Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

10 November 2020 - 22 December 2020

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Action for M.E.	Guideline	General	General	This response is informed by: - our Big Survey of more than 4,000 people with M.E./CFS conducted in 2019 - our NICE Draft Guideline survey of more than 1,500 which ran from November to December 2020 - our frequent and sometimes sustained contact with and support of children, young people, adults and families living with M.E./CFS across the UK, through our Action for M.E. support services. We feel that this guideline is an important step forward and would like to express our thanks to the expert witnesses, guideline committee (especially the lay members) and the M.E./CFS community for engaging in every step of the process. Action for M.E. is pleased to see increased emphasis on the patient experience in this guideline, including a reflection of the disbelief that has been experienced. People with M.E./CFS have repeatedly stated the disbelief and harms they have experienced by healthcare professionals and this draft guideline goes some way to acknowledge that. We also welcome the change in direction away from inappropriate therapies like Graded Exercise Therapy (GET) and Cognitive Behavioural Therapy (CBT) being used as a treatment or cure. Because of the lack of research and evidenced treatments, strong consideration needs to be given to those with lived experience of the condition, with weight given to patient experience. We are however concerned with some of the definitions used in this guideline and the departure from terms used by many	Thank you for your comments. *Black, Asian and ethnic minority populations* An equality impact assessment (EIA) has been completed for this guideline and is available on the guideline webpage. When evaluating all the evidence the committee considered all the groups identified in the EIA, the applicability and generalisability of the evidence was considered by the committee in their discussion of the evidence. Very little specific evidence was identified for any of the groups and the committee agreed that the recommendations should equally apply to all groups and did not discriminate against any particular group and separate recommendations were not thought necessary for any of these groups. The committee agree these factors need to be considered when delivering care and have added, 'Be sensitive to the person's socioeconomic, cultural and ethnic background, and faith group, and think about how these might influence their symptoms, understanding and choice of management.' to recommendation 1.1.3. *Recommendations for research* To raise awareness of this gap in the evidence pregnant women and women in the post-natal period, black, Asian and ethnic minority populations have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations.

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				people with M.E./CFS, such as pacing. Patient experience tells us that this is the most useful method in managing symptoms and we feel this term should be used throughout the guideline with a definition accepted by the patient community. The comments detailed in our submission reflect the positives in the guideline but also detail some areas which we remain concerned about, such as: • the need for more emphasis on the patient's voice and decision making power in the relationship with a healthcare professional • sections on physical activity which need strengthening to ensure that they cannot be misused or misinterpreted • wording around the use of CBT within this guideline • the lack of detail on the experiences of BAME people with M.E./CFS the lack of reference to the level of isolation people with M.E./CFS can experience.	
Action for M.E.	Guideline	General	General	We are pleased to see more emphasis on patient choice and the role patients play in choosing the care they receive. We would like this role strengthened throughout the guidance. We would request that a summary is produced for people with M.E./CFS including options to receive it in 'easy read' and other formats.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.

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Action for M.E.	Guideline	General	General	M.E./CFS is a neurological disease classified by WHO ICD10 G93.3. This classification is also recognised by the Department of Health and Social Care. It is also recognised as a disease by all of the US authorities and by many researchers. It would be consistent if the term 'disease' is used throughout in place of 'medical condition' which does not reflect the impact of M.E./CFS. In our 2020 NICE Guideline Survey almost nine in ten respondents (89%) said that they would like to see NICE make clear that M.E./CFS is a neurological disease. Many people with M.E./CFS have faced disbelief or accusations that it is a psychological condition. A clear statement from NICE acknowledging the physical realities of M.E./CFS and supporting the WHO classification can go some way to addressing this ongoing issue. We request that additional information is added throughout that emphasises the isolation that is experienced by people with M.E./CFS. In our 2020 NICE Guideline Survey 73% of respondents said that having the condition makes them feel very isolated. We would like to see this highlighted with advice on how this isolation could be reduced. We would also like the addition of the benefits of peer support for people with M.E./CFS. 50% of respondents said that being connected with other people who have a similar experience would be helpful to them. We also see this in the Action for M.E. forums.	Thank you for your comment. The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) has been added to the context. Condition is a commonly used term in NICE guidelines and it's use does not diminish the impact of ME/CFS (for example, Multiple sclerosis in adults: management https://www.nice.org.uk/guidance/cg186/chapter/Recommendations). Evidence reviews A and C reported themes of people with ME/CFS having experienced disbelief, prejudice and feeling stigmatised by people, this was supported by the committee's experience. Recognising this and the impact it can have on people with ME/CFS the committee raised awareness this in the principles of care section of the guideline. In the information and support section of the guideline the committee have recommended that people with ME/CFS should be given information about self-help groups, support groups and other local and national resources for people with ME/CFS.
Action for M.E.	Guideline	General	General	Action for M.E. welcomes the recognition that GET should not be offered to people with M.E./CFS. Repeatedly patient surveys have provided evidence of the harms caused by this therapy. Action for M.E.'s Big Survey 2019 found that:	Thank you for your comment. The recommendations address what should or should not be done. With reference to GET the recommendation is clear that a

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				- 47% of those who had GET with support from an M.E./CFS Specialist experienced a worsening effect on their health with 21% seeing no difference at all. It is therefore right that this therapy is removed as a recommendation. There should still be a statement of the likely harms added to ensure people with M.E./CFS are not put at risk by health professionals who have little understanding about the condition. This is further needed because it is a big change from the 2007 guideline, we would like to ensure that GET cannot be considered an option by any healthcare professional.	physical activity programme that does not follow the approach set out in the guideline or uses fixed incremental increases in physical activity or exercise (for example graded exercise therapy) should not be offered to people with ME/CFS. There is no need for a statement of likely harm in the recommendations, Evidence review G includes the detail of the committee discussion on the physical activity and exercise evidence.
Action for M.E.	Guideline	General	General	**Missing – advice on Surgery** Surgery - it is possible for people with M.E./CFS to have major relapses after surgical operations, especially when poorly managed. Specific issues that may need addressing include; orthostatic intolerance, reduced blood volume, lowered temperature control, sensitivity to anaesthetics, and longer recovery times. Certain types of anaesthesia may need to be avoided. For example, detailed guidance is provided in the International Association for CFS/ME Primer, 2014 (Appendix E): https://www.iacfsme.org/assets/docs/Primer_Post_2014_conference.pdf	Thank you for your comment. Advice on surgery for people with ME/CFS was not prioritised by stakeholders during the development of the scope or by the committee when finalising the evidence review questions. As such evidence on surgery has not been searched for or reviewed and the committee were unable to make any recommendations on this topic.
Action for M.E.	Guideline	General	General	Equality Impact Assessment The previous equality impact assessment for this draft guideline reported that *"at the stakeholder workshop, the following populations were identified as having potential equality issues and should be considered within the development of the scope: older people, pregnant women, black and minority ethnic, and men. It was noted that there*	Thank you for your comments. An equality impact assessment (EIA) has been completed for this guideline and is available on the guideline webpage. When evaluating all the evidence the committee considered all the groups identified in the EIA, the applicability and generalisability of the evidence was considered by the committee

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				may be challenges for these groups to be identified and diagnosed with ME/CFS and then to access support services." The current statement states that "there was no or limited evidence identified for these groups." This should have prompted the committee to examine reasons for this by formulating appropriate questions for literature searches and discussion. It should therefore be reflected within the recommendations for research. We feel that the guideline should recognise the additional difficulties faced by black, Asian and ethnic minority people in obtaining a timely diagnosis and adequate care for M.E./CFS. These difficulties were documented in Evidence review C of the draft guideline. Several papers were analysed, including de Carvalho Leite 2011; Bayliss 2014; de Silva 2013; and Hannon 2012. It should also be recognised that in the provided evidence, Guideline commissioned surveys and charity surveys including our 2019 Big Survey, may not be wholly representative of ethnicity. This is further evidence that an additional research recommendation is needed to focus on diagnosis, quality of life and prognosis for BAME populations.	in their discussion of the evidence. Very little specific evidence was identified for any of the groups and the committee agreed that the recommendations should equally apply to all groups and did not discriminate against any particular group and separate recommendations were not thought necessary for any of these groups. The committee agree these factors need to be considered when delivering care and have added, 'Be sensitive to the person's socioeconomic, cultural and ethnic background, and faith group, and think about how these might influence their symptoms, understanding and choice of management.' to recommendation 1.1.3. *Recommendations for research* To raise awareness of this gap in the evidence pregnant women and women in the post-natal period, black, Asian and ethnic minority populations have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations.
Action for M.E.	Guideline	028 - 029	1.11.20	We suggest removing this paragraph entirely from the guideline. It adds confusion and is open to misinterpretation. The draft guideline states that "*physical activity is not a curative or a treatment"* so it is therefore inappropriate to indicate it as a possible approach.	Thank you for your comment. Based on the quantitative and qualitative evidence and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise

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					programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed it was important people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Action for M.E.	Guideline	034 - 035	1.11.50	In our 2020 NICE Guideline Survey we asked respondents for their views on CBT: • 54% said they have used or would like to be offered a different type of talking therapy (eg counselling, acceptance and commitment therapy) that helps them cope with the impact of living with M.E./CFS • 46% said they have used or would like to be offered mindfulness/meditation to help them cope with the impact of living with M.E./CFS. • 41% said they have used or would like to be offered other self-help strategies to cope with the impact of living with M.E./CFS • Just 27% have used or would like to be offered CBT to help cope with the impact of living with M.E./CFS • 19% said they would not consider using any type of talking therapy or self-help strategy in this way. We support the following comments made by Forward-ME: *"In the evidence review at G Page 342 Line 26, the committee summarised the evidence on non-pharmacological interventions for ME/CFS. Their conclusions (from lines 40 – 44) found that: "In addition, the committee made 'do not' offer recommendations for CBT …to treat or cure ME/CFS."*	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).

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				In the light of this finding, Forward-ME are mystified as to why the draft guideline discusses CBT extensively. *This would appear to be discriminatory as the guideline for multiple sclerosis (MS) – a disease that has been compared to ME/CFS, at 1.5.5 states only: 'Consider mindfulness-based training, cognitive behaviour therapy or fatigue management for treating MS-related fatigue.* *Congestive heart failure- also compared with ME/CFS only refers to Depression with reference to the NICE guideline on that topic.* *We can find no other chronic disease for which such extensive advice is given on CBT.* *We are aware that some patients may find psychological support necessary and helpful. CBT is mentioned as having two possible purposes:* *(1) Support in managing symptoms. CBT is only ever relevant when a person is behaving in a maladaptive fashion, grounded in unhelpful beliefs; therapist aims to change mind-set to their benefit in terms of changed behaviour.* *(2) CBT for support with psychological distress as far as we are aware does not exist. Person-centred supportive counselling would be fit for purpose.* *We are asking for this section to be re-written to state:* *'Do not offer CBT to treat or cure ME/CFS as there is no substantive evidence that it is effective. Patients may find supportive, person-centred counselling helpful.'"* It is wrong to include the statement 'aims to improve functioning' within the aims of CBT. This is misleading and can lead to misinterpretation. In the 2019 Action for M.E. Big Survey, of those who undertook a course of CBT:	

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				• Only 8% said they were able to gradually increase their activity. This statement must be heavily caveated to ensure people are aware that for most this is not a possibility and can have a worsening effect on symptoms (13%) Other respondents to our 2020 NICE Guideline Survey said: *"I agree that providing psychological support is very important - to deal with the impact of this condition - but my view, both as a doctor and as a patient, is that CBT is largely promoted based on cost, rather than it really being the best treatment modality. Particularly for people with a more severe disease, I think CBT can be harmful in that it applies a general technique to a vulnerable group who are often unable (physically / mentally) to engage with or benefit from this technique, not through any fault of their own (eg finding 'evidence' to challenge 'negative cognitions' eg of 'being a burden') may well result in more harm than good if the person is actually very disabled and cannot do much for themselves. Other psychological modalities / techniques (including mindfulness, acceptance based strategies) may be far more beneficial."* *"I welcome the way CBT is described as helping people cope with the illness and manage symptoms - but not as a cure. I think most CBT counsellors could help provide this with some training in CFS/ME - possibly professional modules taken through online training - and think this could be explored further."* *"I trained as a person-centred, existential counsellor and worked with people with severe/enduring mental health problems [...] CBT was a rather short-lived success, if*	

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				successful at all [...] My clients would sometimes develop another mental health condition, because the original condition wasn't dealt with appropriately."	
Action for M.E.	Guideline	001	9	This guideline is a new guideline and not a replacement of CG53. Please correct this on the front page.	Thank you for your comment. This has been edited.
Action for M.E.	Guideline	002	Text box	There is evidence suggesting that M.E./CFS can be developed following a viral infection, so we would like to see this wording revised to ensure that it is recognised some people with Long-Covid or similar post-viral illnesses may be diagnosed with M.E./CFS. If the person fits the diagnostic criteria for M.E./CFS in this guideline then the information contained within must override other advice from NICE.	Thank you for your comment. The guideline states it was developed before the COVID-19 pandemic. The committee review the evidence relevant to the key areas of the scope and the recommendations were developed based on evidence reviewed before the COVID-19 pandemic. The committee have not reviewed the evidence on COVID-19 and are not in a position to comment or make recommendations in this area either about the long term recovery from COVID-19.
Action for M.E.	Guideline	004	3	We would like the addition of a principle that recognises that, because of a lack of biomedical research, little is known about M.E./CFS. It is essential that healthcare professionals learn from those with lived experience when overseeing their care.	Thank you for your comment.
Action for M.E.	Guideline	004	4	We would like an additional point that recognises that M.E./CFS can affect any age group. We often hear from people with M.E./CFS who have symptoms discounted because of their age.	Thank you for your comment. A sentence noting that ME/CFS can affect all ages has been added to the context section.
Action for M.E.	Guideline	004	5	Because of the disbelief and misunderstanding that people with M.E./CFS have experienced, we would like to see the wording strengthened here. Change *"can have a substantial impact"* to *"has a substantial impact"*. We feel this is reflected in the physiology of the condition and symptoms that a person will have experienced for several weeks or months before diagnosis.	Thank you for your comment. The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes.. Taking into account the range of comments from

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					stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS. To note other recommendations in this section acknowledge the disbelief and stigma that people with ME/CFS have experienced and that health and social care professionals should acknowledge to the person the reality of living with ME/CFS and how symptoms could affect them.
Action for M.E.	Guideline	004	16	We strongly welcome this addition and the recognition of the injustice and disbelief people with M.E./CFS have faced. We would like to see it repeated throughout the guideline in each of the sections to ensure healthcare professionals are aware of difficulties the person may have faced in the past. One example of the difficulties people have faced is the continued misdiagnosis of Medically Unexplained Symptoms (MUS). In our 2020 NICE Guideline Survey we asked respondents whether they have personal experience of their M.E./CFS being misdiagnosed or incorrectly described as MUS. More than one in three of respondents have experienced this. We feel this justifies stronger wording being used in the diagnosis section that makes clear treatments typically offered by MUS services are inappropriate for people with M.E./CFS.	Thank you for your comment. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. As you note there is further information on prejudices people face in the guideline and for this reason your suggestion has not been added to the recommendation. *ME/CFS specialist services* Throughout the guideline the importance of ME/CFS specialist services is reinforced and where access to these services is required. They have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies.
Action for M.E.	Guideline	005	2	We would like to see the text here strengthened and replace "should" with "must". This is because of the large number of people with M.E./CFS who have reported negative experiences with healthcare professionals. In our 2019 Big Survey we found that:	Thank you for your comment. Must is used in a recommendation when there is a legal duty to apply a recommendation. This is not the case here and no changes have been made to the recommendation.

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				- Just 28% feel they are fully/reasonably confident that their GP understands M.E./CFS and how it affects them. We would also recommend an additional bullet point that details the need for additional time in appointments to allow for any cognitive/brain fog difficulties the person may be experiencing. It is essential that health professionals are patient and are led by the person with M.E./CFS. There should be a further bullet point ensuring that Health Professionals ensure that the person with M.E./CFS understands the options available to them and that they have the power to choose which approach they would like. It is essential that the health professional has informed consent at every stage of the relationship. (Montgomery vs Lanarks Health Board 2015 UK Supreme Court Judgement 11)	Access to care is addressed in detail in section 1.8 and includes your suggestions. The committee agree that the issue of consent and choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person/child centered care is directly reinforced in the guideline sections 'approach to delivering care' and 'assessment and care planning'. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Action for M.E.	Guideline	005	5	In our 2020 Big Survey we found that 64% of respondents do not currently see any health professional about their M.E./CFS. It is therefore important that health professionals know they will need to rebuild trust and this should be reflected in the wording here.	Thank you for your comment. The recommendation is clear that health and social care professionals should build trust, this includes rebuilding trust.
Action for M.E.	Guideline	005	12	Regular monitoring of people with M.E./CFS is important and should be maintained in this guideline. The current guideline says: "Regular, structured review should be undertaken for all people with CFS/ME." (1.8.1.1) People with M.E./CFS often experience a fluctuation of symptoms which would previously not be investigated due to a one-off examination at the start of their diagnosis. This is	Thank you for your comment. After considering the stakeholder comments the committee have added a recommendation in the review in primary care section of the guideline on evaluating and investigating whether new symptoms, or a change in symptoms, are due to the person's ME/CFS or whether they are due to another condition.

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				important to rule out other conditions, which could be having an adverse effect on their symptoms. This would also maintain a relationship between the patient and a healthcare professional. In our 2019 Big Survey we found that almost two thirds of respondents do not see any healthcare professional about their M.E./CFS	
Action for M.E.	Guideline	006	7	It is essential that this section stays so that healthcare professionals know they need to understand severe M.E./CFS and the special accommodations that must be made.	Thank you for your comment. The committee agree that this section is important. Taking into account the range of stakeholder comments on the descriptions of severity in the guideline the committee have moved the recommendations on people with severe and very severe ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS.
Action for M.E.	Guideline	007	4	Delete *'may'*. Insert *'are likely to'*. The reason for this is to ensure that healthcare professionals know to expect that this support is needed and offer the right amount of information to a person with M.E./CFS or their carers. Our 2019 Big Survey found that just 15% of respondents identifying as severely affected had been given information on how to apply for Social Care.	Thank you for your comment. Not all people with severe or very severe ME/CFS will have all of these symptoms all of the time and as such 'may' is appropriate.
Action for M.E.	Guideline	007	8	We feel this section shouldbe elaborated upon so it is clear that aids and adaptions are not just about mobility but reducing the burden of daily living on a person's ability. For example, electric wheelchairs or mobility scooters with the possibility for the carer to control the direction, manual wheelchairs, sunglasses, blue light blocking glasses for screens, ear plugs, shower or kitchen stool, hoists, stair lifts, pressure relieving mattress, hospital style beds, aids to help with hair drying, speech to text computer software, blackout blinds, automatic	Thank you for your comment. After considering the range of stakeholder comments this has been edited to, 'are housebound or bed-bound and may need support with all activities of daily living, including aids and adaptions to assist mobility and independence in activities of daily living (for example wheelchairs)' The section on aids and adaptions provides further information.

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				or adapted cars, blenders for making food less effort to chew, drink with a straw as mugs are too heavy to lift.	These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Action for M.E.	Guideline	007	22	We support the addition of risk assessing interactions with those with Severe ME. It is important that alongside this the health professional has a demonstrable understanding of M.E./CFS and how it affects the person. Our 2019 Big Survey said that: 63% of respondents who identified as being severely affected said that they are not very/not at all confident that their GP understands M.E./CFS or how it affects them.	Thank you for your comment.
Action for M.E.	Guideline	008	1	We are pleased with changes made to this section to recommend early diagnosis.	Thank you for your comment.
Action for M.E.	Guideline	008	9	We would like to see the addition of baseline investigations as it was in the 2007 CG53. This would give patients the knowledge of which investigations should be offered to them so they can challenge the healthcare provider should they not be receiving this. It would also ensure parity between healthcare professionals and the investigations they undertake.	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
Action for M.E.	Guideline	008	16	We feel this is slightly misleading and needs rewording. One respondent to our 2020 NICE Guideline Survey said, *"I had a very specific and sudden onset of ME directly after glandular fever and had a new symptom appear suddenly years into my illness which was not listened to or investigated and instantly lumped in with ME. Some people with ME do not*	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the

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				have a specific onset to their ME but a gradual one they struggle to pin point. They may have also already suffered for years, as I did, before a diagnosis, making things harder to remember and pinpoint."	symptoms have developed and have not always been present covering that the symptoms are not lifelong. This now includes the cohort of people who develop symptoms gradually sometimes over months or even years.
Action for M.E.	Guideline	008	17	It is right that post-exertional symptom exacerbation is recognised as a defining symptom of M.E./CFS. Our 2019 Big Survey of people with M.E./CFS emphasised the commonality of this symptom with 99% of the 4,038 respondents experiencing this following mental or physical activity. It would be helpful for NICE to highlight the importance of using post-exertional symptom exacerbation in both clinical and research guidance. This would ensure there is alignment with those being diagnosed with M.E./CFS and the research studies being undertaken. We also believe that 'unrefreshing sleep which may include' could be replaced by 'unrefreshing sleep and/or sleep disturbances which may include….' so that it encompasses everyone's experiences. We would also like to see a clear definition of "debilitating fatigability" to ensure it is not misconstrued as 'tiredness'.	Thank you for your comment. *Unrefreshing sleep* After considering the stakeholder comments on the description of sleep symptoms the committee edited the bullet points to, 'unrefreshing sleep and /or sleep disturbance, which may include: • feeling exhausted, feeling flu-like and stiff on waking • broken or shallow sleep, altered sleep pattern or hypersomnia. The committee hope this has added some clarity for readers. *Debilitating fatigability.* This has been edited to be more descriptive of the fatigue experienced by people with ME/CFS, 'Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.'
Action for M.E.	Guideline	009	2	We are concerned that the list is not comprehensive and there are some omissions which are common in people with M.E./CFS such as visual problems. Evidence for such: https://pubmed.ncbi.nlm.nih.gov/8201170/ https://pubmed.ncbi.nlm.nih.gov/27799582/	Thank you for your comment. The committee discussed the other symptoms you suggested should be on the list and they agreed to add gastrointestinal symptoms. Based on the evidence reviewed in evidence review D and on their experience the committee did not agree that visual disturbances should be included in the list of associated symptoms. The committee note that visual disturbances are

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				https://pubmed.ncbi.nlm.nih.gov/24187048/ https://www.researchgate.net/publication/327074772_Visual_Aspects_of_Reading_Performance_in_Myalgic_Encephalomyelitis_ME https://www2.le.ac.uk/departments/npb/people/ch190 We would also like to see to addition of gastrointestinal symptoms which are referred to on Page 6 Line 22 for those with severe M.E./CFS.	highlighted in recommendations within the guideline with reference to the description of or the management of symptoms.
Action for M.E.	Guideline	009	4	It should be noted that there is no NICE Guideline for orthostatic intolerance so more information is needed here. They should also be aware of Postural Tachycardia Syndrome, Neurally Mediated Hypotension and Orthostatic Hypotension. The draft guideline says that the medicines usually prescribed for orthostatic intolerance can worsen other symptoms in M.E./CFS - this needs to be much better explained, with specific comments about the various different types of medicines (beta blockers, volume expanders, vasoconstrictors, etc.). There should also be a set of final recommendations.	Thank you for your comment. The orthostatic intolerance section in the section on managing ME/CFS symptoms includes further information. The committee did not make any recommendations on the management of orthostatic intolerance noting that although this can be straightforward it this can involve advice on diet, carrying out daily activities and activity support and should be tailored to the person taking into account their other ME/CFS symptoms. As you note the committee noted medicines usually prescribed for OI can worsen other symptoms in people with ME/CFS and to address this should only be prescribed or overseen by a clinician with expertise in orthostatic intolerance. (see evidence review G).
Action for M.E.	Guideline	010	9	It is essential that healthcare professionals offer to engage with the child's place of education or training as soon as possible to ensure reasonable adjustments can be made. This early intervention can support a child in staying in education and/or prevent symptom exacerbation from pressures to maintain education.	Thank you for your comment. The committee agree early communication with schools and colleges is very important. This recommendation refers to children and young people with suspected ME/CFS and the assumption should not be final diagnosis is ME/CFS. This recommendation is to raise awareness in the short term and

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				Throughout the guideline there should be greater emphasis on the need to rest and not push through activity, whether physical or cognitive. The section needs this addition to ensure that it goes hand in hand with participating in education and learning. We would like it reiterated that children should be encouraged to find a balance between education and social/family life. We would like to see a recommendation that, in communication from the healthcare professional to the education setting, they stipulate the importance of the school/college having a Medical Conditions Policy which will set out commitments in how they will support the person with M.E./CFS. Reference for this is the **Department for Education (Dec 2015)** *Supporting pupils at school with medical conditions: statutory guidance for governing bodies of maintained schools and proprietors of academies in England.*	allows for further communication when the diagnosis is confirmed. Further advice is addressed in the recommendations in section 1.9 supporting people with ME/CFS in work ,education and training. Also see the committee discussion in Evidence review A:Information for people with ME/CFS.
Action for M.E.	Guideline	011	4	In our 2020 NICE Guideline Survey we asked respondents whether they have personal experience of their M.E./CFS being misdiagnosed or incorrectly described as medically unexplained symptoms (MUS). More than one in three of respondents have experienced this. We feel this justifies stronger wording being used in the diagnosis section that makes clear treatments typically offered by MUS services are inappropriate for people with M.E./CFS. We also asked people if they supported the change in diagnosis time to three months for adults. Two thirds (68%) supported this changes with 25% saying they had no strong feelings.	Thank you for your comment. Based on the evidence (Evidence reviews A.B,C,D and I) and the committee's experience referral to ME/CFS specialist care was recommended for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. ME/CFS specialist teams where seen as the most appropriate place for people with ME/CFS to access support with GPs providing ongoing support and review. The guideline is clear that referral is to a ME/CFS specialist team and it is not necessary to include where people should not be referred to. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering

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				We would like it recognised that in practice it has taken people with M.E./CFS significant time to get a diagnosis. In our 2019 Big Survey we asked how long after developing symptoms did they get a diagnosis. • Just 3% said 0-3 months • 13% said 4-6 months • 19% said 7-12 months 59% said over a year	care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Action for M.E.	Guideline	011	7	After 'management' insert 'and support' It should also be recognised that there is a lack of specialist services offering evidenced approaches for people with M.E./CFS and therefore care may be required by a GP. We therefore recommend that GP surgeries identify a lead GP who will specialise in managing and supporting people with M.E./CFS.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Action for M.E.	Guideline	011	13	There is considerable variation in the specialist services offered to people with M.E./CFS with some choosing to travel long distances to see health professionals. This should be reflected in this section or in referral to ensure patients have a choice who they see and are supported to travel to visit the most suitable specialist.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline.
Action for M.E.	Guideline	012	25	We would like the wording here changed to reflect that not all methods in the link are for managing symptoms.	Thank you for your comment. This has been edited to managing ME/CFS and symptom management.
Action for M.E.	Guideline	013	12	It is right and essential that people with severe or very severe M.E./CFS are offered a home visit. This should be extended to those who can evidence that a visit to a surgery or hospital will	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms

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				have a worsening effect on their health. As the condition can fluctuate, there will be some who are mild/moderate but will become severely affected by the physical and cognitive activity of visiting a healthcare setting. It should also be recognised that those who are very severe may only be able to manage a short home visit. Further investigations or queries can be carried out through text or phone calls with the person with M.E./CFS or their carers. We recommend that this flexible approach be adopted by M.E./CFS services to ensure there is a variety of delivery mechanisms to meet need.	experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
Action for M.E.	Guideline	013	14	We would like the addition of a section that recognises the difficulties people with M.E./CFS can experience when applying for disability benefits and the role a healthcare professional should have in this process. Many of those who are unable to work face an uphill battle when asking for this support and proactive communication can reduce stress and symptom exacerbation. We have heard from people with M.E./CFS who struggled to get their doctor to write a supporting letter which then worsens their quality of life.	Thank you for your comment. This section links to the NICE guidance on people's experience in adult social care services and this is further detail on accessing disability benefits. In addition, there is information on accessing social care in this section on information and support.
Action for M.E.	Guideline	014	18	At the end insert: *'and are worsened by exertion'*	Thank you for your comment. The impact of activity is addressed in the energy management section of the guideline.
Action for M.E.	Guideline	014	28	We would like the addition of common triggers here such as points in the menstrual cycle and surgery.	Thank you for your comment. There were several stakeholder comments about the examples of triggers that worsen ME/CFS. Some of the examples were considered potentially misleading information and not always a trigger and as you have commented there are other examples that could be added. After considering the stakeholder comments the committee agreed to delete the examples and not provide any examples in

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					the recommendation recognising the variation in triggers in people with ME/CFS.
Action for M.E.	Guideline	016	6-11	We have concerns that a Safeguarding section within this Guideline may, in some cases, lead to more harm. We would like the language changed to make it clear the reason for the inclusion of this section is because of inappropriate referrals that have been made due to a lack of understanding about the condition. In our 2017 survey of families of young people with M.E.: • 90% of respondents were concerned that professionals involved with their child did not believe them • one in five (22%) said a safeguarding/ child protection referral had been made against them ○ nearly half of these referrals related to claims of fabricated/induced illness or FII (previously known as Munchausen's by Proxy), which occurs when a parent or carer exaggerates or deliberately causes symptoms of illness in the child; this heightened frequency of FII claims sits widely outside the national prevalence rate • 70% of all cases were dropped within a year We agree with comments by Forward ME regarding this: *Replace 2 paragraphs with the following:* *1.7.1 Recognise that people with ME/CFS, particularly those with severe or very severe ME/CFS, are at risk of their symptoms being confused with signs of abuse or neglect. In*	Thank you for your comment. Taking into account the range of stakeholder comments the recommendations in this section have been reordered. This has addressed the point you make about the order. The committee discussion in Evidence review B includes in detail why the recommendations on safeguarding have been included in the guideline and this refers to the lack of understanding and disbelief that parents have experienced.

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				the case of children, ME/CFS should not be mistaken for very rare conditions such as Munchausen's syndrome by proxy or with fabricated or induced illness. *1.7.2 Safeguarding assessments in people with confirmed or suspected ME/CFS should be carried out and overseen by health and social care professionals who have training and experience in ME/CFS.*	
Action for M.E.	Guideline	018	10	We are pleased to see this statement, however, it needs to be strengthened. People can experience a fluctuation of symptoms over the course of a few hours or days, sometimes triggered by unexpected emotional or physical events. We suggest changing the paragraph to: *"Do not discharge someone who misses appointments. Contact them to explore why they could not attend and how to support them in a way that takes into account their functional ability."*	Thank you for your comment. The recommendation is to raise awareness about exploring why people with ME/CFS may miss appointments and as such your suggestion does not add any further clarity and for that reason has not been added.
Action for M.E.	Guideline	018	15	Remove the word 'fear' and replace with 'risk'.	Thank you for your comment. After considering stakeholder comments about the word fear this recommendation has been edited 'risk that their symptoms will worsen may prevent people from leaving their home'.
Action for M.E.	Guideline	018	24	In the line *'supporting their applications for aids and appliances'* add in *'and financial support'.*	Thank you for your comment These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Action for M.E.	Guideline	020	19	We welcome these recommendations but would like to see the addition of information and support in applying for a Blue Badge, recognising the advantages this would have on a patient's ability to plan activity and rest.	Thank you for your comment These are examples in the recommendation and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added

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Action for M.E.	Guideline	020	23	We welcome this recommendation.	Thank you for your comment.
Action for M.E.	Guideline	021	1	We would like to see examples of the type of adjustments a workplace can make to support a person with M.E./CFS in employment. eg. working from home, flexible hours, reduced hours, speech to text, a quieter working space, a space to rest when needed, transport help, parking space closer to the building, adaptations to the lighting levels or type of lighting used, blue light blocking glasses. Make clear that adjustments should be realistic, achievable and solutions-focused based on need, with no employee taking on more than they can manage.	Thank you for your comment. Further information on types of adaptions and adjustments are included in the committee discussion in evidence review A and the points your raise are highlighted there. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.
Action for M.E.	Guideline	021	5	At end add: 'full or part time. Return to these activities is likely to be gradual, if possible at all. Pushing to continue to work or attend school or further education is likely to result in lasting illness and disability.'	Thank you for your comment. This is a general point about returning to work, school or college and the suggestion you make does not add further clarity to the recommendation and has not been added.
Action for M.E.	Guideline	021	12	Include 'Department for Work and Pensions.'	Thank you for your comment. The remit of NICE does not extend to providing guidance for the Department for Work and Pensions (DWP) and insurance companies, the committee are not able to make recommendations about providing information for them.
Action for M.E.	Guideline	022	10-12	We are pleased to see children being advised to find a balance between education and social/family life.	Thank you for your comment.
Action for M.E.	Guideline	022	13	We agree there needs to be a multidisciplinary approach but it may be inappropriate for the specialist care of a person with M.E./CFS to be led by a Psychiatrist or Psychologist. This should be reflected in the statement. Patient surveys conducted by the ME Association and #MEAction UK have both identified that GPs/Consultants are patients' preferred choice in being involved in their care with psychologists being the least preferred option.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be

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				We feel that it should be a recommendation that a physician must be involved in the multidisciplinary team.	available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.
Action for M.E.	Guideline	023	4	At end add: 'if and when able'	Thank you for your comment. This recommendation refers to the expertise that should be available and does not make any judgement about if someone needs the expertise. For this reason your suggestion has not been added.
Action for M.E.	Guideline	023	7	We support this recommendation.	Thank you for your comment.
Action for M.E.	Guideline	023	12	We feel that the addition of a named contact for children and young people is an important step. We would like the recommendation changed slightly to reflect the child or young person should be involved in choosing the named professional. This is also reflected in Evidence Review I page 25 Line 10.	Thank you for your comment. As you comment the committee noted the importance of involving children and young people in their decision making about their named contact in the discussion section however the committee recognised that this may not always be possible or practical and did not put this into the recommendation.
Action for M.E.	Guideline	024	1	We are concerned that there are no references to the complimentary approaches that fall outside of mainstream healthcare/medicine. People who responded to our 2019 Big Survey informed us that they use these methods as part of a management strategy. As these therapies are being sought out by people with M.E., we would like reference to it in the guideline so healthcare professionals are aware of the need to ensure they are kept up to date with any therapies being used by a person with M.E./CFS.	Thank you for your comment. Complementary and alternative therapies were included in the protocol for non- pharmacological interventions and when reviewing the evidence the committee agreed that there is insufficient evidence to recommend any complementary approaches.

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Action for M.E.	Guideline	024	4	We feel this should be reflected in the research recommendations.	
Action for M.E.	Guideline	024	6	We support emphasis that energy management is not curative/a form of treatment. It is about energy management and operating at your baseline. It is essential that NICE recommend additional training for medical professionals on this. In our 2020 NICE Guideline Survey 74% of respondents agreed with the phrase "I am concerned that my GP would not have the expertise to support me to develop a pacing/energy-management plan." Almost four out of five respondents (79%) also said that they would like to see more detail about what energy management means. We would recommend using the term 'Pacing' rather than energy management. Respondents to our survey describe this as a quicker and easier term to grasp, with greater clarity on how it works. It should also be recommended that advice on pacing/energy management from the perspective of a person with M.E./CFS should be provided to demonstrate real life examples. In our 2020 NICE Guideline Survey, we asked respondents for their opinion on this and 62% said they were likely to refer to this approach as pacing. It should also be acknowledged that this approach is still challenging for people with M.E./CFS. In the survey 60% of respondents said that they struggle with pacing/energy management, but it's still the thing that has been most useful.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. *Energy management* Evidence review G provides more information on energy management in the committee discussion section. The recommendation includes that energy management is a self-management strategy that is led by the person. The personalised nature of this makes it difficult to provide examples, as the risk is that examples are seen as the only option. *Pacing* The committee discussed the use of the term pacing agreed that it means something different to different people with many different versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it.
Action for M.E.	Guideline	024	15	We recommend inserting information about 'post-exertional symptom exacerbation' into this line to demonstrate the risk of overexertion. It also needs to be clear than this onset may occur after hours or even days so extra care must be given.	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to,' helps people learn to use the amount of energy

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					they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits'.
Action for M.E.	Guideline	025	3	Please replace 'does not assume' with 'recognises that'. Without this change, there is concern that this could be misinterpreted.	Thank you for your comment. The committee deleted the bullet point on deconditioning noting that this recommendation was about providing advice to people with ME/CFS about the approaches to implement energy management and this point was not useful in this context.
Action for M.E.	Guideline	025	5	We would like the wording around 'goals' clarified. People with M.E./CFS should be informed that a goal could be reducing activity levels to achieve symptom stabilisation.	Thank you for your comment. After considering the stakeholder comments, recommendation 1.11.12 has been edited to include that this is a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse).
Action for M.E.	Guideline	025	21	We would like to see this sentence altered to include references to both physical, emotional and cognitive activity. It should also be clear that this activity could include something as small as sitting up or looking at a clock, whereas for some it may be more of an activity yet have the same level of 'payback'. It is very important to note that "activity" does not just mean physical activity. Mental activity such as reading a book, watching television, having a conversation in person or by phone, also counts – as will emotional activity such as receiving bad news. Some people with M.E./CFS tell us that emotional activity can be the most draining, and the hardest to measure and control. Physical, mental and emotional exertion counts as activity, even in small amounts. Examples include walking, reading a book or having a difficult conversation with a friend or family member.	Thank you for your comment. The principles of energy management are set out in recommendation 1.11.2 and includes that energy management refers to all types of activity (cognitive, physical, emotional and social) and takes into account overall level of activity.

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Action for M.E.	Guideline	026	1.11.8	The wording in this section is not appropriate and could lead to misinterpretation and potentially a form of graded exercise therapy being given to a person with M.E./CFS. The next comments are for the following points in the guideline: "• are ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their M.E./CFS" These points give the impression that this is an inevitability and that all people with M.E./CFS should be ready to increase activity at some point. This interpretation can lead to pressure from a healthcare professional for a person with M.E./CFS to push beyond their capabilities. In order to protect people with M.E./CFS from harm there are changes needed to this section. In our 2020 NICE Guideline Survey, we asked respondents about the effect physical activity as part of self-management has had on their health. Half of respondents said it had a worsening effect. We suggest: • Greater emphasis on patient choice. It should be made clearer that it is up to the person to choose if they wish to make any changes. • Removing the two bullet points and replace with: Choose to make any changes to their activity and energy management plan.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews A, G and H) and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and

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					support plan without it affecting access to other aspects of their care.
Action for M.E.	Guideline	026	8	We are pleased to see a section highlighting severe/very severe M.E./CFS. One respondent to our 2020 Draft NICE Guideline Survey said: "Severe and very severe ME can seem like a different illness to the mild form. Many people and medical professionals only see the "walking wounded" and no idea why a more severe patient can't make it into the surgery for example, and don't believe the patient's explanation. Severe patients should be able to refer doctors to easily accessible guidance."	Thank you for your comment.
Action for M.E.	Guideline	026	16	We feel that some wording should be added to this section to ensure the recommendations are considered in line with other advice given throughout this guideline. We therefore suggest a caveat reminding health professionals to ensure all activity undertaken, including that of daily life, should be within the energy envelope.	Thank you for your comment. 'Strategies need to be carried out in small amounts and spread out throughout the day' has been added to the recommendation

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					to clarify this is in the context of the priorities that people may have. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.
Action for M.E.	Guideline	026	17	Consideration should be given on the severity of the condition when producing a physical maintenance plan in partnership with the person with M.E./CFS. We would like to see emphasis at this point that this is about maintenance as opposed to increasing strength and fitness.	Thank you for your comment. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.
Action for M.E.	Guideline	027	3	We agree with this recommendation	Thank you for your comment.
Action for M.E.	Guideline	027	8	We agree with this recommendation	Thank you for your comment.
Action for M.E.	Guideline	027	14	We believe that families should be given information about the key symptoms. This would ensure they are better able to support the patient but also can look out for new symptoms, which might be a sign of a co-morbid condition.	Thank you for your comment and this information.
Action for M.E.	Guideline	027	20	In our 2020 NICE Guideline Survey, we asked respondents to choose which element of the draft NICE Guideline was most important to them. Almost 80% said that *'the clear advice people with M.E./CFS should not be offered any therapy based on physical activity or exercise as a treatment of cure for their M.E.'* was the most important part.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews A, G and H) and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where

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				In addition to this, 57% said that it is important there is a strong emphasis throughout that any plan put in place to support someone with M.E./CFS must be tailored to the individual, by the individual, with appropriate support from a professional with experience of M.E./CFS if needed. We would also like it clarified that unstructured AND structured exercise (as stated in the evidence review) can be harmful, even with supervision, We would like to see it repeated elsewhere in the guidance to ensure it is understood. In the NICE Survey half of respondents (50%) feel there is not enough warning about the impact of physical activity/exercise. Other respondents to our survey said: "Physical activity has only ever worsened my symptoms. I would like to see realistic examples of how this could help, based on actual M.E./CFS patients and with the acknowledgement that this may not be a suitable approach for many people with M.E./CFS (and that it should not be continued to be pushed in the event that it worsens symptoms). I also have concerns about the assumption that patients are to be supported by a therapist or doctor with knowledge or understanding of the condition - I have been ill for 19.5 years now, and in that time have had maybe 2 doctors who have more than cursory knowledge of M.E./CFS - and many more who continue to refuse to acknowledge that it is exists." "I was helped enormously in the early 90's by a thoroughly competent OT. In 2010, I experienced a 4-weekly 'intensive' GET course which was full-time (9am-3pm, weekday	appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. The committee agree that it is important that people with ME/CFS take into account all types of activity (cognitive, physical, emotional and social) and the overall level of activity when developing and undertaking any energy management plan, this includes how any physical activity might be included.

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				attendance) was a personal disaster for me. I was lumped in with people with Fibromyalgia (I have Fibromyalgia also) but suffered badly, with pain and M.E./CFS crashes." "Some physical activity is required for the basics of living. eg chewing. Many bits of 'normal' physical activity need to be balanced and traded off against each other in a 'robbing Peter to pay Paul' manner. I've been eating recently, but have not been able to have a shower or wash my hair for over two months. Ten years since I've been to a hairdresser. Two years overdue for the dentist and four years overdue for the optician."	
Action for M.E.	Guideline	028	1-11	We strongly support these statements in the guideline and the emphasis that it should not be used as a treatment or cure.	Thank you for your comment. To note after considering the range of stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Action for M.E.	Guideline	028	1.11.18	We support the below comment from Physios4ME. *"We are concerned about the current level of training on ME/CFS for Physiotherapists and Occupational Therapists. Unpublished surveys by Physios for ME found ME was included in less than half of undergraduate physiotherapy courses. Many existing training programmes are based on the deconditioning model and include graded exercise therapy.* *We therefore recommend changing the wording from:*	Thank you for your comment. The committee agree that all health and social care staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline.

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				A physical activity programme, if offered, should only be delivered or overseen by a physiotherapist or occupational therapist with training and expertise in ME/CFS. *To:* *"Any physical activity within an activity management plan should be overseen by a physiotherapist or occupational therapist who has undertaken current, evidence-based training in exercise physiology relating to ME/CFS and can evidence their continuing professional development within this speciality. An awareness of the abnormally lowered anaerobic threshold, lowered VO2 max, increased acidosis post-exercise and their implications are essential.* *Training should reflect the low to very low quality of evidence relating to GET and the additional recent evidence related to adverse physiological responses to exertion and the implications for this on activity management planning."*	
Action for M.E.	Guideline	028	10	We support this recommendation against the Lightning Process. In our 2020 NICE Survey on the draft guideline, a number of people have expressed disappointment that Osteopathy has been included in this section. We would like better clarification here whether the recommendation is against Osteopathy as a whole or when used in combination with life coaching, neurolinguistics programming etc.	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer people with ME/CFS therapies based on the Lightning Process'
Action for M.E.	Guideline	028	12	Remove this paragraph. This paragraph goes against earlier statements we have similar concerns as were set out in Comment 54, page 26 1.11.8	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews A, G and H) and their own experience the committee

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				We suggest: *"Physical activity for people with M.E./CFS should only be considered if they request it and it is part of a maintenance plan for activity and energy management to support activities of daily living. It is essential that post exertional symptom exacerbation is recorded during any activity, and if progression is considered by the patient then accurate recording is needed to ensure any worsening of symptoms is identified and activity stopped."*	concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Action for M.E.	Guideline	028	19	It is essential that people be warned about the risks of additional physical/cognitive activity and the need for accurate monitoring during any activity. It should also be noted that the act of recording symptoms is an activity in itself. We would	Thank you for your comment. The committee agree that it is important that people with ME/CFS take into account all types of activity (cognitive,

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				also like to see the word 'programme' removed from this section as it gives the impression it is a formal exercise programme and not reflective of the small amounts of activity people should be considering. It should be made clear that the majority have found that physical activity programmes make their symptoms worse. The current wording suggests equal proportions for improvement, no difference and worsening when this is not the case when patient feedback is examined.	physical, emotional and social) and the overall level of activity when developing and undertaking any energy management plan (this is outlined in the principles of energy management), this includes how physical activity might be included. The committee agreed not to change the wording, this point was to illustrate that the impact of a physical activity or exercise programme can vary.
Action for M.E.	Guideline	029	18-22	This section needs expanding upon as not enough information is given. • E.g. watching TV, laying on the sofa or listening to an audio book is still a cognitive activity, yet many use this as their rest. • To rest immediately as soon as symptoms feel slightly worse than before they started an activity. Do not push through, as this will result in needing more rest later on and a worsening of symptoms for longer. • Include advice on how to manage sleep disturbances, insomnia and hyper-insomnia. • Sleep quality can get worse during relapses and setbacks during a flare up in symptoms. • More help and support is needed than the general sleep hygiene advice. It should also be made clear that the person must listen to their body and rest when needed and not try to follow strict sleep/awake hours.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Action for M.E.	Guideline	029	14	People should be advised not to rush trying to return to the level of physical activity. Rather than just telling them that the	Thank you for your comment. The committee note this is personalised collaborative programme and advice is specific to the individual. Including time

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				time "varies", explain that it could take several days or weeks, or even months.	frames here could result in people thinking they should be meeting them.
Action for M.E.	Guideline	030	13	This section needs personalising to the individual and the condition. For people with M.E./CFS exercise can be an inappropriate way to manage pain and comes with a potential risk of significant harm. It should be made clear that any approach to manage pain should be done with this in mind.	Thank you for your comments. The committee agree that care for people with ME/CFS should be personalised and recommend a personalised care and support plan in the assessment and care planning section of the guideline. Management of pain should be part of the personalised plan. The committee have noted at the beginning of the managing ME/CFS section and 'managing coexisting conditions that the recommendations in the section on principles of care for people with ME/CFS and section on access to care and energy management should be taken into account when managing symptoms and coexisting conditions in people with ME/CFS.
Action for M.E.	Guideline	031	5	We are concerned at the recommendation not to offer any medicines or supplements to treat or cure M.E./CFS. While there is no treatment or cure, many people with M.E./CFS tell us that medicines and supplements can help their individual symptoms. We therefore request this statement be clarified. Our 2019 Big Survey found that 68% of respondents use medication for individual symptoms, 70% of whom receive them from a healthcare professional. In our 2020 NICE Guideline Survey, we asked respondents for their thoughts on the use of supplements/medication being referred to in the guideline. Three quarters of respondents (74%), said that they would like to see the NICE Guideline make clear that, while there is no current treatment or cure, there are approaches that can be used to help manage individual symptoms.	Thank you for your comment. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.' The committee note the following subsection in the guideline is 'medicines for symptom management' and provides advice for prescribers. The discussion section of Evidence review F: Pharmacological management recognises some people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and this should be discussed on an individual basis.

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				The comments in Evidence Review F page 64 state that a GP should prescribe medication if in their judgement there is potential benefit in terms of symptomatic relief. This should be reflected in the recommendation. In our 2020 NICE Guideline Survey, we asked those who said they use medication or supplements which symptoms it was for: • 72% pain • 55% sleep difficulties • 25% nausea 20% Orthostatic intolerance	
Action for M.E.	Guideline	034	7	The phrasing 'CBT for ME/CFS' suggests that there is an established protocol (like CBT-E for eating disorders and Trauma-Focused CBT for trauma). This is misleading.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Action for M.E.	Guideline	034	16	The use of 'assume' in this line could add ambiguity. This wording should be changed to make clear that 'abnormal' illness beliefs and behaviours are NOT an underlying cause of M.E./CFS.	Thank you for your comment. The committee specifically rejected the assumption that people with ME/CFS have 'abnormal' illness beliefs and behaviours as an underlying cause of their ME/CFS. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their

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					own experience the committee concluded that CBT as described in the guideline could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Action for M.E.	Guideline	034	26	The phrase 'work towards meaningful goals' is open to interpretation and should be clarified to ensure no person with M.E./CFS is pressured to set a goal beyond what they feel are unmanageable. Our 2019 Big Survey showed that one in five people who undertook CBT in the last five years experienced this.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. The recommendations include that CBT is a collaborative intervention and the goals are chosen themselves.
Action for M.E.	Guideline	035	3	The Guideline recommends that CBT should: *"explore their personal meaning of symptoms and illness, and how this might relate to how they manage their symptoms".* This should be removed as it gives the impression that a person with M.E./CFS can reduce their physical symptoms by changing the way they think.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to

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					accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Action for M.E.	Guideline	036	1	Additional wording is needed here to ensure that any management approach for a co-morbid condition is risk assessed against the patient's M.E./CFS. For example, any approach involving increased activity could then lead to post-exertional symptom exacerbation.	Thank you for your comment. The first two recommendations in this section advise that when managing coexisting conditions in people with ME/CFS, the recommendations in the sections on principles of care for people with ME/CFS, access to care and energy management should be taken into account. The NICE guideline on Multimorbidity linked to in this section refers to disease burden and for this to be taken into account when considering the management approach.
Action for M.E.	Guideline	037	7-8	We would like the guideline to acknowledge that for women, having their period or certain stages of the menstruation cycle can cause a flare in M.E./CFS symptoms. The common cold can cause a flare in ME symptoms so it is not always acute illness.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Action for M.E.	Guideline	038	5	It should be made clear here that in the case of a relapse, a person should reduce their activity levels in establishing a new energy envelope and, in some cases, stop altogether.	Thank you for your comment. The committee agree and have recommend general advice to reduce or stop activity, rest and reassess energy limits to stabilise symptoms.
Action for M.E.	Guideline	039	2	This recommendation has been positively received in our 2020 NICE Guideline Survey.	Thank you for your comment.
Action for M.E.	Guideline	040	11	We support this section. It is essential that training be given to health and social care professionals. The overriding theme in our 2020 NICE Draft Guideline Survey was that of medical education and the need for coordinated approaches to health and social care professionals to educate and inform about	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the

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				changes to the guideline and the risks that have been evidenced with previously agreed approaches. In this survey, over half of respondents (56%) are concerned that they are being advised to rely on support from professionals who have experienced/understanding of M.E./CFS – but this is not their experience. This demonstrates the need for coordinated efforts to increase understanding among the medical profession. We would also like a recommendation that training is given to all disciplines. One respondent to our 2020 NICE Survey said: *"Many of us find that detrimental attitudes and incorrect beliefs about ME being psychological/psychosocial make it very difficult to get heard and treated for non-ME health problems as they often ascribe other symptoms to psychological causes, are patronising and sometimes insulting in their assumptions, and most seriously is a real danger of not diagnosing and treating other conditions."* It should be recognised that no amount of training or literature review by a healthcare professional could compare to the knowledge a person with M.E./CFS has about his or her own condition.	recommendations in the training for health and social care professionals section of the guideline. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan.
Action for M.E.	Guideline	040	11	We would like a recommendation that a nationwide information campaign is conducted to inform health professionals about the change in guideline and require new training and assessment to ensure they are able to support people with M.E./CFS.	Thank you for your comment. A nationwide information campaign is beyond the remit of NICE.

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Action for M.E.	Guideline	040	12	Delete 'should'. Insert 'must'	Thank you for your comment. Must is used in a recommendation when there is a legal duty to apply a recommendation. This is not the case here and no changes have been made to the recommendation.
Action for M.E.	Guideline	041	2	Delete 'should'. Insert 'must'.	Thank you for your comment. Must is used in a recommendation when there is a legal duty to apply a recommendation. This is not the case here and no changes have been made to the recommendation.
Action for M.E.	Guideline	041	9	The definition of activity should include activities of daily living	Thank you for your comment. The definition of activity includes physical activity, the committee decided not to include examples of any activity (physical, cognitive, emotional or social) as any list of examples cannot be exhaustive and there is the risk these are taken as the only options available.
Action for M.E.	Guideline	043	11	We would like it to make clear that those with mild M.E./CFS who are able to work often have to reduce hours in order to continue employment. Our 2020 Big Survey found that: • Only 8% of respondents are in full time work • 90% of respondents have had to reduce their hours or stop working altogether It should be noted that many people with M.E./CFS who work might have significantly reduced all non-work activities in their life in order to sustain employment.	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
Barts Health NHS Trust	Evidence Review	General	General	The rejection of almost all the current evidence for the effectiveness and safety of both CBT and GET will lead to services having no evidence based treatments to provide to their patients. Since clinical commissioning groups do not fund services that provide treatments withoEt evidence of efficacy, this will likely lead to decommissioning of existing services. This is a remarkable and inexplicable turn-around compared to the 2007 guideline, which recommended that "Cognitive	Thank you for your comment. *CBT* The management sections of the guideline include recommendations to offer CBT to help people manage their symptoms and reduce the distress associated with having a chronic illness and are options for part of the care and support plan where appropriate and chosen by the person with ME/CFS. To accompany this the committee have made recommendations

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				behavioural therapy (CBT) and/or graded exercise therapy (GET) should be offered to people with mild or moderate CFS/ME and provided to those who choose these approaches, because currently these are the interventions for which there is the clearest research evidence of benefit." Since that time, the research evidence supporting these treatments has grown considerably. Would NICE please explain why a greater body of evidence has led to a reversal of a recommendation that was supported by less evidence back in 2007?	that set out how CBT should be delivered for people with ME/CFS. See evidence reviews G and H for the evidence and the committee discussion on these recommendations. *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes

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					result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Barts Health NHS Trust	Guideline	General	General	This guideline will provide only limited useful guidance to clinicians on effective management of patients with CFS/ME	Thank you for your comment. The committee have taken into account the comments from stakeholders and have made changes to the guideline and hope these will provide further support on the management of people with ME/CFS.
Barts Health NHS Trust	Guideline	General	General	This guideline fails to emphasise a rehabilitative management approach using evidence based treatments to improve symptoms, improve function, promote recovery, and lessen	Thank you for your comment. The committee disagrees that the guideline focuses on passive supportive care and an acceptance of chronicity and disability.

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				debility/disability, but instead focuses on passive supportive care and an acceptance of chronicity and disability.	Throughout the guideline the committee have emphasised the importance of being centred on the patient's needs and wishes, the need to be holistic and to listening to and understanding the patient's perspective and experience. The recommendations in this guideline are based on this focus and in addition the committee have edited the management plan to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.). This further supports the guideline's emphasis upon being centred on the patient's needs and wishes and adopting a holistic approach. The personalised care and support plan supports the person's aims and the management of their health and well-being within the context of their whole life and family situation.
Barts Health NHS Trust	Guideline	General	General	We believe that the general effect of this guideline will be to maintain disability, increase the duration of illness, reduce hope of recovery, and lead to decommissioning of existing specialist services.	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.)
Barts Health NHS Trust	Guideline	General	General	The document 'The principles that guide the development of NICE guidance and standards' states that NICE guidance and standards are underpinned by evidence that is relevant, reliable and robust, recognising the hierarchies of evidence.	Thank you for your comment. As you note all NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual.

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				By disregarding and omitting evidence, introducing arbitrary criteria to re-evaluate published data in post hoc fashion, and putting disproportionate weight on anecdotal evidence, surveys and some qualitative research, NICE will forfeit much credibility in the development of this specific guideline and in the development of guidelines generally.	This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. No evidence that met the protocols was disregarded or omitted from the guideline. The process for quality rating used in NICE guidance is an internationally agreed process and it is not unusual for evidence to be graded as low or very low quality. This does not mean it cannot be used to make recommendations but affects the strength of recommendations. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will take into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing

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					NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Barts Health NHS Trust	Guideline	General	General	Qualitative We believe that the patient feedback has been unbalanced, which may reflect that recovered patients are not so well represented as patients who are sadly still unwell. We provide two anonymous testimonies from two of our ex-patients, who both received GET (and CBT) with good effect, in order to help the committee redress this balance. P1 "To Whom it May Concern Sadly because of the vitriol targeted at patients in the past I request that my feedback remains anonymous. Having lived with M.E. for almost 20 years I was privileged to be referred to Barts Specialist CFS/M.E. service. My diagnosis was confirmed and I was referred for Graded Exercise Therapy which was life changing. Instead of having regular and repeated relapses which I battled through I was eventually able to return to full function without fear of relapse. It was a truly person centred approach which enabled a relationship of engagement and trust for which I am truly grateful. If I could had the management 20 years earlier my life during those years would have been significantly different avoiding weeks, sometimes months off work." P2 "CFS/ME affects every individual differently. This is my experience.	Thank you for your comment and two testimonies. *Underrepresentation from patients who have recovered from ME/CFS* The committee membership had a broad range of professional and personal knowledge about the different experiences of people with ME/CFS and this was discussed and considered at all stages of the decision making. It is true that there is little representation in the literature of people who have recovered from ME/CFS and the committee hope that where this can be published it will be as this can only further inform the care and support of people with ME/CFS.

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				When I first developed what was subsequently diagnosed as CFS/ME in 2012, the most worrying symptom for me was brain fog. At the time, I was a [deleted to maintain anonymity]. The effects of brain fog (combined with severe muscle pain, migraines and debilitating fatigue) were devastating. I was my family's bread-winner and I was no longer able to work. At my worst, I lost the ability to string a sentence together. I was not capable of writing a shopping list let alone, what I was paid to do, a business strategy. However, there was help available at the time from a specialist team at Barts Hospital. I credit the members of this team – together with my own determination to get well – with my recovery. Today, I'm able to function well. I have returned to full-time work, albeit not now as a manager. But my brain and body work again. I can both earn a living and enjoy my life. Why do I think the way my case was handled at Barts was successful? First, I was put through a series of tests, building on what my excellent GP had started, to make sure any obvious physical conditions could be ruled out. That seemed sensible to me. One should not underestimate the positivity that negative results bring the patient. Next, I had a 2-hour session with a psychiatrist who established I was not depressed and so my symptoms where not a reflection of clinical depression. This was also a huge relief. It was a logical start to a resolving a problem. Through a process of exclusion, it meant the medical professionals and I could all now concentrate on my recovery from CFS/ME.	

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				The next thing that happened was a consultation with a physiotherapist, trained to work with CFS/ME patients. I cannot describe the relief, to someone who was feeling so ill, confused and frightened at the time, of having a clear GET programme set out for me, with simple goals that seemed to be, and were, achievable. When you feel so ill that nothing seems achievable, GET is powerful. GET proved to me I could start to regain control of my body and, by extension, my life. After several months of GET, I started CBT. I'd been sceptical about CBT but these sessions taught me to think in a different way. There was, and remains for me, benefit in CBT exercises and mindfulness. Building on the GET that had helped me to get stronger physically, they helped me get stronger mentally. Today, I rarely have relapses but pandemic-related anxiety [deleted to maintain anonymity] has caused me to be slightly unwell again. When this happens, the first thing I do is go back to the calm, logical GET principles, together with some mindfulness, and build myself back to health. This is just my personal experience and my opinion. But, reverting to what I said at the beginning, if everyone's experience of CFS/ME is slightly different, it is illogical to dismiss tried-and-tested techniques that clearly help some patients, myself included, and are also entirely safe interventions. (We are not talking about medication or surgery, for example.) I applaud any research into this horrible condition and welcome any breakthroughs. But let us not throw babies out with the bathwater! Please."	
Barts Health NHS Trust	Guideline	004	7-12	*"ME/CFS….can have a significant impact on people's (and their families and carers') quality of life, including their activities*	Thank you for your comment.

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				of daily living, family life, social life, emotional wellbeing, work and education *• affects each person differently and varies widely in severity – in its most severe form it can lead to substantial incapacity (see recommendations 11 1.1.8 and 1.1.9)"* We entirely agree with these statements about the debilitating effects of this illness on patients, their lives, and their families' lives, which we have seen repeatedly over many years of clinical practice.	
Barts Health NHS Trust	Guideline	006	22-25	"*reduced ability or inability to speak or swallow gastrointestinal difficulties such as nausea, incontinence, constipation and bloating* *• neurological symptoms such as double vision and other visual disorders, dizziness"* The presence of these symptoms and signs should cause a clinician to question the diagnosis, since the majority of these are not related to a diagnosis of CFS/ME.	Thank you for your comment. This recommendation raises awareness about the symptoms people with severe or very ME/CFS may experience and not the symptoms for diagnosis. Taking into account the range of stakeholder comments about the location in the guideline of this section the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. In response to your comment this now means that the criteria for suspecting and diagnosing ME/CFS precedes this recommendation providing clarity about the symptoms that are related to a diagnosis of ME/CFS.
Barts Health NHS Trust	Guideline	008	11-13	*"the person has had all of the persistent symptoms (see box 1) for a minimum of 6 weeks in adults and 4 weeks in children and young people"* Contrary to the committee's assertion and rationale, it is not unusual to have persistent 'key' symptoms beyond 6 weeks following acute illness, including viral illness, e.g. glandular fever, Covid 19. However, the large majority of people who have symptoms 6 weeks after an infection have recovered by six months without any intervention. This time-scale is too	Thank you for your comment. The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms at this point are given advice that may prevent them getting worse. In summary it would be unusual for an acute illness, including a viral illness to persist longer than this with all the symptoms. The committee emphasised it is the combination and interaction of the

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				short to tell patients that they may have an illness with little or no chance of recovery, according to this guideline.	symptoms that is critical in distinguishing ME/CFS from other conditions and illness. See Evidence review D- for the evidence and committee discussion. However after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted for the following reasons: ○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis. • Further investigation/differential diagnoses. The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have added examples of investigations to be done when suspecting ME/CFS and have added that ME/CFS should be suspected if the 'symptoms are not explained by another condition.'
Barts Health NHS Trust	Guideline	008	Box 1	*"Debilitating fatigability,,"*	Thank you for your comment.

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				Although fatigability is a feature of this illness, surely the primary symptom is fatigue and should be listed as such in making a diagnosis?	After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change fatigability. This has been edited to be more descriptive of the fatigue experienced by people with ME/CFS, 'Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.' The committee hope this has added some clarity for readers.
Barts Health NHS Trust	Guideline	008	8	*"psychological wellbeing assessment*" We are not aware of such an assessment, apart from that done by Psychological Well-being Practitioners in IAPT services. Is NICE suggesting that IAPT services provide this for patients? In view of the commonest alternative diagnoses being mood and anxiety disorders and in view of the commonest comorbidities being the same, can NICE explain how such an assessment will capture these important conditions? This is particularly the case when depression is only mentioned once in the guideline and anxiety disorders are not mentioned at all. The only possible risk of premature death is by suicide; will this assessment include a risk assessment for suicide?	Thank you for your comment. The committee agree at this stage the person has not been diagnosed with ME/CFS or any other condition and as you comment it is important to investigate the possibility of other diagnosis and co-existing conditions. The committee note the assessment recommended describes the routine examinations and assessments when a patient has an undiagnosed illness. To clarify this the recommendation has been edited from 'comprehensive clinical history' to 'medical assessment (including relevant symptoms and history, comorbidities, overall physical and mental health). In addition psychological wellbeing has been edited to, 'an assessment of the impact of symptoms on psychological and social wellbeing' to clarify this assessment.
Barts Health NHS Trust	Guideline	009	Box 1	*"…slurred speech,… confusion, disorientation"* These are symptoms that are not part of this illness, and should lead to the assessing clinician seeking alternative diagnoses, such as a neurological or neuropsychiatric disorders.	Thank you for your comment. These have been removed.
Barts Health NHS Trust	Guideline	010	17-19	"*not to use more energy than they perceive they have – they should plan their daily activity to stay within their energy envelope and not push through activity"* Where is the research evidence for such a recommendation? Do NICE believe that such advice, which we believe will	Thank you for your comment. After considering the stakeholder comments the committee agreed that this concept and energy envelope* might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed

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				maintain both disability and duration of ill health, should be given in the absence of any significant research evidence of efficacy? Has 'energy envelope' any specific medical meaning or definition?	with ME/CFS and information on energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits. There is a definition of energy limits in the terms used in the guideline. *Re energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. The energy management section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies).
Barts Health NHS Trust	Guideline	024	7-9	"*Discuss with people with ME/CFS the principles of energy management, its role in supporting them to live with their*	Thank you for your comment.

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				symptoms, the potential benefits and risks and what they should expect." What does NICE mean by 'principles of energy management'? This engineering concept does not have much scientific validity in human biology and appears to be used here as pseudo medical term. How does NICE expect clinicians to explain "the potential benefits and risks" when there is little or no evidence to advise them? The only large trial of such an approach showed that adaptive pacing therapy, based on the principles of energy management and supported by up to 15 sessions from an occupational therapist, was no more effective than specialist medical care, and, if anything, exacerbated physical disability (White et al, 2011, https://doi.org/10.1016/S0140-6736(11)60096-2, Dougall et al, 2014, https://doi.org/10.1016/j.jpsychores.2014.04.002).	*Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS.
Barts Health NHS Trust	Guideline	024	4-5	"*Be aware there is no current treatment or cure (non-pharmacological or pharmacological) for ME/CFS."* This is a very strange statement. Firstly, it is not true, since there are two non-pharmacological treatments with good evidence of efficacy in patients with CFS/ME. Secondly, why use the word "cure", when it is a word hardly seen, if at all, in NICE guidelines for other chronic conditions?	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

10 November 2020 - 22 December 2020

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				Does NICE agree that such a statement is not only inaccurate, but will remove all hope of recovery in patients with CFS/ME? Primum non nocere.	*Cure* Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. The rationale for this recommendation outlines that the committee agreed it was important to raise awareness about the claims that have been made about cures for ME/CFS and that there is often a financial cost to people with ME/CFS when they pursue these. While the committee agree there are people who recover there isn't currently a cure for ME/CFS.
Barts Health NHS Trust	Guideline	025	18-20	"*reduce activity as the first step* • *plan periods of rest and activity, and incorporate the need for pre-emptive rest"* Would NICE advise where clinicians can access research evidence for always reducing "activity as a first step" and the efficacy of "pre-emptive rest"? We already know that there are two, probably three, identifiable patterns of physical activity in patients with CFS/ME (van der Werf et al, 2000, https://doi.org/10.1016/S0022-3999(00)00197-5; King E et al 2020, https://doi.org/10.1016/j.jpsychores.2020.110154). Would NICE please advise how this advice applies to all of these patterns of activity? Is it really a good idea to reduce activity in those who are already inactive all the time?	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to, agree a sustainable level of activity as the first step, which may mean reducing activity.' The committee agreed that rest was an important part of managing activity in people with ME/CFS. The role of rest and sleep are further addressed in section 1.12 and the rationale provides further information on this.
Barts Health NHS Trust	Guideline	025	25-26	"*Advise people with ME/CFS to reduce their activity if increasing it triggers symptoms, or if they have fluctuations in their daily energy levels."* Would NICE please provide the research evidence to support this advice? If it is solely based on the experience of the	Thank you for your comment. After considering the stakeholder comments this has been edited to,' Advise people with ME/CFS how to manage flare-ups and

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

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				committee and patient group surveys, rather than research, why is this advice so strongly recommended in a NICE guideline? In fact, recommendations in the guidelines appear to be weighted more toward selected experiential and qualitative surveys rather than evidential research.	relapses (see the section on managing flare-ups in symptoms and relapse).'
Barts Health NHS Trust	Guideline	027	21-23	"*Do not advise people with ME/CFS to undertake unstructured exercise that is not part of a supervised programme, such as telling them to go to the gym or exercise more, because this may worsen their symptoms."* We entirely agree with this sensible advice, and suspect that this is one of the reasons for the sometimes negative view of GET held by some patients. i.e. that they thought they were receiving GET when they were not. (Gladwell PW et al, 2014, https://doi.org/10.3109/09638288.2013.797508)	Thank you for your comment.
Barts Health NHS Trust	Guideline	028	3-5	"*Do not offer people with ME/CFS… • generalised physical activity or exercise programmes – this includes programmes developed for healthy people or people with other illnesses"* We entirely agree that it is not safe to simply encourage patients to undertake a programme of exercise or physical activity that might be designed for a healthy person.	Thank you for your comment.
Barts Health NHS Trust	Guideline	028	1-2	*"Do not offer people with ME/CFS: • any therapy based on physical activity or exercise as a treatment or cure for ME/CFS"* Why is NICE giving such advice when it flies against the clear evidence of benefit for GET as a treatment for this illness?	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review

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					quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.)

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					The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. . The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.
Barts Health NHS Trust	Guideline	028	6-7	*"Do not offer people with ME/CFS… • any programme based on fixed incremental increases in physical activity or exercise, for example graded exercise therapy"* We entirely agree that patients should not be offered a "programme based on fixed incremental increases in physical activity or exercise". But it is a categorical error to suggest that an example of such a programme is graded exercise therapy. As available manuals, leaflets, and papers make clear, GET is a mutually agreed programme of exercise, designed for each individual patient, which starts with stabilisation of physical activity, before mutually agreeing small increments in the time	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review

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				a patient is physically active, with adaptations of the therapy that depend on symptoms. It is not fixed. Do NICE agree that this is a "straw man" argument, and should be removed.	quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.)

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					The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.
Barts Health NHS Trust	Guideline	028	8-9	*"Do not offer people with ME/CFS… • structured activity or exercise programmes that are based on deconditioning as the cause of ME/CFS"* We are not aware of any studies or reviews that suggest that deconditioning is *a cause* of ME/CFS. Again this is a straw man fallacy. There was one early trial of GET designed as a simple training programme, which involved a high initial intensity of exercise, with consequent significant number of patients dropping out of treatment (Wearden AJ, et al 1998, https://doi.org/10.1192/bjp.172.6.485). But these authors did not suggest that deconditioning was a cause. We now know that GET does not work by improving physical conditioning	Thank you for your comment. The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS.These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable

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				(Chalder et al, http://dx.doi.org/10.1016/S2215-0366(14)00145-X) and GET is not designed as a physical training programme. Such therapies do not have high numbers of patients withdrawing from treatment. Would NICE agree that this false suggestion should be removed from the guideline?	exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G.' The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.
Barts Health NHS Trust	Q1	Q1	Q1	"*1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why.*" This draft guideline means that NHS services would be unable to provide one of the two most evidence based treatments for CFS/ME (graded exercise therapy GET) and only able to provide the second evidence based treatment, cognitive behaviour therapy (CBT), for the relief of distress, and not as a treatment for CFS/ME. This would mean that NHS specialist services would be unable to provide any evidence based treatments, since self-management based on energy management, which this guideline recommends instead, is not an evidence based treatment. The first likely consequence would be that physiotherapists and clinical psychologists would leave the current CFS/ME services to move to other services where they would be able to practise normally and provide these treatments, such as chronic pain services (see current draft NICE guideline for chronic pain) or other rehabilitation based services such as the new "long-Covid" services. The second likely consequence would be the closure of NHS	Thank you for your comment. The committee have revised the wording of their recommendations so that they are less negative regarding CBT and are not restricted to the relief of psychological distress. However, they continue to emphasise the need for patients and clinicians to be informed about the limitations of this therapy for people with ME/CFS. We anticipate there might be a reduced demand for CBT, but it remains an important part of management that many people with ME/CFS will benefit from. The committee assert that this guideline is based on the broad evidence base and are confident that commissioners will demand these services.

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				services for CFS/ME since clinical commissioning groups will not fund services that do not provide evidence based services.	
Blue Ribbon for the Awareness of ME	Guideline	014	16	1.6.4 Replace 'medical condition' with 'disease'	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change condition for disease.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	General	General	Having done this myself, in the past, I just want to say that we appreciate the hard work which has gone into producing this guideline by the group, and the team behind them. We appreciate too the efforts which have gone in to change the tone of these guidelines and the removal of the recommendation of GET and CBT as "treatments" for ME and CFS. We do, however, have concerns still about key areas we feel have still not been appropriately addressed to accurately recognise and reflect the serious neurological diseases of ME and CFS. We hope that you will understand our comments below are constructive feedback, to help create the constructive guidance needed for the acknowledgement, diagnosis, management and implementation of these guidelines for people with neurological ME and CFS.	Thank you for your comments.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	General	General	Why is there no introduction about ME? No mention of the numbers of people with ME and CFS in the UK nor that 25% of people with ME and CFS are severely/very severely affected. Why is the **fact** that ME and CFS are classified as neurological diseases under WHO G93.3 in both ICD 10 and ICD11, and are acknowledged as such by the Dept of Health, not included in the guideline?	Thank you for your comment. The introduction section has been replaced with the context section at the back of the guideline and includes this information. The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) has been added to the context.

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				Putting this statement in, is not stating the opinion of the group, but simply stating the facts that WHO and the Dept of Health classify ME and CFS as neurological diseases. Inclusion of this statement in the guideline would go a long way to give clarity to those who will refer to this guideline and help to dismiss the erroneous myths around these diseases which have not been acknowledged and managed appropriately for decades. We strongly believe the below paragraph drafted by Forward ME should be included: "ME/CFS is a recognised neurological disease classified by WHO ICD10 G93.3. This classification is also recognised by the Department of Health and Social Care. It is also recognised as a disease by all of the US authorities and by many researchers."	
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	General	General	We do not agree with the term ME/CFS as we believe ME and CFS to be 2 separate illness which share similar symptomology, just as long Covid now shares similar symptomology with ME and CFS, and may now either develop into ME or CFS, or become part of the post-viral illness group which shares similar symptomology. When we attended the consultation events prior to the setting up of the group overwhelmingly it was agreed that it should be ME and/or CFS in the document and not ME/CFS. Encephalopathy is not recognised by WHO.	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'*

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					The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) has been added to the context.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	General	General	Why is there no list of exclusionary tests and alternative diagnoses as in the previous guideline? These are helpful signposts for doctors when making a diagnosis and creating a baseline of levels for when reviews are taking place. I still strongly believe that Ferritin should be added to the previous list as many people can have a low ferritin level whilst also displaying a normal/near normal blood picture, a low iron level is easily manageable and could stop someone being sent down a diagnosis and management pathway which is unnecessary.	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	General	General	We support the guideline withdrawing the recommendation of GET and CBT as 'treatments' in this guideline – but a statement must now be made stating that these can potentially cause harm, and NICE in no way recommends these 'treatments' now. We are concerned though that exercise is still included with the support of 'appropriately trained' OTs and PTs and this could still be misinterpreted and lead to exercise programmes which go beyond the anaerobic threshold and cause an exacerbation of symptoms and worsening of condition.	Thank you for your comment. GET
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	General	General	We fully support the need to include the list of physiological effects of exertion in these guidelines as in the evidence provided by Physios for ME. "We were disappointed to see no mention of the physiological effects of exertion in the review. We feel it is essential for health professionals working with people with ME/CFS to have	Thank you for your comment. The guideline includes a definition of post exertional malaise and describes the impact of activity on people with ME/CFS. Exploring the specific physiological effects of exertion was not prioritised by stakeholders during the development of the scope or by the committee when finalising the evidence review questions. As such evidence on the physiological effects of exertion has not been searched for or reviewed and the

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				knowledge of the physiological processes that occur during over-exertion. Research has shown that exercise in people with ME leads to abnormal physiological responses including: 1. reduced maximum heart rate 1-3 2. reduced maximum oxygen consumption 3-5 3. reduced cardiac output 1,2,6 4. insufficient blood pressure increase on exertion 4,7 5. decreased capacity to use oxygen 1 6. anaerobic threshold and maximum exercise are reached at much lower oxygen Capacity 3,8 7. exhaustion reached more rapidly and accompanied by relatively reduced intracellular concentrations of ATP 9 8. increased intracellular acidosis in exercising muscles and reduced post-exercise recovery from acidosis 10,11 9. activation and worsening of symptoms which can be immediate or delayed by several days 12, 13 10. when exercise is repeated the next day, abnormalities are more severe 14 11. decreased cognitive functioning and prolonged reaction time 15 12. prolonged recovery period: usually 24 hours, often 48 but can last days, weeks or cause a relapse 1,14,16 1. De Becker P, Roeykens J, Reynders M, et al. Exercise capacity in chronic fatigue syndrome. Arch Intern Med	committee were unable to make any recommendations on this topic.

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				2000;160:3270-77. [PMID: 11088089] 2. Inbar O, Dlin R, Rotstein A, Whipp BJ. Physiological responses to incremental exercise in patients with chronic fatigue syndrome. Med Sci Sports Exerc 2001; 33: 1463-70. [PMID: 11528333] 3. Jones DE, Hollingsworth KG, Jakovljevic DG, Fattakhova G, Pairman J, Blamire AM, Trenell MI, Newton JL. Loss of capacity to recover from acidosis on repeat exercise in chronic fatigue syndrome: a case-control study. Eur J Clin Invest 2012; 42: 186-94.. [PMID: 21749371] 4. Farquhar WB, Hunt BE, Taylor JA, Darling SE, Freeman R. Blood volume and its relation to peak O2 consumption and physical activity in patients with chronic fatigue. Am J Physiol Heart Circ Physiol 2002; 282: H66-71. [PMID: 11748048] 5. Jammes Y, Steinberg JG, Mambrini O, Brégeon F, Delliaux S. Chronic fatigue syndrome: assessment of increased oxidative stress and altered muscle excitability in response to incremental exercise. J Intern Med 2005; 257: 299-310. [PMID: 15715687] 6. Peckerman A, La Manca JJ, Dahl KA, Chemitiganti R, Qureishi B, Natelson BH. Abnormal impedance cardiography predicts symptom severity in chronic fatigue syndrome. Am J Med Sci 2003; 326: 55-60. [PMID: 12920435] 7. Streeten DH. Role of impaired lower-limb venous innervation in the pathogenesis of the chronic fatigue syndrome. Am J Med Sci 2001;321:163-7.	

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				encephalomyelitis/chronic fatigue syndrome; an experimental study. J Intern Med 2010; 268: 265-78. [PMID: 20412374] 15. La Manca JJ, Sisto SA, DeLuca J, Johnson SK, Lange G, Pareja J, Cook S, Natelson BH. Influence of exhaustive treadmill exercise on cognitive functioning in chronic fatigue syndrome. Am J Med 1998; 105: 59S-65S. [PMID: 9790484] 16. VanNess JM, Snell CR, Stevens SR. Diminished cardiopulmonary capacity during postexertional malaise. J Chronic Fatigue Syndr 2007; 14: 77-85."	
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	General	General	Whilst we appreciate there are multiple references to specialist teams in ME and CFS, we must recognise that there is a dearth of specialist teams around the country, and many of these are set up to provide harmful GET and illness beliefs CBT, and often run by psychiatrists/psychologist/OTs. There is a real genuine concern at the lack of people trained and knowledgeable in neurological ME and CFS. Training and setting up of specialist clinics, providing appropriate care, is urgently needed, especially as numbers are now likely to increase with the addition of long-covid. These clinics also need to provide ongoing care, review and management particularly for the severely/very severely affected and those with co-morbid conditions. A recommendation is needed that specialist multi-disciplinary teams should be urgently set up and to include specialist doctors, nurses, OTs, dieticians, paediatric services and domiciliary services, and should include staff specialised in severe ME, and all staff should be appropriately trained in	Thank you for your comment. The committee agree that there is variation in the delivery of some of the recommended services across the NHS and there are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS.

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				neurological ME and CFS and the clinics provide diagnosis, management and ongoing review and management.	
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	General	General	Although this guideline has tried to improve the tone around ME and CFS, and no longer recommends GET and CBT as treatments, and we welcome this, we still have many concerns around diagnosis and how these guidelines could be interpreted, and misinterpreted, and safeguards must be put in place to ensure that this does not happen. I was assured that this would happen with the last guidelines and it did not. Which areas will have the biggest impact: 1. A dearth of specialist services and appropriately trained HCPs in neurological ME and CFS. 2. Not having correctly trained HCPs who are knowledgeable and understanding of neurological ME and CFS, and the impact of these diseases, will mean implementation of these guidelines will be more difficult, until correct and appropriate medical training is implemented at medical school and throughout. Until this is done, and many HCPs misconceptions of ME and CFS, and the erroneous myths around them, are dispelled and addressed, then they will continue to perpetuate, and therefore will still lead to misdiagnosis, mismanagement, and poor and inappropriate patient care. 3. One of the biggest failures of the document is the section on suspecting ME and CFS and diagnosis. We do understand the need for wide referral criteria, to	Thank you for your comments. *1 and 2. Training* The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. *3.Suspecting and diagnosing ME/CFS* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. For more detail on the committee discussion about the IOM criteria see Evidence review D-Diagnosis. The committee agree these symptoms in the criteria are seen in other conditions particularly fatigue, but note it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS. The committee note all 4 key criteria needing to be present is stricter than the previous CFS/ME NICE guideline. *4. Misdiagnosis* Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude and identify other diagnoses. The committee have now included examples of investigations that

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				catch many, but this is far too wide and is likely to catch anyone with fatigue as a symptom. Once at a specialist clinic/GP specialist, narrower diagnostic criteria must be used to create homogenous groups of people, especially as there is no diagnostic test, ie Fukuda 1994 for CFS and ICC 2011 for ME. We truly fear that the use of IOM for diagnosis will create such a heterogeneous group that it will prove difficult for people to be diagnosed and managed correctly; people with other conditions will not be investigated sufficiently, and just get labelled as ME or CFS, and time-sensitive conditions may be missed, and/or co-morbid diagnoses may be missed. The IOM criteria are neither helpful, nor descriptive, of ME and CFS and how severe, multi-system, multi-organ diseases they can become. It demeans these diseases again to just be fatigue syndromes, and they are so much more, the IOM does not recognise the debilitating neurological disease we all know them to be. The IOM is not helpful for either diagnosis nor research into ME or CFS. These are serious multi-system, multi-organ diseases and should not be demeaned, and dumbed down, all the time to fatigue, just because, presently, science has not found the cause, or fully understands these diseases. They will never be taken seriously, as they deserve to be, until the medical world and the government documentation, takes them seriously, and unfortunately this is yet another failure to do so. 4. A lack of list of basic tests and exclusionary tests, along with the use of IOM criteria could lead to a rise	might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. *5. Introduction* The introduction section has been replaced with the context section at the back of the guideline and includes this information. The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) has been added to the context. *6. Prognosis* This is addressed in the information and support section of the guideline. 7. *Complications of ME/CFS* This was not included within the scope of this guideline as a topic to consider, and therefore the evidence not reviewed and the committee are unable to make recommendations on this topic.

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				in misdiagnosis, and time-sensitive alternative diagnoses being missed, causing not only trauma and distress, and possibly death for the patients if not corrected soon enough, but increased costings for the NHS. 5. There is no introduction or basic overview on ME and CFS at the start of the document. There is no acknowledgement that ME and CFS are classified as neurological diseases by WHO (ICD 10 G93.3) and acknowledged as such by the Dept of Health. There is no mention of the numbers of people in this country thought to have ME – estimated around 250,000 (twice as many as estimate 130,000 with Multiple Sclerosis), nor is there mention that 25% of these will be severely/very severely affected. All of this is information needed when setting up services. 6. There is no real mention of prognosis in these guidelines, nor acknowledgement, as there is in the CMO report, that those who have been severely affected for more than 5 years have a poorer prognosis – this information is especially useful when looking at service provision and for benefits. 7. There is no mention of the research which shows that people can die from either complications of ME and CFS or are more susceptible to die earlier from other co-morbid conditions such as cardiovascular and cancer as shown in the paper by Jason et al 2008. 8. We are extremely pleased that the NICE guidelines are no longer recommending GET or any progressive	

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				exercise programme or regime and CBT as treatment or cures for ME and CFS both of which are not helpful and can be harmful, particularly GET, for people with ME and CFS.	
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	049 - 052	General	We really do not understand this section. There are perfectly valid and extremely useful criteria out there being used. We feel that one of the biggest failures of the document is around diagnosis. We do understand the need for wide referral criteria, to catch many, but the IOM is far too wide and is likely to catch anyone with fatigue as a symptom. Any patient going in with your 4 key symptoms could be a host of different conditions – this 'criteria' does not narrow down to ME it merely muddies the waters. Once at a specialist clinic/GP specialist, narrower diagnostic criteria must be used to create homogenous groups of people, especially as there is no diagnostic test, ie Fukuda 1994 for CFS and ICC 2011 for ME which was written by a multitude of highly respected Drs specialist in ME from around the world. We truly fear that the use of IOM for diagnosis will create such a heterogeneous group that it will prove difficult to820 diagnose and manage people correctly; people with other conditions will not be investigated sufficiently, and just get labelled as ME or CFS, and time-sensitive conditions may be missed, and/or co-morbid diagnoses may be missed. The IOM criteria are neither helpful, nor descriptive, of ME and CFS and how severe, multi-system, multi-organ diseases they can become. It demeans these diseases again to just be fatigue syndromes, and they are so much more, the IOM does not	Thank you for your comment. *Suspecting and diagnosing ME/CFS* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. For more detail on the committee discussion about the IOM criteria see Evidence review D-Diagnosis. The committee agree these symptoms in the criteria are seen in other conditions particularly fatigue, but note it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS. The committee note this criteria with all 4 key criteria needing to be present is stricter than the previous CFS/ME NICE guideline.

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				recognise the debilitating neurological disease we all know them to be. The IOM is not helpful for either diagnosis nor research into ME or CFS. These are serious multi-system, multi-organ diseases and should not be demeaned, and dumbed down, all the time to fatigue, just because, presently, science has not found the cause, or fully understands these diseases. They will never be taken seriously, as they deserve to be, until the medical world and the government documentation, takes them seriously, and unfortunately this is yet another failure to do so.	
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	034 - 035	Whole pages	We agree with the Forward ME submission below: "In the evidence review at G Page 342 Line 26, the committee summarised the evidence on non-pharmacological interventions for ME/CFS. Their conclusions (from lines 40 – 44) found that: "In addition, the committee made **'do not' offer** recommendations for CBT ………to treat or cure ME/CFS." In the light of this finding, Forward-ME are mystified as to why the draft guideline discusses CBT extensively. This would appear to be discriminatory as the guideline for multiple sclerosis (MS) – a disease that has been compared to ME/CFS, at 1.5.5 states only: 'Consider mindfulness-based training, cognitive behaviour therapy or fatigue management for treating MS-related fatigue. Congestive heart failure- also compared with ME/CFS only makes reference to Depression with reference to the NICE guideline on that topic. We can find no other chronic disease for which such extensive advice is given on CBT.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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				We are aware that some patients may find psychological support necessary and helpful. CBT is mentioned as having two possible purposes: (3) Support in managing symptoms. CBT is only ever relevant when a person is behaving in a maladaptive fashion, grounded in unhelpful beliefs; therapist aims to change mindset to their benefit in terms of changed behaviour. (4) CBT for support with psychological distress as far as we are aware does not exist. Person-centred supportive counselling would be fit for purpose. We are asking for this section to be re-written to state: 'Do not offer CBT to treat or cure ME/CFS as there is no substantive evidence that it is effective. Patients may find supportive, person-centred counselling helpful.'	CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	058 - 059	General	Care workers need to be appropriately trained by people knowledgeable and experienced in diseases which are neurological ME and CFS. Any multi-disciplinary team also needs people appropriately trained to understand severe ME and CFS, and working with children/young people with ME and CFS.	Thank for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	008 - 009	1.2	We are extremely concerned by this section. We do understand the need for wider referral criteria, to catch many, but this is far too wide and is likely to catch anyone with fatigue as a symptom. We truly fear that the use of Institute of Medicine (IOM 2015) criteria for suspecting ME/CFS and/or diagnosis will create such a heterogeneous group that people with other conditions will not be investigated sufficiently, and just get labelled as ME or CFS,	Thank you for your comment. *Suspecting and diagnosing ME/CFS* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. For more detail on the committee discussion about the IOM criteria and their decision to

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				and time-sensitive conditions may be missed, and/or co-morbid diagnoses may be missed and people will be mismanaged. Fatigue and cognitive dysfunction, along with several other ME symptoms are not exclusive to ME. We, of course, accept the characteristic, overwhelming and delayed onset fatigue and post-exertional malaise as core symptoms, but we cannot understand why core symptoms of pain and flu-like symptoms have been relegated to the second section, pain in particular, and are not placed in box 1. We will never forget being in a room of about 250 people with ME, with a prominent ME doctor, and when he asked them to put their hands up if fatigue was their most prominent symptom only 6 hands went up, when asked if pain was their most prominent symptom the rest of the room put their hands up. Pain is overwhelming, it is intense, unrelenting, unremitting, throughout the body and often more difficult to manage than fatigue. You will find it extremely hard to find anyone with ME, in particular severe ME who does not have all the symptoms, and people with CFS will have many of the symptoms listed. We are extremely disheartened that once again criteria have been used that are neither helpful, nor descriptive, of ME and CFS and how severe, multi-system, multi-organ diseases they can become. It demeans these diseases again to just be fatigue syndromes, and they are so much more, the IOM does not recognise the debilitating neurological disease we all know them to be.	include pain as one of the commonly associated symptoms and not a key criteria see Evidence review D-Diagnosis. The committee agree these symptoms in the criteria are seen in other conditions particularly fatigue, but note it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS. The committee note this criteria with all 4 key criteria needing to be present is stricter than the previous CFS/ME NICE guideline. *Misdiagnosis* Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.

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BRAME (Blue Ribbon for the Awareness of ME)	Guideline	008 - 009	1.2	Coupled with the disturbing use of the IOM for criteria is the lack of information around which baseline investigations should be done, and other exclusionary diagnoses and co-morbid diagnoses. The baseline investigations list was a helpful signpost last time to guide HCPs on which tests to do. I still strongly believe that Ferritin should be added to the previous list, as many people can have a low ferritin level whilst also displaying a normal/near normal blood picture, a low iron level is easily manageable and could stop someone being sent down a diagnosis and management pathway which is unnecessary.	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	016 - 017	1.7	We have serious concerns on the safeguarding section, we fear that such a large section, rather than preventing the horrendous erroneous safeguarding issues experienced by people with ME and CFS, will instead put safeguarding into the minds of HCPs where it may previously not have been. 2 points, as highlighted by Forward ME, but with some of our own adjustments, with a brief recognition of the horrendous problems, both historically and currently, being faced by children/young people and vulnerable adults is needed, but stating that issues of safeguarding are no more necessary for ME and CFS than any other chronic condition would suffice. Replace 2 paragraphs with the following: 1.7.1 Recognise that people with ME/CFS, particularly children/young people and those with severe or very severe ME/CFS, are at risk of their symptoms being confused with signs of abuse or neglect, especially where physical symptoms do not fit with a commonly recognised illness, or where more than one family member has ME/CFS.	Thank you for your comment. After considering the stakeholder comments the committee have made edits to this section, including moving the second recommendation to the top of the section and clarifying that '*If* safeguarding assessments are needed…' and hope these have added some clarity for readers. The committee agreed this is an important topic for the issues you raise and consider the all recommendations are appropriate.

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				1.7.2 Safeguarding assessments in people with confirmed or suspected ME/CFS, if needed, should be carried out and overseen by health and social care professionals who have training and experience in neurological ME/CFS. We are concerned that more harm than good could happen, and we wish to protect children/young people and vulnerable adults and prevent them being taken down an erroneous, traumatic and damaging path. We recognise that this is a fine balance, but one that must be found, and is not there at the moment.	
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	070 - 071	22 – 2	Our concern again is who is providing the training and ensuring that these people truly do understand neurological ME and CFS.	Thank you for your comment. Evidence review B includes the committee discussion on training programmes on ME/CFS, the committee agreed that should have evidence-based content and training methods (that are developed and supported by ME/CFS specialist services with input from people with ME/CFS) and are run by trainers with relevant skills, knowledge and experience. To note the training recommendations have been edited.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	001	16	It states that "This guideline will update NICE guideline CG53" we were under the distinct impression that this guideline was replacing CG53. Please could you clarify whether this is an 'update' or a 'replacement'.	Thank you for your comment. This has been edited.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	004	5	1.1.1 Replace "medical condition" with "disease" As medical condition diminishes the impact of ME and CFS	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change condition to disease. Reference to the ICD10 classification has been included in the context section of the guideline.

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BRAME (Blue Ribbon for the Awareness of ME)	Guideline	005	2	Replace "should" with "must" there is no 'should' do this, they 'must' do this.	Thank you for your comment. Must is used in a recommendation when there is a legal duty to apply a recommendation. This is not the case here and no changes have been made to the recommendation.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	005	After line 8	1.1.3 Add additional bullet point. "ensure that any management and support plan is mutually agreed with the patient, and that the patient, at every stage, is fully informed of all the benefits and risks to any pharmacological, or non-pharmacological, management, and their informed consent has been obtained."	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. This point is made later and then reinforced in the management section of the guideline and for this reason your suggestion has not been added to the recommendation.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	005	10	1.1.4 We completely agree that accurate diagnosis is essential, the earlier the better, but to do this you need to use criteria that creates a homogeneous group of people, not a large heterogeneous group, which will include any condition with fatigue as a symptom.	Thank you for your comment. Evidence review D- Diagnosis sets out the evidence and the committee discussion for the diagnostic criteria.

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BRAME (Blue Ribbon for the Awareness of ME)	Guideline	005	14	1.1.4 Regular monitoring and review are very important, not only for when symptoms are worsening or changing, but should be ongoing, especially for the severely/very severely affected, and particularly the long term severely affected, and those with co-morbidities, which can cause complications, therefore please add to the end "worsening, changing or the patient is severely/very severely affected or has co-morbid conditions"	Thank you for your comment. Review is addressed in detail in the review in primary care section of the guideline and includes the points you make.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	005	17	1.1.5 I am pleased you kept in 1.1.5 which I fought so hard to have in the previous guidelines, but I still wish that you would remove the "other aspects of" as it should not affect any part of their care if they withdraw from any part of their management plan.	Thank you for your comment. This has been edited to,' any other aspects' to provide further clarity.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	006	9	1.1.9 We welcome the section on severe neurological ME, and the recognition of the additional complexities when managing and assessing these people who are so severely ill, who are in so much pain, and for whom their disease has often become 8multi-system and multi-organ, and have often developed co-morbid conditions. Replace "some" with "many" you will find time and again people who are severely affected will not have 'some' of these, but 'many', if not 'most' of these symptoms, to just say 'some' diminishes the severity of their condition.	Thank you for your comment. Not all people with severe or very severe ME/CFS will have all of these symptoms and as such 'may' is appropriate.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	006	28	1.1.9 In relation to page 7 line 4 and line 8. By definition to be severely/very severely affected you are house/bed bound for the majority of the time and will use aids such as a wheelchair - there is no 'may' about it	Thank you for your comment. As you note not all people with severe or very severe ME/CFS will have all of these symptoms all of the time and as such 'may' is appropriate.

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BRAME (Blue Ribbon for the Awareness of ME)	Guideline	007	After line 16	1.1.9 Additional bullet point needed to read "acknowledge that patients and their carers/families may have become isolated due to the severity of the illness and may need mutually agreed support".	Thank you for your comment. This section highlights the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. The impact on families and carers is recognised throughout the guideline and is highlighted in the supporting families and carers of people with ME/CFS section of the guideline.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	007	18	1.1.10 Extra bullet point needed to read: "appropriately trained and specialised in severe ME and CFS"	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training in line with this guideline and this is included in the recommendations in the training health and social care professionals section of the guideline. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable for this reason your suggestion has not been added to the recommendation.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	010	1.2.7	Are you referring here to specialists in ME or to say specialists in eg neurology, cardiovascular, rheumatology, pathology, gastroenterology etc	Thank you for your comment. Appropriate specialist here refers to expertise in supporting the interpretation of signs and symptoms where there is uncertainty and a possible alternative diagnosis. Throughout the guideline where a specialist refers to a ME/CFS specialist this has been made clearer by including ME/CFS before specialist.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	011	1.4	We reiterate again, you cannot diagnose ME or CFS using the IOM criteria of 1.2.3. This is basically the criteria of a fatigue syndrome it will create too heterogeneous a group of people so that it will be difficult to diagnose and manage people correctly; people with other conditions will not be investigated sufficiently, and just get labelled as ME or CFS, and time-sensitive conditions may be missed, and/or co-morbid diagnoses may be missed. The impact from this will not only be on the person and the trauma they go through with misdiagnosis and	Thank you for your comment. *Suspecting and diagnosing ME/CFS* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. For more detail on the

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				mismanagement, and possibly death if a time sensitive diagnosis is not made in time, but also it will increase costs to the NHS. Diagnosis of CFS should be made using the Fukuda 1994 criteria and diagnosis of ME using the International Consensus Criteria (2011)	committee discussion about the IOM criteria see Evidence review D-Diagnosis. The committee agree these symptoms in the criteria are seen in other conditions particularly fatigue, but note it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS. The committee note this criteria with all 4 key criteria needing to be present is stricter than the previous CFS/ME NICE guideline. *Misdiagnosis* Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	012	10	1.5.2 Replace "management plan" with "management and support plan" as you manage the disease but support the patient.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	012	25	1.5.2 Symptom management should be the first bullet point in this list as the management of the symptoms should be the first step when developing a management and support plan.	Thank you for your comment. The bullet points are not in any order of priority.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	013	13	1.5.5 Adjust sentence to read 'assessment, development and provision of their management plan as well as regular review and monitoring of their condition.'	Thank you for your comment. *Provision of care*

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				Continuity of care should be included as it is vital for building up a mutually trusting relationship and to enable the HCPs to recognise any change in the person's symptoms, which may indicate a co-morbid condition developing.	The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. Review The review in primary care section of the guideline recommends a review of the care and support plan at least once a year depending on the person's circumstances. The committee recommended a named contact in the multidisciplinary care section of the guideline and continuity of care is further addressed in the awareness of severe or very severe ME/CFS and its impact.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	014	18	1.6.4 Add on to end of sentence "and are worsened by physical and cognitive exertion"	Thank you for your comment. The impact of activity is addressed in the energy management section of the guideline.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	014	23	1.6.4 Very few people 'recover' it is thought that the disease remains dormant waiting to come to the surface again at any time.	Thank you for your comment. After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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BRAME (Blue Ribbon for the Awareness of ME)	Guideline	015	10	1.6.7 Replace 'condition' with 'disease'	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change condition to disease. Reference to the ICD10 classification has been included in the context section of the guideline.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	018	18	1.8.1 Need an extra bullet point of "have prepared for appointment by resting"	Thank you for your comment. This recommendation raises awareness about the reasons people may miss an appointment not about preparation for an appointment and for that reason your suggestion has not been added.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	019	1	1.8.5 Need to add in 'taking into account section 1.1.8" so that it reads "discuss with people who need inpatient care, taking into account 1.1.8, and whether any aspects of…."	Thank you for your comment. This recommendation refers to all people with ME/CFS and recommendation 1.1.8 is specific to people with severe or very severe ME/CFS. For this reason your suggestion has not been added. To note after considering the stakeholder comments the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	019	17	1.8.6 Replace 'management plan' with 'management and support plan'	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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BRAME (Blue Ribbon for the Awareness of ME)	Guideline	021	5	1.9.1 Add to the end of the sentence 'even part-time'	Thank you for your comment. This is a general point about returning to work, school or college and the suggestion you make does not add further clarity to the recommendation and has not been added.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	021	10	1.9.1 Add to the end of the sentence 'even part-time'	Thank you for your comment. This is a general point about returning to work, school or college and the suggestion you make does not add further clarity to the recommendation and has not been added.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	023	4	1.10.1 Add to end of sentence 'when able'	Thank you for your comment. This recommendation refers to the expertise that should be available and does not make any judgement about if someone needs the expertise. For this reason your suggestion has not been added.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	025	21	1.11.4 Agree with Physio's for ME the need to recognise that both cognitive and physical activity can cause symptom exacerbation, so the sentence needs to read: "Alternate and vary between different types of activity eg cognitive and physical, and break them into small chunks to avoid triggering Post Exertional Symptom Exacerbation"	Thank you for your comment. The principles of energy management are set out in recommendation 1.11.2 and includes that energy management refers to all types of activity (cognitive, physical, emotional and social) and takes into account overall level of activity.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	025	25 & 26	1.11.6 Please signpost the "managing flare and relapse" section on page 37	Thank you for your comment. After considering the stakeholder comments this has been edited to,' Advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).'
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	026	1.11.8	1.11.8 Have serious concerns about this section, any referral must only be made if mutually agreed with the patient and all the risks and benefits have been fully explained allowing them to make an informed choice. I have concerns about the inclusion of any of the bullet point in this section, as explained below:	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews A, G and H) and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS

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				Would suggest a rewriting of the entire point 1.11.8 to read "Refer people with ME/CFS to a specialist service if they require additional support with activity and energy management planning, and if mutually agreed with the patient"	where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	026	3	1.11.8 Have concerns about people just being referred because they have had reduced mobility or physical activity levels for a while, this could lead to people who are severely affected, in severe pain being referred as well as people who do not wish to	Thank you for your comment. After considering stakeholder comments this bullet point has been edited to, 'have difficulties caused by reduced physical activity or mobility (also see the sections on physical functioning

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				be referred, as any activity leads to an exacerbation of symptom. I would remove this bullet point	and mobility and care for people with severe and very severe ME/CFS)'. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	026	4 & 5	1.11.8 I would also remove this bullet point, as who is making the decision that a person is ready to progress their activity beyond their current abilities – this sounds like it is an HCP making this decision and not the person themselves, as this suggests that the person can achieve activity when "ready" not when physically able to do so without exacerbation.	Thank you for your comment. After considering stakeholder comments this bullet point has been edited to,' feel ready'. Based on the quantitative and qualitative evidence (evidence reviews A, G and H) and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into

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					managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. In line with this someone could decline a referral to a specialist ME/CFS physiotherapy or occupational therapy service
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	026	6 & 7	1.11.8 This is the only bullet point that states the wishes of the person to incorporate physical activity ie it is their choice, but caution should also be used, as you should not just refer people when they say they want to do physical activity, as they may end up causing a relapse, or flare up, by trying to do too much too soon. Physical activity incorporates a wide range of activity, including daily activities, and should be within the confines of their energy envelope and without triggering symptom exacerbation.	Thank you for your comment. The committee agree that this needs to discussed alongside the expertise of physiotherapist or occupational therapist working in a ME/CFS specialist team and this is why they have recommended referral at this stage.
BRAME (Blue Ribbon for the	Guideline	026	18	1.11.11 Need to add in at end of sentence "taking into account a patient's pain, ability and ensuring it does not cause	Thank you for your comment.

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Awareness of ME)				exacerbation of symptoms and keeps below their anaerobic threshold" Should be more emphasis on maintenance in this section rather than endurance etc which could be misinterpreted as need for progression.	'Strategies need to be carried out in small amounts and spread out throughout the day' has been added to the recommendation to clarify this is in the context of the priorities and symptoms that people may have. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	027	1.11.14	Need to add in the importance of families and carers understanding that a person may not be able to achieve things every day, that they need to keep within their energy envelope and help the person to minimise symptom exacerbation.	Thank you for your comment. After considering the stakeholder comments, 'strategies need to be carried out in small amounts and spread out throughout the day' has been added to the first recommendation in this section to clarify that any strategies implemented are in the context of the priorities and symptoms that people may have. This would be part of the information that families and carers receive. In addition the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	027	1.11.15	We strongly support the inclusion of this statement as it can cause a serious exacerbation of symptoms and abnormal physical response (see comment 6)	Thank you for your comment.
BRAME (Blue Ribbon for the	Guideline	028	1.11.16	We strongly support that NICE are no longer recommending the use of structured and progressive exercise programmes and	Thank you for your comment. *Treatment or cure*

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Awareness of ME)				regimes for people with ME or CFS. These were never a treatment nor a cure, and patient evidence repeatedly showed that it could caused a worsening of symptoms, supported by the multiple research papers showing the abnormal physical response to exercise seen in people with ME and CFS. We are pleased that the NICE evidence review itself has now found the quality of evidence of clinical effectiveness of GET ranged from low to very low	After considering the range of stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	028	1.11.17	Concerned again about the language here of "ready to progress" it should be when a person wishes to increase, and, more importantly, is 'able' to increase their physical activity whilst maintaining their energy envelope, without symptom exacerbation and below their anaerobic level.	Thank you for your comment. After considering stakeholder comments this bullet point has been edited to,' feel ready'. At this point the person is referred to a physiotherapist or occupational therapist working within a ME/CFS specialist team to explore this.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	028	1.11.18	As with all through this document, the training must be appropriate and in relation to neurological ME and CFS. With particular regard to OTs and PTs they need specific training and awareness in the adverse reactions and symptom exacerbation experienced by people with ME and CFS to exercise, and the abnormal physical reactions experienced by people with ME and CFS eg lowered anaerobic threshold etc.	Thank you for your comment. The committee agree that all health and social care staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	031	14	1.11.31 Add another bullet point "Avoid giving further medication to counter side effects"	Thank you for your comment. The committee have included in the other considerations section of Evidence review F:Pharmacolgical management that it is important that medicines management is tailored to the person with ME/CFS and as a result could not provide detailed advice on how to manage intolerance.
BRAME (Blue Ribbon for the	Guideline	034	1.11.43	Please add another bullet point "People with ME and CFS should not be automatically directed to IAPT pathway"	Thank you for your comment. The committee agree and it is clear in the recommendations that CBT is only delivered to people with ME/CFS by healthcare

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Awareness of ME)					professionals with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	036	5 and 6	1.12.2 Please add to the end "whilst taking into account any hypersensitivities and exacerbations of symptoms" Many people with ME and CFS suffer from hypersensitivity to medication, and medication, where possible, should be started at a lower level and then gradually increased. Some co-morbid conditions include exercise within the management of the condition, and the person's ME should be taken into account.	Thank you for your comment. In the medicines for symptom management section of the guideline there are recommendations addressing the points you raise. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason you suggestion has not been added.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	039	14	1.14.3 Add to the end "and evaluate and investigate whether these new symptoms, or change in symptoms, are due to the patient's ME or CFS or whether it is due to a diagnosed/undiagnosed co-morbid condition"	Thank you for your comment. The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another recommendation to ensure that any new symptoms or a change in symptoms are investigated.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	040	12	1.15.1 Change 'should' to 'must'	Thank you for your comment. Must is used in a recommendation when there is a legal duty to apply a recommendation. This is not the case here and no changes have been made to the recommendation.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	040	13	1.15.1 Remove the words "what" and "is" and add in to read "understanding that ME and CFS are neurological diseases which can become multi-system/multi-organ, and its diagnosis and management" Though you talk of diagnosis, this guideline is not helpful for the diagnosis of ME or CFS, only for diagnosing general fatigue conditions, to properly diagnose then the use of Fukuda criteria 1994 for CFS and the ICC 2011 for ME, which was written by specialists in ME from around the world, should be used.	Thank you for your comment. The committee discussed the level of detail that should be included in training programmes and agreed on a general description to avoid a prescriptive interpretation of the content allowing the recommendations to remain relevant as research in the area develops.

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					To note the text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) has been added to the context. *Diagnosis* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in Evidence review D-Diagnosis. The committee note it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	041	2	1.15.3 Replace 'should' with 'must'	Thank you for your comment. Must is used in a recommendation when there is a legal duty to apply a recommendation. This is not the case here and no changes have been made to the recommendation.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	043	3	Management Plan – replace with "management and support plan"	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	043	4	Add in new points to read "The personalised management and support plan, which should be mutually agreed and developed between the patient and the specialist team,"	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans. https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) The definition is a summary and includes an overview of what is within the care and support plan, it is not meant to be exhaustive. For this reason you suggestions have not been added. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the

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					NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	045	4	Replace "may" with "usually"	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	046	6	This was recommended last time, and the diagnostic criteria, which is still the best for diagnosing ME (ICC) and CFS (Fukuda) are still being ignored, for a catch all fatigue syndrome criteria, which is of no use to anyone.	Thank you for your comment.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	050	17-20	Until these guidelines actually recommend helpful criteria then the practices of diagnosing will not be standardised, the IOM criteria will diagnose nothing more than a fatigue syndrome and will lead to misdiagnosis and so wide a heterogeneous group that it will not be helpful to anyone.	Thank you for your comment. The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in Evidence review D-Diagnosis. The committee agree these symptoms are seen in other conditions particularly fatigue, but note it is the combination and the interaction of the

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					symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	051	14-16	If the IOM criteria continue to be used then there may be additional costs to the NHS as people are misdiagnosed and potentially time critical illnesses are missed, in addition to the trauma and illness impact to the patient.	Thank you for your comment. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted. As you note this combination of symptoms cannot be considered normal and should be investigated but the committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. • Further investigation/differential diagnoses. The committee have similar experience of people being referred and having another diagnosis and throughout the section on suspecting ME/CFS the committee have recommended that investigations should be done to exclude other diagnoses and this should continue where ME/CFS is suspected. If in any doubt specialist advice should be sought. The committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'. See evidence review D-diagnosis for the evidence and committee discussion on the diagnostic criteria.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	052	4-15	We cannot agree that no one criteria is better overall because clearly the ICC 2011 criteria creates a homogeneous group of people which fit the diagnosis of ME.	Thank you for your comment and information See evidence review D-diagnosis for the evidence and committee discussion on the diagnostic criteria.

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BRAME (Blue Ribbon for the Awareness of ME)	Guideline	056	2 & 3	'expertise' is a loaded phrase as it depends on who classes the person as an expert, their beliefs on ME and CFS and the education, information and training they have received.	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. This applies to this section on safeguarding.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	060	14-17	Research is only valid and useful if the research criteria used creates a homogeneous group of people such as Fukuda for CFS, and ICC for ME, to allow for an accurate diagnosis of the conditions. To use the Oxford or IOM (which is only one step up from Oxford) will lead to just anyone with a fatigue syndrome being used, and therefore the results cannot be extrapolated for use for people with ME or CFS. These guidelines dangerously recommending the IOM criteria will not help in any way for diagnosis or research and may lead to misdiagnosis and research extrapolated for use for the population it is supposed to be for.	Thank you for your comment. *Suspecting and diagnosing ME/CFS* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. For more detail on the committee discussion about the IOM criteria see Evidence review D-Diagnosis. The committee agree these symptoms in the criteria are seen in other conditions particularly fatigue, but note it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS. The committee note this criteria with all 4 key criteria needing to be present is stricter than the previous CFS/ME NICE guideline.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	062	14	Add to the end of the sentence "….management and support plan, where appropriate and mutually agreed with the patient"	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	063	2-8	Still have real concerns, I am pleased that the group acknowledges that exercise should not be used as a treatment or cure, but concerned that in effect by saying that the programme should only be delivered by a PT or OT who has	Thank you for your comment. Based on the evidence (see evidence review G) and their own experience the committee concluded that it was important that a

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				training in ME/CFS, then it is still saying exercise programmes are ok. There is also the concern as to the training and whether it is appropriate.	physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed it was important people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	069	15-19	It should also be recognised that sometimes a flare up or relapse can happen for no reason whatsoever even when the person is managing everything within their envelope.	Thank you for your comment. After considering the stakeholder comments a recommendation raising awareness that flare- ups and relapses can happen in ME/CFS even if the person's symptoms are well managed has been added to the flare up and relapse section of the guideline.
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	071	10-14	We cannot agree that there is little pathological evidence, as there are multiple papers showing differences in the grey and white matter of the brain and inflammation of the spinal cord has been observed in post mortems such as that found in a young woman whose post mortem has been well documented in the public domain. As we have stated before, we believe that ME and CFS are 2 different diseases which share similar symptomology and	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly*

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				management techniques, and therefore the guideline should have separated them throughout to ME and CFS or ME and/or CFS. This was also agreed by just about everyone that came to the consultation event pre guidelines.	*defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'*
BRAME (Blue Ribbon for the Awareness of ME)	Guideline	072	1	We agree that there is no diagnostic test but many do accept that ICC creates an accurate diagnosis for ME and Fukuda for CFS and these should be used, as to use the IOM will create too heterogeneous a group of patients leading to a very likely high potential of misdiagnosis and time sensitive alternative diagnoses being missed – we believe the use of the IOM is potentially dangerous and could also lead to an unnecessary increase in cost for the NHS.	Thank you for your comment. See Evidence review D-Diagnosis for evidence and committee discussion on the diagnostic criteria.
British Neuropsychiatric Association	Guideline	General	General	Dear committee members, We were pleased to see the release of the recent update to ME/CFS guidance, and note the preliminary recommendations on assessment and management for this complex group. The British Neuropsychiatric Association is the leading scientific society for medical practitioners, and professionals allied to medicine in the UK, working at the interface of the clinical and cognitive neurosciences. Our objective has always been the advancement of health for the public benefit by bringing about improved health care for people with neuropsychiatric disorders, in particular by increasing, integrating, and disseminating knowledge of the relationships between brain function and human behaviour through open learned meetings.	Thank you for your comments.

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				Our members have considerable expertise in the management of this condition, and we have canvassed opinion from our Committee to provide commentary on the document. We hope you find the attached commentary on specific sections of the guidance helpful, which is focused on improving the quality of care and patient experience for this highly disabling condition.	
British Neuropsychiatric Association	Guideline	005	006	"Use a person-centred approach". [We would suggest the addition of the wording "incorporating a biological, psychological, and social model of care" about here], "to assess people's needs", as is common in all neurological, neuropsychiatric and psychiatric disorders (e.g. Epilepsy, stroke, multiple sclerosis, Parkinson's, Huntington's schizophrenia, obsessive-compulsive disorder).	Thank you for your comment. This recommendation refers to involving people in their own care not models of care. For this reason your suggestion has not been added.
British Neuropsychiatric Association	Guideline	008	017	Box 1. 'Dyslexia' is a term that is a specific psychiatric diagnosis equivalent to a reading disability. 'Dyscalculia' again relates to a specific learning disability, or damage sustained from a brain (parietal lobe) injury. There is no recognised term for "temporary dyslexia or dyscalculia" within the medical literature. The working understanding is that extreme fatigue impairs attentional processes that result in problems reading, speaking, or performing higher-order cognitive tasks such as calculation. We would suggest simply stating "impaired activities of daily living e.g. problems with reading or calculation", in order to avoid confusion.	Thank you for your comment. This has been edited to,' including problems finding words or numbers, difficulty in speaking'.
British Neuropsychiatric Association	Guideline	011	013 - 018	Given there is no known cause for this condition, we would suggest that the standard approach to medicine (full history, symptoms, physical and mental health) is necessary. We would point out that in such circumstances an individual	Thank you for your comment.

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				patient formulation becomes more important - incorporating potential predisposing, precipitating (e.g. trigger by a virus), and identification of factors pertinent to therapy - even more important than in other areas of medicine. This goes on to inform the management plan. We suggest inclusion of this point in the guidance.	After considering stakeholder comments about the assessment the recommendation was edited to,' If ME/CFS is suspected, carry out: • a medical assessment (including relevant symptoms and history, comorbidities, overall physical and mental health) • a physical examination • an assessment of the impact of symptoms on psychological and social wellbeing assessment • baseline investigations to exclude other diagnoses, (for example (but and not limited to)….' The committee have now included examples of investigations that might be carried out and include those you mention. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. The committee discussed the inclusion of triggering events but decided not to include reference to this as it is not clear what causes ME/CFS and the inclusion of any examples of triggers may be taken as an absolute list. The context section notes that in many cases, symptoms are thought to be triggered by an infection.
British Neuropsychiatric Association	Guideline	017	011 - 012	We recognise the need to be understanding of the complex interplay of a parent caring for a child with a disabling condition, especially when that condition is poorly understood. We feel the statement, however, to be too vague. The physical symptoms still need to have a biological plausibility to them. For instance, a patient suddenly going blind would not be consistent with the condition. There is a risk that this reads as if all symptoms should be recognised as linked to chronic fatigue. We would appreciate it if the panel thought to	Thank you for your comment. The importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families.

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				operationalise this further, as it may otherwise affect clinical management (for instance justifying unnecessary investigations, or even worse, unnecessary treatments).	Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The NICE guidelines on child maltreatment and child abuse and neglect should be followed. This is clear that if a professional has concerns they should be addressed in the same way as with any person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
British Neuropsychiatric Association	Guideline	017	017 - 018	Again, we feel that this comment warrants further clarity. It is clearly important that parents support their children, and that we take a flexible approach to care that does not place children under duress. Similarly, it is important that healthcare professionals have access to the child, in whatever agreed format is deemed acceptable in order to provide the best care available. This sentence runs the risk of unquantified amounts of time where a healthcare worker may be unable to speak to the child patient.	Thank you for your comment. The importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The principle applies to adults. This is clear that if a professional has concerns they should be addressed in the same way as with any person. Recognising that this can be compounded by the risk of symptoms being

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					misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
British Neuropsychiatric Association	Guideline	017	019	Non-attendance at school would be deemed somewhat of an emergency, and would be an indication for specialist services involvements, if not already involved in the care of the child. We would advise this be made explicit in the document. We would hope that such a comment would be helpful in escalating concerns about the child should they not be receiving adequate help and support.	Thank you for your comment. These recommendations are to raise awareness about the difficulties that some children and young people and their families have experienced when safeguarding concerns have been raised. The section of the guideline on supporting people with ME/CFS in work, education and training has further detail on providing support for children and young people at school.
British Neuropsychiatric Association	Guideline	020	001	There is no mention of Lasting Power of Attorney in this section. For instance, if a patient is admitted to hospital, how might they continue to deal with existing obligations such as bills etc…	Thank you for your comment. After considering the stakeholder comments the committee have added that the points listed are a minimum, taking into account that an assessment should be personalised and for this reason no other examples have been added.
British Neuropsychiatric Association	Guideline	025	003	We very much agree that deconditioning is not a cause of ME/CFS. However, as this document is intended in part to inform those less familiar ME/CFS, we feel some acknowledgement that deconditioning is often present as a result of prolonged (understandable) inactivity should be mentioned here, as it would be for any disorder such as stroke, brain injury or multiple sclerosis. This is pertinent to management, and is in line with other comments in the document about the risk of further muscle loss or contractures.	Thank you for your comment. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.
British Neuropsychiatric Association	Guideline	030	006	We wonder what the panel means by 'neurally-mediated hypotension' and the evidence for this in this condition. We feel the paragraph warrants greater explanation, and an underlying clarity on the referenced source of this view and data supporting it.	Thank you for your comment. After considering the stakeholder comments this has been deleted.

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British Neuropsychiatric Association	Guideline	034	016 - 018	We have significant concerns that this comment is in a NICE guidance document, and is not pertinent to CBT used for other medical conditions (e.g. CBT for cancers or neurological conditions such as Parkinson's disease). This reads as if referencing personal grievance against healthcare professionals who may perhaps be less familiar with the condition. We suggest a less emotive approach may be achieved with the following: "is a method designed to help the individual develop understanding in the manner that their physiology, thoughts, feelings, and behaviour may have a contributory role to their level of disability." However, we do agree, that in line with modern CBT principles, you do not need to assume that everything (or indeed anything) is 'abnormal', in therapy and completely normal coping responses (like avoidant coping) and cognitions ("I'm a failure") can still be a cause of disability when they end up as important components in cycles of maintenance for a particular problem. CBT is agnostic to what gets identified as 'abnormal' (it attempts to use the patient's own label) and it has moved away from the early Beck focus on 'irrational' beliefs to a focus on **'unhelpful'** beliefs.	Thank you for your comment. The committee agreed that it would not be correct to suggest a causative role between a person's thoughts or beliefs and their development of ME/CFS, but recognised that thoughts, feelings, behaviours and physiology interact with each other, in line with modern CBT principles. Thus CBT, as described here, aims to support people with ME/CFS to adapt to and manage the impact of symptoms of ME/CFS. This is consistent with your comment, but does not allow the interpretation that ME/CFS is caused by a person's illness beliefs, abnormal or otherwise.
British Neuropsychiatric Association	Guideline	051	022 - 026	In relation to a suggestion that the criteria should be amended by the duration of fatigue to three months to meet caseness for disorder, we ask the committee for justification on such a decision. Specifically, what is known of the percentage of those who might meet ME/CFS at three months, who no longer, meet criteria at six months? Given NICE guidance should follow robust evidence, we feel information needs to be explicit to justify such a change. Additionally, it is unclear how such recommendations tie into earlier comments about mild, moderate, and severe symptoms.	Thank you for your comment. After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. See evidence review D-diagnosis for the evidence and committee discussion on the diagnostic criteria.

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British Neuropsychiatric Association	Guideline	052	011 - 024	Fatigue is a common symptom within a range of neurological, and neuropsychiatric disorders. It has been studied and investigated in a large number of conditions without reliable replication of a severity tool that satisfactorily/accurately reflects real-world (also referred to as ecologically valid) measures of severity. This is part-related to the subjective component of fatigue, akin to the subjective nature of pain. This does not in any way imply that the experience is "made up, or all in the head". Whilst a range of measures of fatiguability are used in the research setting, and should continue to be investigated and developed, we would emphasise equal understanding needs to go into how these measures impact on social and occupational functioning. Our rationale for this is that this is clearly what our patients tell us to be the most disabling aspects of living with ME/CFS.	Thank you for your comment and information.
British Neuropsychiatric Association	Guideline	054	008 - 012	We agree home visits provide useful information in patient management. Given the significant duress, travel can impose in this condition, we would suggest the committee consider additional mention of teleconferencing. Our view is that this is clearly not suitable for initial contact but may be suitable for some (although not all) follow-up contacts, especially in the earlier stages when fatigue may be more marked.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
British Neuropsychiatric Association	Guideline	059	001 - 009	It is our view that navigating secondary care services often proves more difficult for patients (once they have received a diagnosis) than primary care. We wonder about the committee's views on recommending, where possible, a single	Thank you for your comment. In the multidisciplinary care includes a recommendation that people with ME/CFS have a named contact to coordinate their

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				physician in secondary care, in addition to a single physician in primary care, to help navigate the different health care professions in this area, especially in those with significant comorbidity.	management plan, help them access services and support them during periods of relapse (Evidence review I).
British Neuropsychiatric Association	Guideline	064	017 - 022	We ask the committee for the evidence of outcomes in those who may have received treatment for orthostatic intolerance. We feel it is important to differentiate any suggestions that such services may be preferred by ME/CFS sufferers from evidence for efficacy. In other words, we feel inclusion of this recommendation should only be justified if there is a sufficient level of evidence on (1) definition of this range of syndromes, and (2) efficacy of treatment.	Thank you for your comment. The recommendation on referral is not about preference of services but about ensuring that the most appropriate care is accessed if symptoms related to orthostatic intolerance are severe or worsening, or there are concerns that another condition may be the cause. The importance of seeking advice from an appropriate specialist is highlighted throughout the guideline.
British Neuropsychiatric Association	Guideline	065	008 - 014	We welcome this inclusion of an evidence base for the management of pain which as mentioned above has some similarities in terms of a subjective symptom. It is notable that the NICE guidance on chronic pain has, in our view very appropriately, a biopsychosocial approach at its heart, and psychological therapies are recommended as part of treatment in view of this.	Thank you for this comment.
British Neuropsychiatric Association	Guideline	068	015 - 017	Our understanding is that this document is intended to inform clinicians, and sufferers of ME/CFS. Given this, we feel it would be helpful to comment on what the committee means by benefits and harm. Such information may serve to forewarn individuals, should they be involved in patients who start to develop stated evidence of such harms.	Thank you for your comment. This is the short rationale for the recommendation. The recommendations link to Evidence review G and H provides detail on the evidence and the committee discussion, these includes the benefits and harms.
British Society of Rehabilitation Medicine	Evidence Review D		8-59	Diagnostic criteria We have concerns about the diagnosis of chronic fatigue syndrome, and we question the wisdom of straying from the evidence used by the guideline group concerning the	Thank you for your comment.

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				diagnosis. The concerns are as follows: A. The paper by Rowe et al (2017) highlights the range of symptoms that have been considered central by some people, and not included by other people. B. The choice to use this particular set of criteria suggests that there is a 'correct' and 'definitive' way to reach a diagnosis that is separate from all other conditions. C. The evidence review has therefore discounted research based on earlier sets of criteria as if the researchers were researching some completely different phenomenon. D. The list of "possible conditions which might be considered" (as differential diagnoses) on page 57-58 overlooks the most important, and difficult ones: chronic pain syndrome, fibromyalgia, functional neurological disorders and others, all being common, having a very similar early stage, and sharing most if not all symptoms.	Evidence review D-diagnosis reviews the seven diagnostic criteria for adults and two diagnostic criteria for children and young people that met the inclusion criteria set out in the protocol, these are criteria that are commonly recognised in the clinical practice of ME/CFS. It is commonly acknowledged that there is ongoing discussion in the ME/CFS community about which diagnostic criteria should be used to diagnose ME/CFS. If there was an agreed set of criteria there would be no need for the committee to have addressed this question. The committee recognised this guideline adds another set of consensus criteria to the literature but noted the evidence calling for clarity over diagnostic criteria (see Evidence review B:Information and Support for health and social care professionals) and agreed that it was important to have a set of criteria that is informative and enables health and social care professionals to recognise ME/CFS. The committee made a consensus decision based on their interpretation of the evidence review comparing the criteria that the IOM 2015 criteria were a useful set of criteria, having advantages over other criteria in terms of usability and an optimum balance of inclusion/exclusion criterion. Recognising that their recommended criteria are untested and this is an absence of validated diagnostic criteria they made a research recommendation to develop validated criteria. *Discounted research* All NICE guidelines follow the process for evidence synthesis as set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis

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					before the data is collected. Accordingly, no study has been excluded that met the review protocols. This point about discounted research we think refers to the decision by the committee to downgrade evidence that did not use a diagnostic criteria that includes post exertional malaise (PEM) as essential. PEM is widely acknowledged in ME/CFS specialist practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just do not know how many if the information is not reported. Where this is the case, the trial population could include people that do not have ME/CFS and this makes it difficult for the committee to be confident of the benefits and risks of the interventions on people with ME/CFS. Using GRADE and CERQual the committee agreed that evidence without this information would be 'indirect' (relevance in CERQual) acknowledging this uncertainty about the population. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and CERQual. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative and qualitative evidence and the application of indirectness and relevance. As part of this they agreed that any evidence with a

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					population ≥ 95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) *Differential diagnosis* Other chronic pain disorders, including fibromyalgia is included in the list. After considering the stakeholder comments the committee agreed to edit this section of the discussion to add clarity to the conditions that are commonly co-existing or result in a differential diagnosis in people with ME/CFS. The committee note that exhaustive lists are not possible and these are examples.
British Society of Rehabilitation Medicine	Guideline	General	General	We welcome the guideline's emphasis upon being centred on the patient's needs and wishes, and upon promoting the need to be holistic, and we also welcome the emphasis given to listening to and understanding the patient's perspective and experience. We noted that there are aspects of the guideline that are obviously reasonable. They include an emphasis upon: • taking a holistic approach • working with the patient (although the guideline is written as if most people do not work with the patient, which is unlikely to be the case) • explaining the risks and benefits of any particular course of action • tailoring recommendations to the specific needs of the specific patient, including the specific symptoms that are troublesome • involving a multidisciplinary team familiar with the condition	Thank you for your comment. In addition the committee have edited the management plan to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.). This further supports the guideline's emphasis upon being centred on the person's needs and wishes and adopting a holistic approach. The personalised care and support plan supports the person's aims and the management of their health and well-being within the context of their whole life and family situation.

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				- recognising the role for treatments such as cognitive behavioural therapy, gradually increasing the amount of daily activities that an individual undertakes, and the use of medication for mood disturbance - educating the patient (and family if appropriate) about the condition - considering plausible alternative or additional diagnoses The many features mentioned are all central to a rehabilitation approach. We therefore find it surprising that the guideline only mentions rehabilitation once, and then incidentally (1.10.1, bullet 7). We strongly **suggest** that embedding rehabilitation within the guideline will simplify and strengthen the guideline, because the **approach** used by rehabilitation is precisely that being suggested. Only holistic rehabilitation services will have this approach built-in to their clinical practice.	
British Society of Rehabilitation Medicine	Guideline	General	General.	We welcome the guideline's concern with prevention of chronic fatigue syndrome, but we question the incorporation into the guideline of any specific recommendations for several reasons. A. There is no evidence that allows identification of specific individuals who are at high risk of developing chronic fatigue syndrome. B. The number of patients who have some of the features suggested is very large, and indeed it is 'normal' (i.e. expected and seen) to have these symptoms not only after presumed viral illness but after many other acute health events. C. Many of the people with these symptoms are managed well by GPs, rehabilitation services and general services and would overwhelm any more focused service.	Thank you for our comment. The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. For the points you make see Evidence review D-Diagnosis. *Advice for people with suspected ME/CFS* The committee note in the rationale for suspecting ME/CFS that it is the combination and interaction of the symptoms that is critical in distinguishing ME/CFS from other conditions and illness. The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the evidence

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				D. There is no specific evidence on which to base any specific recommendations, other than to note that common rehabilitation interventions – education about the symptoms, and self-management; psychosocial interventions; undertaking physical activity within a person's capability, practising and extending performance with guidance; and a range of specific, interventions tailored to a person's needs – are likely to be helpful. E. The guideline concerns a diagnosis that, according to its own preferred diagnostic criteria (Rowe et al, 2017) requires symptoms to be present for six months. We **suggest** that it is both confusing and outside the scope of this guideline to make any specific recommendations about diagnosis and management before six months. We **recommend** a generic statement that anyone with symptoms similar to those seen in chronic fatigue syndrome for less that six months should be seen as soon as possible in a rehabilitation service or other similarly experienced service for active assessment and management in the hope that it will reduce the risk of developing long-term problems.	and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. The committee recognised that not everyone with suspected ME/CFS will have a diagnosis of ME/CS and that the advice recommended at 4 and 6 weeks (for the next 8 and 6 weeks) would not be detrimental to people who are then not diagnosed with ME/CFS. Diagnosis is now clarified in the guideline at 3 months with referral to ME/CFS specialist services for confirmation of the diagnosis and development of a care and support plan.
British Society of Rehabilitation Medicine	Guideline	General	General	We have concerns about the guideline's approach to diagnosis, and its loosening of diagnostic criteria which were derived for an extensive review. There are several concerns: A. As noted above, the guideline has selected to base diagnosis upon one set of criteria (out of many possible sets of criteria), and the criteria require symptoms to be present for at least six months before making the diagnosis. B. If this is a guideline on the diagnosis and management of chronic fatigue syndrome, then it should be bound by the evidence it chose to use, and **not** give any advice concerning any aspect of diagnosis or management prior to that. C. The guideline, as presented, has three major sections	Thank you for our comment. The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. For the points you make see Evidence review D-Diagnosis. *Advice for people with suspected ME/CFS* The committee note in the rationale for suspecting ME/CFS that it is the combination and interaction of the symptoms that is

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				(principle of care, suspecting the condition, and managing the suspected condition) before making a diagnosis. Clinical practice starts with making the diagnosis, and a clinical guideline should do the same. We suggest that the guideline should restrict itself to its own definition of the diagnosis. As soon as the guidelines strays outside this, it needs to recognise that there are very many patients who have the same set of symptoms who get better, or, if they do not get better, are often diagnosed with a functional disorder such as a functional neurological disorder, chronic spinal pain, and fibromyalgia. It also needs to consider a very much broader range of evidence.	critical in distinguishing ME/CFS from other conditions and illness. The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. The committee agreed this should be a separate section of the guideline to avoid confusion with the management of ME/CFS. The committee recognised that not everyone with suspected ME/CFS will have a diagnosis of ME/CS and that the advice recommended at 4 and 6 weeks (for the next 8 and 6 weeks) would not be detrimental to people who are then not diagnosed with ME/CFS. Diagnosis is now clarified in the guideline at 3 months with referral to ME/CFS specialist services for confirmation of the diagnosis and development of a care and support plan.
British Society of Rehabilitation Medicine	Guideline	General	General	The BSRM is concerned at the large number of recommendations made without any supporting evidence. They are presumably based on the opinions of committee members, and the invited experts. These opinions do not constitute evidence, and (as in all other areas of medicine and guidelines), opinions are subject of bias from many causes. The BSRM feels that a national document should base recommendations on published evidence of an appropriate quality, and it should otherwise admit that there is insufficient evidence. The BSRM is also concerned that evidence for the benefit of exercise has been downgraded inappropriately because: 1. It is not possible to use the same methodology for rehabilitation interventions as is used for drug trials. The intervention needs to be personalised, the	Thank you for our comment. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that

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				important outcomes are by definition subjective and it is never possible to be truly double blind 2. Results from trials of exercise in closely linked conditions, and in this condition before syndromic criteria were changed in 2015, were discounted Note was taken only of the longest follow up data available. Many patients will have changed their behaviour by then and groups will have become contaminated and converged.	were identified as underrepresented in the literature. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). *Methodology* Developing NICE guidelines: the manual. Chapter 4 *Developing review questions and planning the evidence review* addresses the topic about approaches to take when considering the design of studies to be included in a systematic review. In summary the effectiveness of an intervention is usually best answered by a RCT because a well-conducted RCT is most likely to give an unbiased estimate of effects. Where such evidence is not available (for example, where interventions it can be difficult or unethical to assign populations to control and intervention groups). In such cases, a non-randomised controlled trial might be a more appropriate way of assessing association or possible cause and effect. The Medical Research Council (MRC) has produced guidance on evaluating complex interventions (Craig et al. 2008) and using natural experiments to evaluate health interventions delivered at population level (Craig et al. 2011).

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					When developing the protocols for the intervention reviews, a RCT was agreed to be the most appropriate study design to evaluate clinical effectiveness. This was informed by the committee's knowledge that there was a body of RCT evidence in this area. In recognition that the views of people with ME/CFS who had experienced the interventions was important a qualitative review was done with an accompanying call for evidence to identify any unpublished evidence. Risk of bias was assessed using Randomised Controlled Trial: Cochrane RoB (2.0) in the studies and then using GRADE in evaluating the quality of the evidence (as described in Developing NICE guidelines: the manual.) We agree that there are difficulties in blinding in some trials and the result of this is a risk of bias. The role of the committee is then to discuss this limitation and the impact it has on the results and then in turn on the making any recommendations about practice. As noted above the decision making for developing recommendations is multifaceted and complex. *Downgrading and indirectness* This point about discounted trials on exercise we think refers to the decision by the committee to downgrade evidence that did not use a diagnostic criteria that includes post exertional malaise (PEM) as essential. PEM is widely acknowledged in ME/CFS specialist practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100%

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					ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just do not know how many if the information is not reported. Where this is the case, the trial population could include people that do not have ME/CFS and this makes it difficult for the committee to be confident of the benefits and risks of the interventions on people with ME/CFS. Using GRADE and CERQual the committee agreed that evidence without this information would be 'indirect' (relevance in CERQual) acknowledging this uncertainty about the population. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and CERQual. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative and qualitative evidence and the application of indirectness and relevance. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) *Follow- up data* Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for

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					ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.
British Society of Rehabilitation Medicine	Guideline	General	General	We have every sympathy with patients who feel they have been disbelieved, or treated in a rigid and unyielding way, or not offered the support they need. We understand that this no doubt is the experience of some patients with chronic fatigue syndrome. Similar comments are made by patients with many other conditions such as people whose diagnosis of cancer is delayed, people who develop Parkinson's disease, and people with multiple sclerosis. Rehabilitation clinicians see many disabled patients who recount similar stories, usually very believable. We feel the guideline is much more likely to improve care if it is written in a positive manner that values all that is good, validating the efforts that almost all clinical teams make. We feel that the current guideline will be rejected by many clinical readers, in that they will simply not read it when faced with many statements that can only be interpreted as being critical. Very similar feelings were expressed in a national audit of services for people with multiple sclerosis, but the guideline does not present such a critical tone.	Thank you for your comment. The evidence reviews and the discussion sections summarise and reflect the evidence and the committee agree that some of this evidence, in particular Evidence review A and the commissioned reports (Appendices 1 and 2), is challenging. However challenging and uncomfortable it is, it is important that this evidence is heard and considered when making the recommendations. Please see comment 228 for a summary of decision making. The committee note that the evidence highlights that disbelief and prejudice was common where health and social care professionals lacked knowledge and did not understand ME/CFS. It was much less reported in specialist services. The training section of the guideline addresses this recommending that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline (see evidence review B).
British Society of Rehabilitation Medicine	Guideline	General	General	We accept fully that services for patients with chronic fatigue syndrome are not optimal, either in the number of patients that can be managed or in the quality of services, and this is the implication of many of the statements. However, it must be	Thank you for your comments. The population for this guideline is people with suspected or diagnosed ME/CFS and the guideline has no remit to make

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				recognised that identical comments are made by people with many other conditions. Patients routinely feel that they have been deserted by healthcare by six months after their stroke, and many published qualitative studies record similar perceptions in most long-term disabling conditions. There is nothing exceptional about the implied observation that there are insufficient resources to provide either healthcare or social care and support for patients with chronic fatigue syndrome. Rehabilitation services are faced with this problem many times each day. We are therefore concerned that many of the statements and recommendations imply that patients with chronic fatigue syndrome should have a quality of service that exceeds that available for the very many other patients in a similar situation with, for example, Huntington's disease, stroke, spinal cord injury, most childhood disorders where someone survives into adulthood, chronic mental health problems and so on. The guideline is implying a discrimination in favour of one group at the expense of all others, and this is not acceptable in a national guideline. Patient groups can and do campaign for better treatment for their disorder; and national guideline should not imply that one group gets preferential treatment.	recommendations for other conditions. The guideline reflects the evidence for best practice for people with ME/CFS, accordingly, the committee have made recommendations about appropriate care for people with ME/CFS. The committee note that much of the guideline reflects care that anyone with a long-term condition should be able to access and has not always been available to people with ME/CFS. The aim of NICE guidance is to provide advice to improve health and social care and to reduce inequity in the access and provision of services and not to accept where services are suboptimal.
British Society of Rehabilitation Medicine	Guideline	001	5	We note the change in the title from 2007, to give preference to Myalgic Encephalomyelitis, a change that we consider unwise. (a) The term, chronic fatigue syndrome is the term used in the majority of research, (b) the term, chronic fatigue syndrome is a much better reflection of the uncertainty around and difficulty in determining a precise diagnosis, (c) the term, myalgic encephalomyelitis suggests a specific pathology, for	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context

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				with there is no evidence – Rowe et al, 2017 say "The aetiolgy has not been established." as their second sentence. We recommend retaining chronic fatigue syndrome as the diagnostic term, to avoid generating additional fears in patients who might, reasonably, conclude that they had a diffuse disease of the brain and spinal cord.	section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'*
British Society of Rehabilitation Medicine	Guideline	004	5	(1.1.1 first bullet) The word, medical, should be removed. It does not clarify anything, as there is no obvious contrast; a healthcare guideline would not be written about a non-medical condition. We are concerned that it is implying that there is some specific biological abnormality, for which there is as yet no evidence. Furthermore, stating that it is "affecting" multiple body systems is again not supported by evidence. What is true is that symptoms that might be attributed to disturbance in multiple body systems occur. We suggest it would be better to state that it is "a complex and chronic condition liable to relapses and remissions where both the factors causing it and the pathophysiological mechanisms underlying it are unknown."	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change the terms used. The committee agree the pathophysiology of ME/CFS is an ongoing area of investigation and have edited the bullet point to reflect this.
British Society of Rehabilitation Medicine	Guideline	004	10	In this part of the guidance, there is no justification for picking out the severe form. It would be more important, if something is to be said, to emphasise that for many people it is relatively minor, short lived, and not necessarily liable to recurrence. It would be better to finish the point at the word, severity. This is an example of the lack of balance and sense of proportion in the guideline.	Thank you for your comment. The committee agreed that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes.. Taking into account the range of comments from stakeholders about the importance of representation for all

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					people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS. In the 'information about ME/CFS' section of the guideline the variation in long-term outlook is highlighted and includes that a proportion of people recover.
British Society of Rehabilitation Medicine	Guideline	004	13	It is unnecessary to specify the range, and again is emphasising severe debility (not debilitation) and ignoring the fact that some people can live normally for much of the time. This statement should end at the word, longer.	Thank you for your comment. The committee agreed that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes.. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS.
British Society of Rehabilitation Medicine	Guideline	005	9-11	This statement is, on one level, self-evidently good. **But**, the definition states that it cannot be diagnosed until six months so, by definition, an 'early and accurate diagnosis' is simply not possible. Everything that flows on from this is invalid.	Thank you for your comment. After considering the stakeholder comments the committee have replaced 'early' with 'timely' and hopes this adds clarity.
British Society of Rehabilitation Medicine	Guideline	005	2	This statement, and many others which we will not comment on individually, is a generic statement of good clinical practice. Every rehabilitation service would use this approach and, as it is central to advice from the General Medical Council and, no doubt, many other professional regulatory bodies, it seems unnecessary to say it. It simply adds to an impression that all clinical readers are being criticised, as it is stating the obvious.	Thank you for your comment. The committee agree this is good clinical practice. This recommendation is supported by the evidence. Lack of belief in ME/CFS and understanding about the impact of their symptoms was reported by people with ME/CFS in Evidence review A, Appendices 1 and 2 and supported by the committee's experience.

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British Society of Rehabilitation Medicine	Guideline	005	27	This is an example of a statement likely to upset any person working with children, because it is central to the philosophy of paediatric care.	Thank you for your comment. The aim of the recommendation was to raise awareness that children and young people with ME/CFS have experienced prejudice and stigma and is based on the evidence identified in the Evidence reviews A and C and the committee's experience.
British Society of Rehabilitation Medicine	Guideline	006	8	It is not clear what the point of this series of statements (and other similar statements elsewhere) is. It seems more appropriate for a textbook on chronic fatigue syndrome.	Thank you for your comment. This section highlights the difficulties that people with severe or very severe ME/CFS may have and is supported by Appendix 2, Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these difficulties and the support that may be needed to live. Taking into account the range of stakeholder comments about the location in the guideline of this section the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. In response to your comment this now means that the criteria for suspecting and diagnosing ME/CFS precedes this recommendation providing clarity about the symptoms that are related to a diagnosis of ME/CFS.
British Society of Rehabilitation Medicine	Guideline	007	17-21	This statement is an example of requesting exceptional treatment because of the diagnosis. Every single person receiving personal care and support, for whatever reason, would like this, stating it in official national guidance risks placing commissioners and providers in an invidious position. Do they act ethically, and continue to give everyone with equal need and equal priority, risking criticism for failing to adhere to a national guideline, or do they capitulate and knowingly discriminate in favour of one group simply on account of their diagnostic label, thereby infringing the equality and diversity discrimination action?	Thank you for your comment. This recommendation reflects good practice for all people accessing health and social care services. See NICE guideline on Patient experience in adult NHS services: improving the experience of care for people using adult NHS services.

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British Society of Rehabilitation Medicine	Guideline	008	1	While we fully understand why this might have been included, the logical and practical difficulties are such that this section should be removed – as we have made clear in a general comment. We have suggested a general recommendation that anyone who has persisting problems that are attributed by the patient, to an acute illness or other event should be referred to a rehabilitation service if the patient is not recovering spontaneously and at an expected rate.	Thank you for your comment. We think you refer to removing the section om suspecting ME/CFS. This was identified by stakeholders as an important area to review and provide advice on in the guideline. The evidence for the diagnostic criteria in the guideline and times to diagnosis and referral is set out in Evidence review D_Diagnosis. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters.
British Society of Rehabilitation Medicine	Guideline	009	17	We have already stressed our concern about making a diagnosis at a time when it cannot be made, by definition. We have grave concerns that this statement, for which there is no evidence, will lead to a self-fulfilling prophesy particularly if the patient reads this guideline with its emphasis upon the severity and incurability of the condition.	Thank you for your comment. This recommendation was to ensure that clinicians were alerted to the possibility of ME/CFS as soon as possible. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. See Evidence review D- for the evidence and committee discussion. However after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted for the following reasons: ○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months.

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					○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis
British Society of Rehabilitation Medicine	Guideline	010	18	We are uncertain about what is being said here, but if it refers to avoiding the so-called "Boom and Bust" approach to activity, then we agree with the underlying idea but are worried about the terminology used. Although several of our members have found the clinical term, 'energy envelope' useful, it is nebulous. It is not derived from any scientific theory and not based on any evidence. We think that this phrase and the many statements associated with it and its derivative is trying to make the following points: • it is unwise for anyone to increase, suddenly and without preparation, the amount of activity (usually but not necessarily involving exercise) they undertake by two or more times because, in anyone including people with chronic fatigue syndrome, the person will be more tired afterwards and will often experience other symptoms. It is a normal phenomenon. • any increase in activity should be planned, and done in small increments, expecting to feel that more has been done but not excessively. The size of the increment and the rate of change, needs to be agreed between the patients and his or her clinical advisor. One approach is to increase the minimum level of activity undertaken over a 24 hour period, rather than to aim to increase the maximum amount. • the effect of any increase needs to be evaluated by the patient and clinician at an agreed point.	Thank you for your comment. After considering the stakeholder comments the committee agreed that this concept and energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on PEM and energy limits* may not be helpful. At such keeping a diary at this stage may not be appropriate. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits.

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				We think this is what is being said, albeit in a series of unconnected statement scattered around, and it is an approach we would support wholeheartedly, given the evidence for the effectiveness of this approach in many conditions. It appears to be vital for the patient to establish some control of their symptoms and not be subject to frequent worsening.	
British Society of Rehabilitation Medicine	Guideline	011	5	This is making a diagnosis outside the agreed diagnostic criteria used by this guideline. No evidence is given to support this statement which does not acknowledge or discuss the fact that people with fibromyalgia and chronic spinal pain will also be captured,	Thank you for your comment. In summary based on the evidence and the committee's clinical experience, they agreed the four criteria for the diagnosis of ME/CFS were fatigue, post-exertional malaise, unrefreshing sleep and sleep disturbance (or both), and cognitive difficulties. Key to the diagnosis of ME/CFS is the presence and combination of the four symptoms. Pain may be associated but is not exclusive to with ME/CFS, this was supported by the IOM diagnostic criteria (2015). The committee note that pain is the dominant symptom in fibromyalgia and in chronic spinal pain as such the two populations are differentiated.
British Society of Rehabilitation Medicine	Guideline	011	7	This suggests referring **every** patient, and we doubt this is sensible. Many patients are managed successfully by GPs or existing services, and they will be de-skilled if this recommendation is followed. It will also lead to a much higher workload for services that are already insufficient, further reducing their ability to help patients with more needs. It should be qualified.	Thank you for your comment. Based on the evidence (Evidence reviews A.B,C,D and I) and the committee's experience referral to ME/CFS specialist care was recommended for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. ME/CFS specialist teams where seen as the most appropriate place for people with ME/CFS to access support with GPs providing ongoing support and review. In reference to your point the committee acknowledged that non-specialists may not feel confident in diagnosing ME/CFS and recommended that people with suspected ME/CFS are referred

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					to a ME/CFS specialist service for confirmation of the diagnosis (Evidence review B). **The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.**
British Society of Rehabilitation Medicine	Guideline	011	13	The BSRM notes the frequent reference to "a specialist ME/CFS team". The BSRM is fully supportive of patients with complex or difficult problems being seen by a team that has the experience and expertise to assess, advise and if needed manage the patient's needs. The BSRM has significant concerns about reference to 'a specialist ME/CFS team' which carries two implications. First, that the team only sees patients with ME/CFS and will not see any other patients, however much the needs of other patients might overlap. Second, that patients with chronic fatigue syndrome should only be seen in a labelled specialist team. Our concerns are clinical and practical. The practical concern, which is not trivial, is that there are currently few Specialist ME/CFS teams that are truly multi-disciplinary. There may be many small 'teams' of 2-3 physiotherapists and/or occupational therapists, but the number of patients that would need to be seen if this guideline were acted on would greatly exceed capacity. Coupled to this is a very pertinent and practical concern about proliferation of	Thank you for your comment. Based on the evidence (Evidence reviews A.B,C,D and I) and the committee's experience referral to ME/CFS specialist care was recommended for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. ME/CFS specialist teams where seen as the most appropriate place for people with ME/CFS to access support with GPs providing ongoing support and review. The committee acknowledged that non-specialists may not feel confident in diagnosing ME/CFS and recommended that people with suspected ME/CFS are referred to a ME/CFS specialist service for confirmation of the diagnosis (Evidence review B). The committee does not think that being part of an ME/CFS specialist team necessarily precludes them from also working with patients who have other conditions as well, especially if this makes services more viable. However, they have concluded that it is essential that ME/CFS patients are cared for by staff with experience of the disease, since their care needs are so different to other patients, particularly with respect to exercise and activity.

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				specialist teams for long-term conditions. They are suggested or campaigned for to see people with: stroke, multiple sclerosis, post-Covid syndrome, traumatic brain injury, chronic pain etc etc. The core expertise needed across all these conditions is shared. The proliferation of teams will make each one too small to accumulate expertise, survive one or two people leaving, manage fluctuations in demand, etc. The consequence of this implied recommendation would simply be a general deterioration of all services as the same number of rehabilitation experts are split up into smaller and smaller teams. At the same time, the focus on single, narrowly defined conditions will lead to more people not being able to access a service that could meet all their needs because they have not been given the 'correct' or necessary label. This is already a major problem. The clinical concern is that the term specialist is being misused. The important point is not that a team only sees patients with the condition; the important point is that they have the knowledge and skills required to assess, advise and manage the person. This need only be one or two particular people, who can support other team members. A third concern is that general services that are offering thoroughly appropriate services to patients with CFS/ME will no longer be viewed as compliant because they are not 'Specialist'. Therefore, the BSRM recommends a more nuanced approach, referring to services that have the appropriate knowledge and skills within the team.	The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I-Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.

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British Society of Rehabilitation Medicine	Guideline	011	15	This recommendation is directed at a 'specialist team'. Two points arise. First, we would support the processes recommended as a rehabilitation service offering a holistic approach. We do note, however, that the list of items to be covered is incomplete and misses some important areas such as: • the patient's wishes, expectations and beliefs • the patient's core values and "life purpose" (i.e. what aspects of their life are important and what their lifetime aspirations are) • factors that may have precipitated or made them vulnerable to the illness • factors that may be exacerbating, maintaining or perpetuating the illness together with relevant protective factors • information that indicates potential risk or need for safeguarding • their emotional state • their past medical history, and illness experiences. Second, this recommendation suggests that a 'specialist team' will not know what to do, which is perhaps not the best way to encourage clinicians to pay attention to this guideline. If you are in fact aiming this at, for example, commissioners then it should be rephrased, e.g. "Commissioners should ensure that a holistc assessment is carried out covering …."	Thank you for your comment. These are the minimum areas to be considered in the assessment the list is not meant to be exhaustive and does not exclude the areas you have mentioned. While it's recognised that clinicians working in this area are likely to be carrying out this sort of assessment there is variation in the access to services and it was important to set this out in the guideline so as to ensure good quality care. As you note this is important information to commissioners when planning services.
British Society of Rehabilitation Medicine	Guideline	012	10	We would like to comment on something that is **absent** but should start on line 10. In every health encounter in any service for any condition, the important step after history and examination is to **formulate** the situation. In acute situations, this is usually just a disease diagnosis, but in every long-term condition it is far more. It is developing a shared understanding	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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				with the patient how various factors interact and contribute to the problems faced. It is the start of a process coming to an agreed management plan. At present it reads as if the clinician develops a plan which is then discussed, without any explanation as to how she or he has arrived at the suggested plan. It is a vital stage in any rehabilitation plan for any person with a complex long-term condition, and should be part of any patient-centred, holistic service. We strongly recommend adding this stage. It might also help the guideline group to have a rehabilitation expert to advise on normal rehabilitation practice and how it can help patients.	The plan is developed in collaboration with the person with ME/CFS and explores their aims and the management of their health and well-being within the context of their whole life and family situation. It should be proportionate, flexible and coordinated and adaptable to a person's health condition, situation and care and support needs. The committee composition was agreed during the scoping phase as appropriate for the expertise for the guideline scope. Great care was taken to ensure the committees was formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. The committee membership does reflect the multidisciplinary approach to treating ME/CFS and includes medically qualified clinicians and allied health professionals who lead and work in specialist ME/CFS services.
British Society of Rehabilitation Medicine	Guideline	013	1	We agree that the patient's goals play a major role, and that the clinical team should establish them and check them over time. Identification and setting of goals is a central rehabilitation skill, and it is axiomatic that all actions should be concordant with their overall goals. However, this section misses some important aspects of rehabilitation planning: • practical considerations must be considered in any plan; it is not fair to the patient to develop an ideal plan that cannot be delivered, and often in current circumstances less than ideal plans are devised for almost all patients with long-term disability. The role of the clinical team under these circumstances is to balance what should be done with what can be done, and to support the patient with this.	Thank you for comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.). In line with this the bullet points have been deleted as this is reflected in the aims of a care and support plan. The personalised care and support plan is based on the person's needs and includes the areas listed. The plan is developed in collaboration with the person with ME/CFS and explores their aims *and the management of their health and well-being within the context of their whole life and family situation. It should be proportionate, flexible and coordinated and adaptable to a person's health condition, situation and care and support needs.*

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				helping the patient re-establish control. The goal of most rehabilitation is to maximise a patient's autonomy, their ability to make choices and to exercise control. Having autonomy and control infers taking on again their roles and responsibilities. This may have to be re-learned, and part of planning management with a patient is to help them re-establish control over their life.	
British Society of Rehabilitation Medicine	Guideline	014	15	We believe that this series of statements is unnecessarily nihilistic. As an example, no guideline on spinal cord injury would recommend explaining that the person will never regain movement, or sensation, and would always be incontinent etc etc. A rehabilitation approach, which is much more patient-centred than this, would explain that, although no absolute cure is likely, and the future is unpredictable, nevertheless a person can develop a new, meaningful life. We believe that this section should be recast to explain that people with chronic fatigue syndrome can still participate in life, and the focus of rehabilitation is not exclusively aimed at care and support.	Thank you for your comment. After considering the range of stakeholder comments the committee agreed to edit this recommendation to: Explain that ME/CFS: • is a fluctuating medical condition that affects everyone differently, in which symptoms and their severity can change over a day, week or longer • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS • varies widely in its impact on people's lives, and can affect their daily activities, family and social life, and work or education (these impacts maybe severe) • can be worsened by particular triggers – these can be known or new triggers or in some cases there is no clear trigger • can be self-managed with support and advice (see the section on energy management) • can involve flare-ups and relapses even if symptoms are well managed, so planning for these should be part of the energy management plan. The previous section on assessment and care and support planning by a specialist team describes the process of the holistic assessment and development of a personalised care and support plan that underpins management planning in this guideline. The personalised care and support plan is based on

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					the person's needs and includes the areas listed. The plan is developed in collaboration with the person with ME/CFS and explores their aims and the management of their health and well-being within the context of their whole life and family situation. It should be proportionate, flexible and coordinated and adaptable to a person's health condition, situation and care and support needs.
British Society of Rehabilitation Medicine	Guideline	014	19	Is there any epidemiologically sound evidence to support your contention that it is less common to have long periods of remission. Can you point to an inception cohort of patients followed up over time? This is one of many statements for which there is no evidence other than anecdote. Evidence from support societies is necessarily biased, because people who recover will rarely join a support society. People who receive good care and get better rarely publicise it!	Thank you for your comment. After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS.
British Society of Rehabilitation Medicine	Guideline	016	9	We believe that this is a dangerous statement. It is equally if not more serious to contemplate that signs of abuse and neglect are interpreted as being attributable to chronic fatigue syndrome when they are in fact due to abuse. It is a one-sided approach, not recognising that there may be other equally plausible and valid explanations for observations. The statement poses a significant risk to some vulnerable patients.	Thank you for your comment. The importance of this section is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The NICE guidelines on child maltreatment and child abuse and neglect should be followed.

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					This is clear that if a professional has concerns they should be addressed in the same way as with any person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
British Society of Rehabilitation Medicine	Guideline	017	8	Although we are not specialised in paediatric matters, we believe this is another dangerous statement. It will make it very difficult for any professional to suggest that a child is being neglected or abused, particularly if the parent states that their child has chronic fatigue syndrome, a statement that would be difficult to refute. This is a one-sided statement, that does not acknowledge that there are often many potential explanations for observation, and that abuse is one (a new medical condition would be another, and side-effects of drugs might be another). This statement, if left as it stands, risks leaving children who are being abused to continue being abused because, if the parent states that "the guideline in paragraph 1.7.6 says what it says, and that this paragraph explains everything that has been recorded and more besides.", it would be very difficult for any team to continue. Given how much child abuse is already not acted on, partly because of the fear of legal or other forms of 'counter-attack', this statement needs to be removed or heavily qualified with counter-recommendations.	Thank you for your comment. The importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The principle applies to adults. This is clear that if a professional has concerns they should be addressed in the same way as with any person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
British Society of Rehabilitation Medicine	Guideline	017	21	We think that this series of statements suggests that everybody should adapt their service to the wishes and requirements of the patient. WE agree that this is an ideal, or aspiration, that most healthcare services and social services	Thank you for your comment. The committee agree that flexibility in accessing services is important for all people and is best practice (see NICE guidelines on patient experience in adult NHS services).This guideline is

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				would like to do for every patient, and in principle there is no problem with this. Our serious concern is that this recommendation appearing in this national guideline implies that services should favour patients with chronic fatigue syndrome over other people requiring the same services and wanting the same standard of flexibility. If that is how it is interpreted, then it is discriminatory against other people with similar needs and problems arising from other causes. There is no reason given to suggest discrimination is justified, and this is contrary to the spirit of the Equality and Diversity Act.	about people suspected or diagnosed with ME/ CFS and refers to this population and highlights the needs they may have. The committee do not in any way wish to promote the needs of people with ME/CFS over those of patients with equal need. Conversely, the committee are highlighting that these people will have additional needs to those of some other patients. There is evidence from our reviews of qualitative studies that people with severe or very severe ME/CFS often find it difficult to access services. If they are unable to access services due to these disabilities, then that would be contrary to equality legislation. This might be aspirational, but it highlights that reasonable steps should be taken where possible.
British Society of Rehabilitation Medicine	Guideline	018	10	We believe that this is an unnecessary and, to many clinicians, hurtful recommendation. Somebody with chronic fatigue syndrome can always contact the hospital either before the appointment, or after the appointment, to explain that they are not attending, and why or that they did not attend, and why. Furthermore, many clinics either phone or write to the patient. This also seems to be privileging patients with chronic fatigue syndrome above other patients, if it is intended that there should be a greater effort for these people. If this recommendation is left in, then it should be counterbalanced by a recommendation that people with chronic fatigue syndrome should make every effort to keep any appointment made, should cancel an appointment if they cannot make it explaining why, and if necessary phone after missing an appointment. The aim should be effective cooperative shared management of the condition. The guideline needs to recognise that the management of all long-term conditions is a joint responsibility between the	Thank you for your comment. This recommendation is supported by the evidence that people with ME/CFS reported that some health and social care professionals did not understand ME/CFS and difficulties they may sometimes have in attending appointments (see evidence reviews A and C). This was supported by the committee's experience and they agreed that the relationship with health and social care services is collaborative. This recommendation highlighted the difficulties people with ME/CFS have had in accessing services. After considering the range of stakeholder comments the committee edited this recommendation to, 'an appointment' and deleted,' contact the'' to recognise that it is a collaborative relationship between the healthcare professionals and the person with ME/CFS and it could be the person with ME/CFS that contacts the service.

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				patient (and the family, if involved) and the clinical team. Both parties have responsibilities and duties.	
British Society of Rehabilitation Medicine	Guideline	019	1	We feel that this statement, like others, implies that people with chronic fatigue syndrome should have a standard of care above that experienced by anybody else. In every patient there will be some consideration, when there is choice, about where a bed is situated. Accessibility of toilets and washrooms is or should be a central concern in relation to all ward structures, and it is well recognised that lighting, noise and other environmental factors are less than optimal for most patients, but the environment is often inevitable given the nature of acute hospital wards. These are systemic issues within healthcare, and they are common across all conditions.	Thank you for your comment. The committee agree that these considerations are applicable to all people accessing health services and is an example of best practice (see Patient experience in adult NHS services: improving the experience of care for people using adult NHS services).This is a guideline on people with ME/CFS and highlighted here as consideration for people with ME/CFS.
British Society of Rehabilitation Medicine	Guideline	021	1	The BSRM welcomes the attention being given to patients being involved in educational and vocational activities. Nevertheless, we think that this section continues the generally nihilistic attitude of problems being inevitable **and** irresolvable except by not doing things. Many people with identical specific problems (but a different diagnostic label) are helped to manage, and also rehabilitation services can liaise with employers and occupational health service both to minimise the risk of problems and to improve the chance of recovery sufficient to return if necessary. We suggest that this section is re-considered, and written with an emphasise upon facilitating and maintaining work and education, rather than as recommending support in not working or being educated. Such an approach would not only benefit patients, but would contribute (a small amount) towards educating employers, teachers and the public so that they have a better understanding of this common condition.	Thank you for your comment. After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support.

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British Society of Rehabilitation Medicine	Guideline	022	13	The BSRM supports the use of multidisciplinary teams in the assessment and management of people with chronic fatigue syndrome whose needs cannot be met by less well resourced service, such as general practice.	Thank you for your comment.
British Society of Rehabilitation Medicine	Guideline	022	14	The BSRM is slightly concerned that this statement and list shows a misunderstanding of teams. A team is or should be a group of people who work together towards common goals as a group. The statement is written as if a team is constructed for a single patient, but 'virtual teams' are known to be much less effective because the group do not develop shared ways of working and shared expertise, knowledge and skills. We therefore strongly recommend rephrasing this to emphasise the need for a team, to which the patient is referred. The team will determine the particular people needed for the individual patient. The BSRM has long experience of the problems of saying what professions should be in a team, and no list is ever satisfactory or agreed. It is important to highlight that, between the team members they have the knowledge and skills to manage most of the problems from within team membership. It also has to recognise that some patients will have rare or unusual problems needing assistance from others (e.g. someone who is blind or deaf, who also has chronic fatigue syndrome), and therefore the team should be responsible for engaging other teams or individuals when needed. Third, it needs to be recognised that the team, as a whole, needs to include someone with specific knowledge about the condition of a particular patients (chronic fatigue syndrome in this case).	Thank you for your comment. People with ME/CFS often require the input of different professionals, and the committee agree the optimal approach is good communication between the different professionals and that care is coordinated to avoid duplication of assessments and appointments for the person with ME/CFS. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. In addition, the committee discussed the value of naming which professionals should be in a team and as you comment no list is ever satisfactory or agreed. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (see Evidence review I _Multidisciplinary care) The committee note that throughout the guideline there is reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support plan and supervision for the management of some symptoms. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS

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				Last, the list of areas of knowledge and skill given in the nine bullet points has overlooked the need for medical expertise. The medical needs, which require a doctor, include: • reviewing existing and emerging symptoms and signs, to check that in fact that the original diagnosis remains correct and to be alert to the development of a new disease or diseases • managing drugs, especially any given for pain, fatigue, or mood disturbance • assisting in the management of many of the symptoms where medical interventions may help (depression, vomiting, pain, anxiety etc) • maintaining a holistic overview, ensuring that all resolvable problems are identified and managed • acting as an authoritative interface with other teams, organisations, and agencies (e.g. employers) • contributing to team leadership and function, specifically advising and educating on any medical concerns raised by other team members leading on the most complex cases raising legal, ethical and other concerns.	the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.
British Society of Rehabilitation Medicine	Guideline	024	4	The BSRM has concerns about this bald statement, questioning particularly its nihilistic implications and the effects of that. There are many treatments available, proven and unproven, that help someone with chronic fatigue syndrome to regain autonomy, more involvement in social and other activities, and a better quality of life. The statement was probably written from within a non-holistic, biomedical framework with an assumption that (a) there is a unique, single specific cause for the condition and that (b) the only 'treatment' would be one that 'cured' the disorder by, somehow, reversing or removing the single unique cause. This	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. However the committee agree there currently isn't a cure for ME/CFS and it is important that people with ME/CFS are aware of this. For this reason, the committee have not further edited the recommendation.

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				simplistic conception does not apply to many diseases or disorders, and this statement could be added to almost every guideline, for example that for stroke, multiple sclerosis, of the management of backpain. More importantly, the implication of this statement both for patients and their families, and for clinicians and the public, is that, once the diagnostic label has been attached, it is downhill only and there is no prospect of improvement or recovery. This overlooks the large number of people who do recover and return to a full or nearly full life. Equally importantly, there are treatments that can help many patients regain some of their lost activities and experience less pain and distress: exercise (in general, not graded exercise therapy as characterised in this guideline); cognitive behavioural therapy, anti-depressants for people with depression, etc. This statement should be removed.	
British Society of Rehabilitation Medicine	Guideline	024	6 to p25 line 7	The BSRM is very supportive of self-management as an integral part of any rehabilitation plan for any person with a long-term disabling condition. The BSRM also agrees that deconditioning is not **the cause** of chronic fatigue syndrome. On the other hand, the BSRM has suggestions to improve this section 1.11.2 to 1.11.8. they are: • self-management needs to be seen as a whole, not picking off separate bits • energy management is a misnomer – the accurate term would be the management of symptoms associated with activities (of any type, including cognitive)	Thank you for your comment and information. The committee note that this is one element of the care and support plan incorporating a holistic approach to a person's care. Energy management is a term and concept that is understood in the ME/CFS community and is described as a strategy to manage symptoms and includes taking into account all types of activity (cognitive, physical, emotional and social) and takes into account overall level of activity. The approach is to reach stabilisation and then increase after periods of stability where possible. Energy management is part

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				• deconditioning (lack of cardiovascular. respiratory and muscular fitness) is not the **cause** of chronic fatigue syndrome, but it is undoubted a **consequence** of chronic fatigue syndrome and reducing its effects needs to be integral to any self-management plan • the emphasis on avoiding "Boom and Bust", more accurately described as undertaking proportionately large changes in levels of activity suddenly but for a short-time, is correct and this approach is unwise in anyone with any condition. Sports enthusiasts are routinely advised to increase their activity at a controlled rate • on the other hand, discussion with the patient on methods to increase their tolerance of activities that are part of normal life should take place, and any method needs to be reviewed after starting to check its appropriateness. This will include, inevitably, minor increases in symptoms as fitness (even in thinking) increases – that is normal in everyone • exercise, when referring to activities such as attending a gym, or doing exercises **for their own sake** are not essential, and it should only be included if the person specifically enjoys that type of activity • Instead, the focus should be on increasing, slowly, the amount and range of activities undertaken that the person wants or needs to undertake • During this process, the focus should be on activities achieved, not symptoms. This is the approach that is used by rehabilitation services for almost all patients with long-term disabling conditions, most of whom have deconditioning as a secondary consequence.	of the care and support plan and developed with a ME/CFS specialist team. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility. To note management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management

Consultation on draft guideline - Stakeholder comments table

10 November 2020 - 22 December 2020

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British Society of Rehabilitation Medicine	Guideline	027	24	The BSRM feel it is unusual to make recommendation **not** to undertake something unless there is incontrovertible evidence of a high risk of harm in everyone and no evidence of any possible benefit. These criteria do not apply to any of the mentioned activities. This is an example of a negative and nihilistic approach.	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people

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					with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.

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					Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
British Society of Rehabilitation Medicine	Guideline	028	1	The BSRM has two concerns with this statement. The first is in the use of the terms, therapy, treatment, and cure. If therapy means treatment, then the statement is tautologous. If cure refers to a complete reversal of everything, then it might be defended, but exercise has not been proposed as a cure, only as one of many interventions that will help some problems in some people. We recognise that some enthusiasts may over-sell exercise, and some patients may misunderstand what might be gained, but the assumptions underlying this are invalid. The second concern is that, if the person never considers or discusses increasing the activities they undertake, then the person can never get better. The concern here is with the word, exercise. Exercise should not be considered as some form of external 'treatment', analogous to taking a medication. Rather it is used as short-hand (unfortunately) for doing more	Thank you for your comment and information. *Treatment or cure* After considering the range of stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The definitions in the guideline clarify the difference between physical activity and exercise and these are linked to in this section. The committee have not reordered the recommendations. These recommendations are preceded by one in the energy management section that is to refer people who feel ready to progress their physical activity or would like to incorporate physical activity or exercise programme into managing their

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				activities that are or might be part of life – getting dressed, going up or down stairs, shopping etc. This section might be usefully re-ordered so that it starts with 1.11.20 and works backwards to 1.11.15 before covering deterioration in their conditions in 1.11.20 and 1.11.21	ME/CFS. The physical activity section then outlines the elements before developing a personalised programme.
British Society of Rehabilitation Medicine	Guideline	028	6	The BSRM agrees that no intervention should be recommended on some externally-given, fixed 'dose' or schedule. We agree that all interventions must be tailored to a patient's needs and wishes.	Thank you for your comment.
British Society of Rehabilitation Medicine	Guideline	028	8	The BSRM agrees that any management suggested to reduce the effects of deconditioning should **not** be put forward as treating 'the cause' of chronic fatigue syndrome, though we were unaware that this was being undertaken.	Thank you for your comment.
British Society of Rehabilitation Medicine	Guideline	028	10	This statement will, no doubt, be commented on by paediatric specialists. The BSRM has concerns that it is specifically suggesting that a treatment for which there is some evidence should not be offered, and this seems odd for a guideline that is supposed to be based upon evidence. The BSRM feels that, in the absence of evidence of comparable quality that the Lightning Process is harmful, sufficient to counter the evidence suggesting that it is beneficial, it is quite inappropriate for a guideline to recommend against it. The BSRM is also concerned that at least one member of the guideline committee has publicly stated that he does not support the Lightning Process as a treatment, a clear conflict of interest and of concern.	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer people with ME/CFS therapies based on the Lightning Process'. The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H). *Pre stated views or an interest in a particular outcome* The NICE Policy on declaring and managing interests for NICE advisory committees sets out the processes for : • what interests need to be declared and when • how declared interests should be recorded

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					• when a declared interest could represent a conflict of interest and the action that should be taken to manage this. As with any other guideline this Policy has been applied to this guideline. The Interests Register for the committee is published on the NICE website (https://www.nice.org.uk/guidance/indevelopment/gid-ng10091/documents) . The register has been updated throughout the development of the guideline and includes the decisions and actions made on the interests declared.
British Society of Rehabilitation Medicine	Guideline	028	12	The BSRM support this approach, but would prefer to frame it **not** as a 'programme', which carries implications of being an independent treatment. The rehabilitation approach is "If you wish to improve/increase activity 'A', then we need to help you develop a plan for you to carry out whereby you incrementally improve or increase activity 'A'".	Thank you for your comment. The programme is part of the care and support plan and the energy management plan, 'programme' is used to illustrate it is addresses physical activity or exercise in particular.
British Society of Rehabilitation Medicine	Guideline	029	6	The BSRM understands that a patient's clinical state fluctuates. This is seen in almost all people with long-term disability, albeit rarely with such dramatic fluctuations as may be seen in some people with chronic fatigue syndrome. The BSRM is concerned about the use of the term 'flare' which implies some kind of inflammatory process, and the word 'relapse' which implies some new tissue damage; there is no evidence for either process. A better term would be 'drop in level of activity', 'decompensation' or, conversely, 'increase in symptoms'.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
British Society of Rehabilitation Medicine	Guideline	029	18	The BSRM is concerned that this paragraph contains a series of recommendations without any evidence to support them. The recommendation is, anyway, very imprecise. What is the role of rest? Is rest deleterious? As there is no evidence, it is unhelpful because the clinician can only express an opinion.	Thank you for your comment. The committee considered that giving advice on planning rest and activity was a fundamental part of any management strategy for people with ME/CFS. In their experience, understanding the

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					role of rest and how to introduce rest periods was important in successful energy management. As you note there was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice. It is important that the advice comes from health care professionals with expertise in ME/CFS. This advice would be part of the care and support plan that is developed by the ME/CFS specialist team and they are knowledgeable about the role of rest and sleep in people with ME/CFS.
British Society of Rehabilitation Medicine	Guideline	030	15	The BSRM agree wholeheartedly with the importance of controlling pain. The committee also agreed that it could not make any recommendation. However, by referring the reader to a guideline on neuropathic pain, the guideline is implying strongly that the pain has a neurological origin. While some pain might possibly be neuropathic, there are many other likely causes including secondary to depression, and secondary to immobility and failure to move naturally. Most people reading this will simply start a drug for neuropathic pain, which will in all probability worsen fatigue and cognition without any benefit. If any recommendation is made, it should be to consult either a rehabilitation service (evaluation and management of pain in people with long-term complex disability is part of their expertise) or a pain service.	Thank you for your comments. Although pain relief was included in the protocol for pharmacological interventions no evidence was identified and the committee agreed they were unable to make any recommendations for specific medications. The committee linked to NICE guidance that was relevant to people with ME/CFS, the committee acknowledged that this does not address all the type of pain that people with ME/CFS may experience. The committee agree that care for people with ME/CFS should be personalised and recommend a personalised care and support plan in the assessment and care planning section of the guideline. Management of pain should be part of the personalised plan. The committee have noted at the beginning of the managing ME/CFS section and 'managing coexisting conditions that the

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					recommendations in the section on principles of care for people with ME/CFS and section on access to care and energy management should be taken into account when managing symptoms and coexisting conditions in people with ME/CFS. *Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. As such the difference between the guidelines is not a problem. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate. The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS.
British Society of Rehabilitation Medicine	Guideline	031	6	The BSRM is concerned with this statement. We assume that, if someone has, for example, severe pain then it would be acceptable to use, or at least try a drug such as ibuprofen. Yet this statement, taken at face value, would stop this as the ibuprofen is being used to 'treat' a part of the syndrome. Most people with a long-term condition nevertheless take treatments	Thank you for your comment. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.'

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				to alleviate symptoms, and sometimes to reduce progression, without any expectation of a cure. The BSRM suggests that this statement is removed, especially as it has already been emphasised that the condition is not 'curable'.	The committee note the following subsection in the guideline is 'medicines for symptom management' and provides advice for prescribers.
British Society of Rehabilitation Medicine	Guideline	031	10	The BSRM support this; it is standard practice when managing most people with long-term disabling conditions.	Thank you for your comment.
British Society of Rehabilitation Medicine	Guideline	032	15	This statement seems to contradict or, at least, conflict with 1.11.29.	Thank you for your comment. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.' Recommendation 1.12.24 recognises it is the person's choice to take vitamins or supplements but that this should be an informed choice with an awareness about potential side effects.
British Society of Rehabilitation Medicine	Guideline	034	1	The BSRM is familiar with cognitive behavioural therapy, and it is an integral part of many rehabilitation plans for many patients. The BSRM is uncertain whether the text accurately reflects the process and content of the treatment but expects a psychological organisation to pass comment.	Thank you for your comment.
British Society of Rehabilitation Medicine	Guideline	037	1	The BSRM agrees fully that the more marked fluctuations in symptomatology need analysis and management. The BSRM has concerns about the terms 'flare' and 'relapse' as already explained. The BSRM also has a concern about trying to distinguish between the two categories. As the basis for these more marked fluctuations is unknown, there is no rational basis for making such a distinction. The clinical reality is also that there is no clear-cut, easily defined separation.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse. Flare ups and relapse are further defined in the terms used in the guideline with flare up recognising that flare ups usually occur as part of PEM andis transient with and a relapse as a sustained

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				The BSRM recommends (a) avoiding categorisation on duration or any other feature and (b) that each person's fluctuations need analysis on an individual basis, with a tailored plan for prevention and management.	and marked exacerbation of symptoms lasting longer than a flare-up. The committee agree that each person's fluctuations need analysis on an individual basis, with a tailored plan for prevention and management in the care and support plan. This is recommended in the assessment and care planning section of the guideline.
Connect Health Ltd	Evidence Review F	007	General	The PICO table does not include pain interference or pain-related self-efficacy. Pain is a common symptom in CFS. Please can you confirm that the absence of evidence for interventions for 'pain' (p88 L8) would also apply to these constructs. Otherwise, you may be missing treatments that may be beneficial.	Thank you for your comments. Pharmacological interventions aimed at treating pain in people with ME/CFS were included in the review protocol, however none were found. Additionally, pain was included as an outcome (visual analogue scales and numeric rating scales were eligible for inclusion) in this review. See the review protocol in Appendix A.
Connect Health Ltd	Evidence Review G	006	General	The PICO table does not include pain interference or pain-related self-efficacy. Pain is a common symptom in CFS. Please can you confirm that the absence of evidence for interventions for 'pain' (317, L14) would also apply to these constructs. Otherwise, you may be missing treatments that may be beneficial.	Thank you for your comments. Non-pharmacological interventions aimed at treating pain in people with ME/CFS were also included in the review protocol (for example, TENS), however none were found. Pain was also included as an outcome (visual analogue scales and numeric rating scales were eligible for inclusion) in this review. We have noted that the pain interference sub-scale of the Brief Pain Inventory was reported in Jason 2007, and this has now been extracted and included in the review. See the full review protocol in Appendix A of Evidence review H.

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Connect Health Ltd	Guideline	General	General	Thank you for updating this important guideline. It balances both quantitative methods for evaluating published papers along with a qualitative analysis of patient experience. We understand that a guideline needs to be implementable and support this approach to help make the guideline acceptable to people with CFS whilst making best use of scarce public resources.	Thank you for your comment.
Connect Health Ltd	Guideline	008	17	The symptoms used by the committee for suspecting CFS do not mention pain. However, in Evidence review 4 (diagnosis), p44 table 4, chronic pain appears in 8 out of 9 of the diagnostic classifications. A systematic review (Meeus 2006) showed that chronic widespread pain occurs in 84-94% of people with CFS. Further, in evidence review 6 (pharma), p87, L 19 "The committee agreed that pain though not key to the diagnosis of ME/CFS, is a common symptom in people with ME/CFS and should be considered by the committee in their decision making". It therefore seems perverse that this guideline should choose diagnostic criteria that do not include chronic widespread pain and that the guideline avoids management of chronic pain in people with CFS. In our view it would be helpful if the guideline committee advised on principles for adapting recommendations in the chronic pain guideline and other relevant guidelines (low back pain, osteoarthritis) for people with CFS. Mira Meeus, Jo Nijs, Kenny De Meirleir, Chronic musculoskeletal pain in patients with the chronic fatigue	Thank you for your comment. The committee agree that pain and decreased pain threshold were identified in most of the criteria as symptoms for suspecting ME/CFS and diagnosis and the committee agreed they were important to be aware of. They also noted that other symptoms, including having flu like symptoms in the initial stages of ME/CFS, temperature hypersensitivity, neuromuscular symptoms, intolerances and sensory sensitivities were all mentioned to some extent in the criteria and were common symptoms they were aware of. The four symptoms (debilitating fatigue, PEM, unrefreshing sleep and sleep disturbance (or both) and cognitive difficulties) were agreed by the committee as the best basis for identifying people with ME/CFS and as essential to a diagnosis of ME/CFS. The committee emphasised it is the combination and interaction of the symptoms that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). *Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population '

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				syndrome: A systematic review, European Journal of Pain, Volume 11, Issue 4, 2007, Pages 377-386,https://doi.org/10.1016/j.ejpain.2006.06.005.	chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. As such the difference between the guidelines is not a problem. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that any when managing any co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account.
Connect Health Ltd	Guideline	008	17	Please include guidance on the management of chronic pain, or cross-refer to the NICE Guideline on chronic primary pain as pain is a very common symptom in people with CFS even if not a defining diagnostic feature. The symptoms for suspecting CFS do not mention pain. However, in Evidence review 4 (diagnosis), p44 table 4, chronic pain appears in 8 out of 9 of the diagnostic classifications. A systematic review showed that chronic widespread pain occurs in 84-94% of people with CFS. Collin 2016 suggests 20% of people with CFS have widespread pain, and a further 33% have multiple symptoms in including chronic pain (53% of total cohort). Many patients with CFS also meet the diagnostic criteria for fibromyalgia (see Evidence review 4 (diagnosis), p10, table 2 and the following references: In our view it would be helpful if the guideline committee advised on principles for adapting recommendations in the chronic pain guideline and other relevant guidelines (low back pain, osteoarthritis) for people with CFS.	Thank you for your comment. The committee agree that pain and decreased pain threshold were identified in most of the criteria as symptoms for suspecting ME/CFS and diagnosis and the committee agreed they were important to be aware of. They also noted that other symptoms, including having flu like symptoms in the initial stages of ME/CFS, temperature hypersensitivity, neuromuscular symptoms, intolerances and sensory sensitivities were all mentioned to some extent in the criteria and were common symptoms they were aware of. The four symptoms (debilitating fatigue, PEM, unrefreshing sleep and sleep disturbance (or both) and cognitive difficulties) were agreed by the committee as the best basis for identifying people with ME/CFS and as essential to a diagnosis of ME/CFS. The committee emphasised it is the combination and interaction of the symptoms that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). *Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population '

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				Collin SM, Nikolaus S, Heron J, Knoop H, White PD, Crawley E. Chronic fatigue syndrome (CFS) symptom-based phenotypes in two clinical cohorts of adult patients in the UK and The Netherlands. J Psychosom Res. 2016 Feb;81:14-23. doi: 10.1016/j.jpsychores.2015.12.006. Epub 2015 Dec 23. PMID: 26800634. Mira Meeus, Jo Nijs, Kenny De Meirleir, Chronic musculoskeletal pain in patients with the chronic fatigue syndrome: A systematic review, European Journal of Pain, Volume 11, Issue 4, 2007, Pages 377-386,https://doi.org/10.1016/j.ejpain.2006.06.005.	chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. As such the difference between the guidelines is not a problem. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that any when managing any co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account.
Connect Health Ltd	Guideline	023	6	What constitutes a specialist team? This is important for both commissioners and providers to be defined. Maybe add to glossary and include in section on training?	Thank you for your comment. A definition of a ME/CFS specialist term has been added to the terms used in this guideline.
Connect Health Ltd	Guideline	024	General	There is no rec and no research rec regarding the provision of multidisciplinary programmes. This is in scope for this review (Final scope, p7, para 3.4). There is nothing covering this in the rationale and impact section either. We note that one cost–utility analysis found that multidisciplinary rehabilitation was not cost effective compared to cognitive behavioural therapy for adults with ME/CFS (evidence review 7 non-pharma, p198 L28). Should such programmes in use in the UK continue? It would be helpful for commissioners and providers to have guidance on this.	Thank you. The committee have recommended a specialist team approach to the care of ME/CFS including assessment and development of a management plan. The skills required by the team are described in the recommendations. 'Multidisciplinary rehabilitation' is a specific intervention that was not found to be cost effective. It is evident from the recommendations that the committee are not advocating this intervention. However, a "do not do" recommendation was not made, since there was no evidence that it is harmful to patients.
Connect Health Ltd	Guideline	026	18	Rec 1.11.11 should be laid out differently as it is ambiguous. The first sentence is fine. The activities in the bullet points are a subset of exercise and physical activity, which you want included as part of physical maintenance. Maybe this should be a separate rec: "Think about incorporating the following physical activities (in the management plan/as part of physical maintenance)"?	Thank you for your comment. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice

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					on maintaining and preventing the deterioration of physical functioning and mobility. The bullet points are not in particular order and are examples of areas to think about when considering how to support someone with long term immobility.
Connect Health Ltd	Guideline	027	20	The terms 'exercise', 'physical activity', 'physical maintenance' and 'movement' are used interchangeably by general public, physiotherapists and clinicians. Although these terms are defined as the committee wished to use then in the glossary, these different terms may lead to confusion for clinicians and patients because it is not how they use the terms. Is it possible to reduce the number of terms in use in separate places in the document? In many cases you could refer to 'exercise or physical activity' even though the terms are not synonymous; the guidance would apply to both.	Thank you for your comment and information. The definitions used in the guideline are from the World Health Organization advice on physical activity. After considering the stakeholder comments, physical activity or exercise has been added to aid clarity. To note after considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.
Connect Health Ltd	Guideline	027	21	Please consider rewording this rec to include advice on maintaining physical activity for wider health benefits perhaps as part of a management plan or discharge plan. There are considerable public health benefits from being physically active. (Nice Public Health guideline PH44, CMO Physical Activity Guidelines 2019.) People who are the most inactive are the group most likely to get health gains from increased physical activity. The question is how to do this? There will be some people with CFS who have improved with the treatments recommended in this guideline, or whose condition has plateaued. Once their treatment in an NHS setting is completed (even if they are kept on long term review)	Thank you for your comment. In section 1.5 the holistic assessment includes assessments of physical health and the care and support plan include planning to address physical functioning and mobility. This recommendation directly addresses exercise.

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				they would still benefit from tailored advice regarding maintaining their physical fitness for all the other health benefits this brings.	
Connect Health Ltd	Guideline	027	21	We suggest that this rec should be softened as 'do not use' is not justified by the clinical evidence review. Maybe "advise people with CFS that unstructured exercise may worsen their symptoms" Rationale: This is because unstructured, unsupervised or un-tailored advice on physical activity may not be helpful as a treatment for CFS, particularly if this results in them exceeding their 'energy envelope.' Although we suggest this wording, some of our contributors were unsure about referring to 'energy envelope' as it is not a commonly used term by clinicians outside the tight sphere of chronic fatigue syndrome management i.e. most clinicians in England.	Thank you for your comment. The committee agree there is little dispute amongst clinicians working with people with ME/CFS that they should not undertake exercise that is not part of a programme overseen by a ME/CFS specialist team, such as telling them to go to the gym or exercise more. It is commonly agreed that people with ME/CFS experience post exertional malaise (PEM) after activity. PEM is a worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated. It is in this context, and recognising the evidence from people with ME/CFS indicating that misunderstanding of the impact of PEM and inappropriate advice on how to incorporate physical activity (and exercise) into their lives has resulted for some in a deterioration of their condition, that this guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS

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					that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms. This is linked to terms used in the guideline with further explanation of the meaning.
Connect Health Ltd	Guideline	027	21	Please consider rewording or deleting this bullet point because it may result in physios not being able to use the word "exercise" with this patient group and being very worried about doing anything with a patient that may increase their symptoms. In some cases, particularly when pain is a significant feature, encouraging movement and exercise is a very important part of giving some people with chronic fatigue "agency" over their management. This bullet point also fails to acknowledge the skills physios use in combination with exercise/movement including facilitating patient choice, helping them understand their condition better and working with them to help them towards their values and goals in life.	Thank you for your comment. The committee agree there is little dispute amongst clinicians working with people with ME/CFS that they should not undertake exercise that is not part of a programme overseen by a ME/CFS specialist team, such as telling them to go to the gym or exercise more. It is commonly agreed that people with ME/CFS experience post exertional malaise (PEM) after activity. PEM is a worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated. It is in this context, and recognising the evidence from people with ME/CFS indicating that misunderstanding of the impact of PEM and inappropriate advice on how to incorporate physical activity (and exercise) into their lives has resulted for some in a deterioration of their condition, that this guideline has recommended that people with ME/CFS should be supported by a

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					physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. *Pain* The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist with ME/CFS and these should be investigated and managed in accordance with best practice. This section also lists related NICE guidelines and recommends the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS.
Connect Health Ltd	Guideline	028	1	The bullet point not to offer therapy based on physical activity is a non-sequitur. . Dissecting the statement, what is the point you are trying to make here: is it that you are not recommending physically-based **therapies**, is it that you do not recommend **physical activity**, is it that you don't think CFS can be **treated**, or that you don't think CFS can be **cured** (by physical therapy or physical activity)? To a non-expert this	Thank you for your comment. *Treatment or cure* After considering the range of stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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				bullet point is a confusing variance to the rest of the advice from recs 1.11.17 – 1.11.22. There is a further inconsistency with this bullet point: The energy envelope theory requires tailoring physical activity to within the envelope (P42 L8). Further, you suggest including physical activity (p28 lines 12, 16, 19, 23), and in the bullet points p27 L19 onwards.	The committee have slightly edited recommendation 1.11.20 to, 'a personalised collaborative physical activity or exercise programme'. Any activity would take into account a person's energy limits.
Connect Health Ltd	Guideline	028	1	This bullet point is at variance with the Cochrane Review, which states "Key messages: People who have exercise therapy probably have less fatigue at the end of treatment than those who receive more passive therapies. We are uncertain if this improvement lasts in the long term. We are also uncertain about the risk of serious side effects from exercise therapy." Larun L, Brurberg KG, Odgaard-Jensen J, Price JR. Exercise therapy for chronic fatigue syndrome. Cochrane Database of Systematic Reviews 2019, Issue 10. Art. No.: CD003200. DOI: 10.1002/14651858.CD003200.pub8	Thank you for your comment. With reference to Larun 2017: This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion from evidence review G are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity levels, return to school/work, exercise performance measures, and mortality. However, all studies included in this Cochrane review were included in our review. Also we note that Cochrane has acknowledged issues with this review in terms of the methods used and the population definition and they plan to conduct a full update of this Cochrane review. *Treatment or cure* After considering the range of stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to

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					avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Connect Health Ltd	Guideline	028	1	Please consider rewording or deleting this bullet point because it may result in physios feeling unable to use the words “physical activity” or “exercise” with this patient group and being very worried about offering therapeutic advice to a patient that may increase their symptoms. In some cases, particularly when pain is a prominent feature, encouraging movement and exercise is a very important part of giving some people with chronic fatigue “agency” over their management. This bullet point also fails to acknowledge the skills physios use in combination with exercise or movement including: facilitating patient choice, helping them understand their condition better, and helping them towards their values and goals in life.	Thank you for your comment. After considering the stakeholder comments, the committee have added exercise into the recommendations on considering a physical activity programme to clarify where these apply to exercise. The recommendation describes the types of physical activity or exercise programmes that should not be offered to people with ME/CFS. The previous recommendation in the energy management section includes that people who feel would like to incorporate a physical activity or exercise programme into managing their ME/CFS (see the section on physical activity and exercise) should be referred to a physiotherapist or occupational therapist working in a ME/CFS specialist team to explore this. The following recommendation in the physical activity section reinforce this and include that if a physical activity or exercise programme is offered, it should be overseen by a physiotherapist in a ME/CFS specialist team. The guideline is clear that access to support for a physical activity or exercise programme should be available for people with ME/CFS. *Treatment or cure* After considering the range of stakeholder comments on the wording ‘treatment or cure for ME/CFS’ the committee agreed to remove the word ‘treatment’ from these recommendations to

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					avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. *Pain* The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist with ME/CFS and these should be investigated and managed in accordance with best practice. This section also lists related NICE guidelines and recommends the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS
Connect Health Ltd	Guideline	028	3	This bullet point implies that physical activity advice or programmes are not helpful for people with chronic fatigue syndrome. From the evidence presented in evidence review 7 (non-pharma), we think that the quality of the research investigating a link between physical activity and mental health is poor (GRADE Very Low for almost all comparisons of physical activity and mental health outcomes). There is strong evidence from a number of Cochrane systematic reviews that physical activity improves mental health. However, with regards the specific CFS population, the Cochrane review also found "The effect of exercise therapy on pain, quality of life and depression is uncertain because evidence is missing or of very low certainty." We therefore think that a research recommendation rather than a 'do not use' recommendation for physical activity would be more appropriate in respect of generalised benefits of physical activity.	Thank you for your comment. The bullet point is clear that generalised physical activity or exercise programmes – this includes programmes developed for healthy people or people with other illnesses should not be offered to people with ME/CFS. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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				Larun L et al, Exercise therapy for chronic fatigue syndrome, Cochrane Database of Systematic Reviews, 2019 https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD003200.pub8/full Posadzki, P., Pieper, D., Bajpai, R. *et al.* Exercise/physical activity and health outcomes: an overview of Cochrane systematic reviews. *BMC Public Health* **20,** 1724 (2020). https://doi.org/10.1186/s12889-020-09855-3	and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). With reference to Larun 2017: This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion from evidence review G are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity levels, return to school/work, exercise performance measures, and mortality. However, all studies included in this Cochrane review were included in our review. Also we note that Cochrane has acknowledged issues with this review in terms of the methods used and the population definition and they plan to conduct a full update of this Cochrane review.

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					We note the Posadzki et al review is not specifically about ME/CFS although it does include the Larun review. *Research recommendation* The committee have made recommendations to address the difficulties and limitations in diagnosing ME/CFS (see Evidence review D for the committee discussion on this). The committee identified these as high priority for research. This committee hope this will enable future research to accurately identify people with ME/CFS and determine the impact of interventions on them. They thought this was particularly important before recommending any research trials on physical activity or exercise interventions.
Connect Health Ltd	Guideline	028	16	Physical activity programme: please can you suggest guidance about whether this can be provided in a group setting, caveated with any requirement to take into account individual needs. Although there is discussion about group treatments in the narrative review, there is no conclusion about this.	Thank you for your comment. No evidence was identified to make recommendations on the mode of delivery of programmes and the committee agreed not to comment on this recognising it will be individual to the person and there will be local variation in implementation. .
Connect Health Ltd	Guideline	028	16	Physical activity programme: You have discounted the clinical approach (GET) taken in McCrone 2012, yet this is the only cost-effectiveness evidence provided for physical activity. Please therefore explain on what basis a physical activity programme or intervention is likely to be cost effective? Would it be more-so if in a group setting?	Thank you for your comment. McCrone 2012 showed GET to be of marginal cost effectiveness. However, the qualitative evidence indicated that outside of a trial context there is a risk of harm with GET. The committee felt that only if there is more emphasis on keeping with the person's energy limits and less emphasis on achieving targeted increases, can a physical activity programme be safe and cost effective. To be confident of this the committee sought to ensure that such a therapy was overseen by an ME/CFS specialist. There are different ways in which this could be conducted. It might be more cost effective conducted remotely and/or in a group setting.
Connect Health Ltd	Guideline	028	19	We agree with this rec, but it seems to be at variance with p28, line 1 (do not offer physical activity). Whilst the individual recs may make sense, this whole section on physical activity contains contradictions.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical

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					activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
Connect Health Ltd	Guideline	030	14	Please link to the NICE guideline on chronic primary pain. This is more applicable than the neuropathic pain guideline, which only refers to pharmacological management of patients with conditions such as diabetic neuropathy, post herpetic neuralgia and trigeminal neuralgia, which may co-exist but are not associated with chronic fatigue syndrome. The symptoms used by the committee in this guideline for suspecting CFS do not mention pain. However, in Evidence	Thank you for your comments. *Neuropathic pain* The committee disagree that reference to the neuropathic pain guideline isn't relevant. People with ME/CFS report many different types of pain, neuropathic pain and headaches included. These are examples of NICE guidelines on pain and is not intended to be an exhaustive list of the types of pain people with ME/CFS may experience.

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				review 4 (diagnosis), p44 table 4, chronic pain appears in 8 out of 9 of the diagnostic classifications. A systematic review showed that chronic widespread pain occurs in 84-94% of people with CFS. Collin 2016 suggests 20% of people with CFS have widespread pain, and a further 33% have multiple symptoms in including chronic pain (53% of total cohort). Many patients with CFS also meet the diagnostic criteria for fibromyalgia (see Evidence review 4 (diagnosis), p10, table 2 and the following references. For all these reasons, a cross reference to the NICE guideline on chronic primary pain seems essential. Collin SM, Nikolaus S, Heron J, Knoop H, White PD, Crawley E. Chronic fatigue syndrome (CFS) symptom-based phenotypes in two clinical cohorts of adult patients in the UK and The Netherlands. J Psychosom Res. 2016 Feb;81:14-23. doi: 10.1016/j.jpsychores.2015.12.006. Epub 2015 Dec 23. PMID: 26800634. Mira Meeus, Jo Nijs, Kenny De Meirleir, Chronic musculoskeletal pain in patients with the chronic fatigue syndrome: A systematic review, European Journal of Pain, Volume 11, Issue 4, 2007, Pages 377-386,https://doi.org/10.1016/j.ejpain.2006.06.005.	*Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that any when managing any co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account. *Suspecting ME/CFS* Pain is listed as one of symptoms that may be associated with ME/CFS. Based on the evidence (Evidence review D) and the committee's clinical experience, they agreed the four criteria for the diagnosis of ME/CFS were fatigue, post-exertional malaise, unrefreshing sleep and sleep disturbance (or both), and cognitive difficulties. Key to the diagnosis of ME/CFS is the presence and combination of the four symptoms. Pain may be associated but is not exclusive to with ME/CFS, this was supported by the IOM diagnostic criteria (2015). The committee note that pain is the dominant symptom in fibromyalgia and as such the two populations are differentiated.
Connect Health Ltd	Guideline	034	General	There is no guidance on whether to deliver CBT in groups for some people. Whilst the evidence review did not show differences in benefit from one-to-one, group or web-based interventions (evidence review 7 non-pharma, p323 L27), there	Thank you. The committee did not think that the evidence was strong enough to give guidance. However, we have added a brief discussion to Evidence Report G: "Whilst the evidence review did not show differences in benefit from one-to-one, group or web-

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				is nevertheless a cost implication. There is no modelling or threshold analysis. It would be helpful for commissioners and providers to know whether, if CBT is being provided, what is the most cost-effective method of delivery and the cost-impact.	based interventions, there will be differences in resource use and cost. For patients where it is of equal efficacy, web-based therapy would clearly be more cost effective followed by group-based therapy. Although some people with ME/CFS might get additional therapeutic benefits from meeting in a group, for many, the benefits might be greatest from web-based CBT, as it would not involve travel that could trigger post-exertional malaise."
Connect Health Ltd	Guideline	034	5	The problem with the phrase "do not offer CBT…" is that the next recs describe how CBT should be used, who should deliver it, preparing people to engage with CBT. If this was a stand-alone rec rather than 1.1.43, it would be even less justifiable than tucking at the end of the rec about who to offer it for. We understand the committee wished to reflect the negative qualitative evidence about experience of people receiving CBT (evidence review 7 non-pharma, p326 L10). However, the committee goes on to say that CBT has a role in improving sleep, depression and dietary issues (evidence review 7 non-pharma, p326 L20). Whilst these symptoms are common across many physical and mental conditions, it is incorrect to state that CBT is not a treatment for use in people with CFS. This will be easily mis-interpreted that CBT should not be used in people with CFS. We believe that these evidence reviews show that CBT is an intervention or treatment that is of benefit for some symptoms experienced by people with CFS. We suggest that you could separate rec 1.11.43. The last sentence could either be removed (although the committee were keen to reflect patient experience of CBT) or a stand alone rec "Do not offer CBT as a cure for CFS".	Thank you for your comment. After considering the range of stakeholder comments the first recommendation in this section has been edited to remove the word treatment. The committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. The recommendation now starts with, 'explain to people with ME/CFS that cognitive behavioural therapy (CBT) may help them to manage their symptoms but it is not curative'

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Connect Health Ltd	Guideline	039	2	We are pleased to see the consensus recommendation to review in primary care rather than routinely by a specialist team. However, given the few numbers of people with CFS at practice level you may wish to discuss in the rationale that delivery in primary care includes "in primary care networks…" This would allow primary care expertise to be built up and consistent across local area population.	Thank you for your comment. This has been added to the committee discussion in Evidence review J.
Connect Health Ltd	Guideline	039	8	We agree with the rec to "ensure you have access to the management/discharge plan". Our experience is that is poorly done and leads to inconsistent messaging between different clinicians in primary care and unnecessary prescribing, investigations and referrals, which can be harmful for the person with CFS.	Thank you for your comments.
Connect Health Ltd	Guideline	042	4	Please improve the definition of "energy envelope". The definition used in the NICE guideline is not the same as the studies on which this is based. Energy envelope is a theory. It proposes that patients with CFS will experience improved functioning when maintaining expended energy levels at the same level as the available energy level. (Jason 2009) The NICE definition mentions 'The amount of energy a person has to do all activities'. The paper by Jason showed improvements in both physical activity and fatigue severity scores. These constructs are not the same thing, and it would be less misleading to stick to the original definition by Jason (2009). The NICE definition mentions 'an increase in their symptoms' and one might conclude that this is everything from page 8 line 17 to page 9 line 16 as well as a person's mental health. But this is not the case (Jason 2009, Brown 2013). One might conclude erroneously from the NICE guideline that the focus on energy envelope, particularly reducing activity at initial	Thank you for your comments. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.

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				assessment (p25 L18) will improve **all** their symptoms. But even in some groups of people with adaptive coping strategies associated with the energy envelope theory, they experience severe limitations of function. Brown AA, Evans MA, Jason LA. Examining the energy envelope and associated symptom patterns in chronic fatigue syndrome: does coping matter?. *Chronic Illn*. 2013;9(4):302-311. doi:10.1177/1742395313478220 Jason L, Benton M, Torres-Harding S, Muldowney K. The impact of energy modulation on physical functioning and fatigue severity among patients with ME/CFS. *Patient Educ Couns*. 2009;77(2):237-241. doi:10.1016/j.pec.2009.02.015	
Connect Health Ltd	Guideline	042	4	We are unsure about the guideline referring to 'energy envelope' as it is not a commonly used term by clinicians outside the small sphere of chronic fatigue syndrome management services i.e. most other clinicians in England. We thought this term might be misunderstood although defined in the glossary.	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
Connect Health Ltd	Guideline	053	5	With regards a specialist team: you mention that there are 250,000 people in the UK with CFS (p71 line15). Will there be enough specialist teams to deliver this guideline? (In Review 9 (MDT), p24, line 16 "The committee acknowledged that specialist teams are limited in number and in some areas of England and Wales are non-existent.) So will the impact of this recommendation be fully costed and timetabled?	Thank you for your comment. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services , to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken

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					into account when commissioning services for people with ME/CFS. The NICE implementation team are developing a resource impact analysis for this guideline. However, it will be up to local health economies to fully cost and timetable the impact in their area.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Evidence review D	050	033	'Debilitating fatigue' – user friendly word to replace fatigability.	After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change 'Debilitating fatigability to 'debilitating fatigue'.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Evidence review D	057	032 - 040	Removal of exclusion blood tests of other possible conditions with fatigue and 'any tests are then specific to the condition suspected by the clinician based on the persons symptoms' – It is beyond the professional competencies of clinical nurse specialists in ME/CFS services to identify symptoms of multiple other conditions. To clarify this is carried out by GP's before referral to specialist services.	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to identify and exclude other diagnoses. The committee have now included examples of investigations that might be carried out and that investigations should continue where ME/CFS is suspected. The committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Evidence Review G	034	016 - 018	There is a concern that this message leads with a negative message. Switch to 'Recognises that thoughts, feelings, behaviours and physiology interact with each other and does not assume people have 'abnormal' illness beliefs and behaviours as an underlying cause of their ME/CFS' for a more optimistic message.	Thank you for your comment. This section intended to highlight some of the negative criticism of non-pharmacological interventions recommended in previous guidance. The committees full discussion about CBT and other non-pharmacological interventions can be found in Section 3 of Evidence review G.
Epsom and St Helier University Hospitals NHS	Guideline	General	General	There are a number of roles for specialist ME/CFS services identified in the draft including referrals to social care, overseeing safeguarding assessments, supporting families	Thank you for your comment. The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as training development, to implement some

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Trust – Chronic Fatigue Syndrome Service				and carers, liaising with employers and education, providing advice and consultation & training to primary care health and social care professionals, and acting as a single point of contact. These recommendations will be a challenging change in practice because of the balance of clinical activities and non-clinical activities. These roles would impact on clinical capacity and with existing resources significantly add to waiting times.	recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. A strong theme from the evidence was the lack of understanding about ME/CFS and training in health and social care professionals and the committee agreed it was important to make recommendations about training. The development of training by ME/CFS specialist service reflects the evidence in Evidence reviews A and B and the committee's experience that ME/CFS specialist services provide valuable training, information and support to non-specialists and people with ME/CFS. To note the training recommendations have been edited. Your comments will also be considered by NICE where relevant support activity is being planned.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	004	006	There is concern of the accuracy of the statement "its pathophysiology is unclear" – There is a growing body of research explaining the dysregulation model of several body systems for a better understanding of ME/CFS. This model is a positive message for patients offering a pragmatic approach to start their rehabilitation. Risk of ME/CFS being mis-labelled as 'medically unexplained symptoms'.	Thank you for your comment and information. The committee agree there is published research in this area and also that there is much controversy, which is reflected in the stakeholder comments. This bullet point has been edited to,' and its pathophysiology remains under investigation' to clarify that there is not enough evidence to make any conclusions about the pathophysiology of ME/CFS and this is an active area of research.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	008		Box 1 Fatigability and post-exertional symptom exacerbation – The concern is that this is not a patient user friendly term. Equality risk due to non-accessible language for service users.	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms and hope this has added some clarity for readers

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					- *Debilitating fatigability.* This has been edited to be more descriptive of the fatigue experienced by people with ME/CFS, 'Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.'. - *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	008	009	CG53 guidelines – recommended blood tests identifying other medical issues reduces inappropriate referrals to specialist ME/CFS services. Improves patient care and avoids patient being bounced between ME/CFS services and primary care delaying patient treatment.	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	008	012	Suspecting ME/CFS (minimum 6 weeks) – The concern is of a risk of people being incorrectly diagnosed with ME/CFS at this early stage. Once a provisional medical label is suggested it is difficult to remove from a patients' medical history and can impact future medical care. To clarify that patients with provisional diagnosis are managed in primary care to reduce the risk of inappropriate referrals to specialist services with limited resources.	Thank you for your comment. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: - 'Provisional' diagnosis has been deleted for the following reasons:

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

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					○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis • Further investigation/differential diagnoses. The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have added examples of investigations to be done when suspecting ME/CFS and have added that ME/CFS should be suspected if the 'symptoms are not explained by another condition.'
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	013	012	Home visits -this recommendation will be challenging in practice because of the resource implication for specialist ME/CFS service large catchment area. Holistic assessments are likely to require several home visits. Offering a domiciliary service is likely to reduce the number of outpatient clinic appointments and increase waiting times.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.

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					The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as flexible access to care, to implement some recommendations in the guideline. guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	014	022 - 024	The concern is that the language is negative –This sentence should be factual rather than a leading interpretation. E.g., 'although' to be removed. 'Many' to be replaced with 'Others'.	Thank you for your comment. After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS. See evidence review A for the committee discussion on information about the long term outlook for people with ME/CFS
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	024	004 - 005	Prefix with what is available, e.g. "There are several psychosocial interventions available" to support patients.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The section on symptom management for people with ME/CFS then outlines the available interventions.

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Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	024	010	Move this statement to the end of 1.11.2. The concern is that it biases the rest of the section. State what it is first, then state what it isn't.	Thank you for your comment. The committee agreed to keep, 'is not curative' at the beginning of the recommendation. In the rationale for managing ME/CFS the committee outline why it is important that it is clear there are not any cures for ME/CFS.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	027	015 - 018	There is a concern that the mention of 'no cure' in the draft and the cautious undertones of the draft undermines the evidence review comment 'patients hoped that referral to a specialist service would give them positive direction for the future' and 'maintain hope that symptoms can improve'.	After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. However while the committee agree there are people who can improve through managing their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	028	012	The concern is by using the word 'only' risks instilling fear. Omitting this word changes it to a confident statement of use of a physical activity programme where appropriate. The concern is that this is biased language undermining the positive message in the sentence.	Thank you for your comment. This recommendation is preceded by one in the energy management section to refer people who feel ready to progress their physical activity or would like to incorporate physical activity or exercise programme into managing their ME/CFS. This recommendation (1.11.11) refers to the discussion between the person with ME/CFS and the ME/CFS specialist physiotherapist or occupational therapist about considering a personalised collaborative physical activity or exercise programme under the circumstances listed..
Epsom and St Helier University Hospitals NHS Trust – Chronic	Guideline	029	008 - 009	As ME/CFS is a fluctuating condition, a management plan should include a 'flexible setback management plan' for long term patient self-management which includes physical activity adjustment guidelines. The concern is that specialist ME/CFS	Thank you for your comment. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas

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Fatigue Syndrome Service				physiotherapy service is a limited resource and does not currently have the capacity to support patients from primary care adjusting physical activity after a flare or relapse and this would reduce the specialist ME/CFS physiotherapist clinical capacity and increase waiting times.	that may need support and investment, such as access to ME/CFS specialist services , to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	034	009 - 010	There is concern of the use of the language 'adapt' and 'manage' where the balance has shifted away from rehabilitation and symptom improvement. Suggestion to include in the principles of CBT 'learn new ways of responding to symptoms of ME/CFS' and to replace 'adapt' & 'manage' with 'manage' and 'improve'.	Thank you for your comment. The following bullet point includes that CBT aims to improve quality of life, including functioning, and to reduce the psychological distress associated with having a chronic illness.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	034	019 - 020	This sits better within the 1.11.46 section as it comes under 'what to expect'.	Thank you for your comment. This bullet point has been moved to the following recommendation.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	034	001	Cognitive behavioural therapy (CBT) is a psychological intervention which is an integral option of care for people with ME/CFS. It does not fall into either category of 'treatment' or 'support'. The concern is that 'psychological support' implies an adjunct option rather than an intervention in its own right. The heading 'Psychological intervention: cognitive behavioural therapy' is recommended.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. After considering the range stakeholder comments about the title not being representative of this section the committee edited the

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					title of this section to remove psychological support recognising this only referred to CBT.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	034	002	The concern that the use of the word 'only' is nuanced and implies negative bias. An alternative suggestion is, 'Offer people CBT for support in managing and in some cases improving their symptoms of ME/CFS and to reduce the psychological distress associated with living with a chronic illness. Clarify the principles of CBT to help the person decide whether this intervention is right for them' (see 1.11.45)	Thank you for your comment. After considering the range of stakeholder comments the first recommendation in this section has been edited to remove the word treatment. The committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. The recommendation now starts with, 'explain to people with ME/CFS that cognitive behavioural therapy (CBT) may help them to manage their symptoms but it is not curative'
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	034	005	There is a concern that the draft is using medical language of 'treatment' to describe psychological/psychosocial therapies. CBT is a psychological intervention used with long term conditions. The sentence 'there are a variety of psychosocial interventions that help many people live well with ME/CFS' can be inserted earlier in the draft which can be used to describe CBT, energy management, physical activity programmes and relay a positive message for hope and engagement in interventions. There is a concern of the over use of the word 'cure' in the draft – a word that is not used in other NICE guidelines for other long term health conditions.	Thank you for your comment. After considering the range of stakeholder comments the first recommendation in this section has been edited to remove the word treatment. The committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. The recommendation now starts with, 'explain to people with ME/CFS that cognitive behavioural therapy (CBT) may help them to manage their symptoms but it is not curative'

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Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	034	012	'is not curative' – there is concern that the use of this word for the second time in the space of 11 sentences is nuanced and risks negative bias and messaging.	Thank you for your comment. This has been deleted here.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	034	030	There is concern that a CBT specific component is missing. E.g., 'learning to respond differently to thoughts and feelings associated with ME/CFS with the aim of changing behaviours to improve the use of self-management strategies.'	Thank you for your comment. Recommendation 1.12.30 sets out what CBT involves and includes working closely with their therapist to establish strategies to work towards goals and priorities that they have chosen themselves. The following recommendation includes developing a self- management plan and reviewing strategies.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	037	014	There is concern that the CG53 'setback' terminology has been removed and replaced with 'relapse'. Whilst it is recognised that both are nouns, 'setbacks' as an obstacle has a more hopeful language of something that can be overcome.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	039	021 - 022	As ME/CFS is a fluctuating condition, the management plan should include a 'flexible setback management plan' for long term patient self-management including deteriorating aspects of their condition. This will reduce the number of referrals to specialist services with limited resources adding to the pressure of demand exceeding clinical capacity.	Thank you for your comment. This is included in the care and support plan (see recommendation 1.5.2). To note management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
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Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	040	011	There is a concern that the resources required for ME/CFS specialist services to train non specialist staff will remove resources from outpatient capacity and increase waiting times.	Thank you for your comment. The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. A strong theme from the evidence was the lack of understanding about ME/CFS and training in health and social care professionals and the committee agreed it was important to make recommendations about training. Your comments will also be considered by NICE where relevant support activity is being planned.
Epsom and St Helier University Hospitals NHS Trust – Chronic Fatigue Syndrome Service	Guideline	325	042	There is a concern of the conclusion CBT 'showed no clinical difference'. This is highlighted by an editorial piece in BMJ 16.12.2020 by Turner Stokes & Wade. These authors highlight NICE use of the GRADE system poor applicability to evaluating complex rehabilitative interventions.	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient

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					experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). *NICE methodology and complex interventions* Developing NICE guidelines: the manual. Chapter 4 *Developing review questions and planning the evidence review* addresses the topic about approaches to take when considering the design of studies to be included in a systematic review. In summary the effectiveness of an intervention is usually best answered by a RCT because a well-conducted RCT is most likely to give an unbiased estimate of effects. Where such evidence is not available (for example, where interventions it can be difficult or unethical to assign populations to control and intervention groups). In such cases, a non-randomised controlled trial might be a more appropriate way of assessing association or possible cause and effect. The Medical Research Council (MRC) has produced guidance on evaluating complex interventions (Craig et al. 2008) and using natural experiments to evaluate

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					health interventions delivered at population level (Craig et al. 2011). When developing the protocols for the intervention reviews, a RCT was agreed to be the most appropriate study design to evaluate clinical effectiveness. In recognition that the views of people with ME/CFS who had experienced the interventions was important a qualitative review was done with an accompanying call for evidence to identify any unpublished evidence. In clinical practice a holistic personalised approach to care may typically combine a range of physical, cognitive and psychological approaches depending on patients' needs, preferences and priorities. These may include elements of different intervention varied proportions, incorporated where possible into everyday activities. Current NICE methods do not discount any RCTs of this approach. In ME/CFS the protocol for non-pharmacological interventions includes combinations of treatments (including combinations with pharmacological treatments). Unfortunately, very few RCTs combining any treatments were identified.
F.O.R.M.E.	Equality Impact Assessment	002	3.4	We believe that the preliminary recommendations do make it more difficult for a specific group to access services due to the discrimination against people with ME/CFS who wish to benefit from osteopathic techniques. We ask that the committee omit the "do not offer… therapies derived from osteopathy" recommendation. A patient's management plan may include interventions not yet funded by the NHS but this does not mean that they are any less suitable or successful.	Thank you for your comment. After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. However no evidence was identified to support recommending treatments and osteopathy services for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy.

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				F.O.R.M.E. set up a petition to NICE calling for health equality and patient choice for osteopathy based techniques in the treatment and management of ME/CFS and in just over two weeks has attracted almost a thousand signatures. This reflects the need for healthy equality for people with ME/CFS.	
F.O.R.M.E.	Evidence Review D	148	Table 14	We are concerned about the disregard of the blind controlled study by Hives et al 2017 which demonstrated an 86% accuracy in correctly diagnosing ME/CFS patients using the presence of specific physical signs, without the use of any other clinical data such as case history or symptom picture. The NHS Physician in the study was only able to identify the illness in 44% of the patient group, using standard NHS clinical tests. We ask the committee to review the paper and consider the presence of these signs be explored further, as a cost effective screening tool to aid the clinician in making the correct diagnosis, in addition to the standard clinic methods.	Thank you for your comment. The review question was, 'what are the predictive accuracies of specific clinical symptoms/signs, to identify those who will subsequently be given a clinical diagnosis of ME/CFS?' and not about the effectiveness of screening tools. This is a different question with a different reviewing approach and for this reason the paper was excluded from this review on specific signs and symptoms. In addition, the paper did not include the signs and symptoms the committee had identified to evaluate. The protocol sets out the process for how the committee agreed on the signs and symptoms to be included in this review.
F.O.R.M.E.	Evidence Review G	342	42	With regards to the "do not offer" recommendation of "therapy based on physical activity or exercise therapies derived from osteopathy" - This generalisation about osteopathy based therapies is incorrect and detrimental. Therapies derived from osteopathy are not exercise therapies, nor are they based on physical activity. Osteopathy includes gentle techniques which aim to improve overall joint mobility, muscle flexibility and postural and positional support – all of which are detailed in the draft guidelines management plan for physical maintenance.	Thank you for your comment. Please note that the wording of the recommendations has been amended and Osteopathy has been removed from this section. Considering the worsening of symptoms reported in the qualitative evidence, as well as their experience of the effects of when people exceed their energy limits, the committee concluded that programs involving fixed incremental increases in exercise or that are based on deconditioning as a cause of ME/CFS are not appropriate. However, they acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been acknowledged in the recommendations made to ensure this type of support is available. The committee agree that the way interventions are delivered is crucial and have also included specific recommendations about the content of

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					programmes involving physical activity or exercise as well as for whom such programs should be considered. In developing recommendations on physical activity and exercise, the content, approach and delivery of physical activity management, the committee considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their own.
F.O.R.M.E.	Guideline	008	7	There is evidence, which has not been taken into account by the committee, that an easy to use physical examination can be an effective clinic screening tool to aid diagnosis alongside standard NHS clinic methods, via specific physical signs detailed in the study by Hives et al 2017. Making clinicians aware of these physical signs may allow for an earlier, accurate diagnosis which is paramount for ME/CFS patients. Early diagnosis improves patient outcomes.	Thank you for your comment and information. The committee have not included specific assessments in the physical examination as these are based on clinical judgement and individual to the person's symptoms. In addition any list could not be exhaustive and there is the risk that the examples given are seen as the only assessments to do. For this reason the committee did not add your suggestion.
F.O.R.M.E.	Guideline	028	10	NICE recommend patient choice with regards to the treatment and management of their illness and the committee agree it is important that people with ME/CFS are provided with all the information regarding interventions. Therefore, it is of great concern that this choice is being taken away from ME/CFS patients with the recommendation of "do not offer… therapies derived from osteopathy". We ask that this is omitted from the guidelines to ensure people with ME/CFS have patient choice for management of their own illness. Evidence exists that many ME/CFS patients benefit from osteopathic techniques, such as The Perrin Technique. Osteopathy based treatment addresses and aims to improve overall joint mobility, muscle flexibility, postural and positional support, muscle strength and endurance, cardiovascular health (all of which are included in the management plan detailed on page 26 line 19), as well as aiming to improve central neurological and immune support via the neuro-	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer people with ME/CFS therapies based on the Lightning Process'

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				lymphatic system – which has now been finally proven to exist. To recommend against osteopathic therapies is to remove patient choice, and would remove the option for people with ME/CFS to self-fund their own management and treatment plan.	
F.O.R.M.E.	Guideline	028	10	The following comment has been submitted to F.O.R.M.E. by an individual: I am extremely concerned to read that osteopathy based therapies are not investigated within the draft guidelines for ME/CFS: diagnosis and management. As the NHS states: "osteopathy is a safe and effective form of prevention, diagnosis and treatment of a wide range of health problems" which is why it is a therapy used within and by the NHS. Osteopathy has been proven by research, done in conjunction with three NHS Trusts and published in the BMJ Open in late 2017, to aid diagnosis of ME/CFS, and has been proven by research done by the ME Association to help patients suffering from ME/CFS. NICE 'provides national guidance and advice to improve health and social care' and utilises 'up-to-date policies, procedures and publications'. If that is the case, why is osteopathy not fully investigated within these draft guidelines? And why is the 2017 published research not even mentioned? How can you possibly justify ignoring it? I have personal experience of the efficacy of osteopathy in the treatment of ME/CFS, which I was left with after suffering from Flu B at age 16. After 14 years I thought I would never have a normal life again with enough energy for basic expectations like a family or a job. I was lucky enough to discover the osteopathic treatment called The Perrin Technique. This is not the place to list all the reasons why my very physical response	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer people with ME/CFS therapies based on the Lightning Process'

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				to the treatment convinced me of the validity of the theory – but it is a fact that the very visible swelling of my lymph nodes in reaction to the treatment proved something was draining and the gradual reduction of the swellings over the following year directly correlated with my recovery. After a year of treatment I had recovered enough to be hopeful of a more normal life. After another two years stable at about 90% energy I was able to start a family and have a social life. After eight years I am still stable at about 90% energy. It is not a cure and does not claim to be, to maintain my level health I still do daily stretches and lymphatic massage myself and have a (Perrin Technique) treatment every three months. However, every day I feel so lucky to have stumbled across this treatment, and I am constantly shocked by how little attention is paid to the impact of osteopathy on ME/CFS. Make sure you are not allowing the personal prejudices of any committee members to bias these guidelines and miss out valid research, experiences and treatments. Do not doubt the importance of these guidelines. Not only for sufferers of ME/CFS but it would not be surprising if these guidelines also become of great interest to those suffering from and treating Long Covid, which seems to share many of the same symptoms. If I am right and Perrin's theory and treatment is the key to unlocking post viral illnesses and you fail to explore that, history may not judge you kindly. Don't dismiss what you don't yet understand, it might just end up being the solution. A section to include osteopathy at this point doesn't promise anything but it does leave the door open.	

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
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F.O.R.M.E.	Guideline	028	10	The following comment has been submitted to F.O.R.M.E. by an individual: Please take this as actual evidence of the success of osteopathic treatment having a life-changing positive effect on me, an M.E. sufferer. Nothing else helped, the NICE recommended GET and psychology interventions proved to be damaging, degrading and 'gas lighting'. Thankfully, these have been removed. I eventually was able to fund Dr Perrin to treat me as per his 30 years of successful experience. His explanations of the condition came as a huge relief psychologically, then gradually my physical symptoms started to improve as each month of sustained osteopathic treatment from one of his trained colleagues. I cannot express enough my gratitude to osteopathy and Dr Perrin, and wish his scientific explanation could be made available to all fellow sufferers, even if it's too much to ask the NHS to adopt it as the proven successful treatment that it is.	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer people with ME/CFS therapies based on the Lightning Process'
F.O.R.M.E.	Guideline	028	10	The following comment has been submitted to F.O.R.M.E. by an individual: I would like to let you know that my daughter benefitted greatly from being treated by Raymond Perrin in about 1996. She was very ill and bed bound when she should have been in the sixth form. We had already had a diagnosis (and no treatment of course, except pacing) but Raymond Perrin treated her and showed me how to do the treatment for her at home and for her to do herself. She slowly improved after this and was later able to earn a BSc in Business Studies and then become fully qualified as a Management Accountant. With this treatment she would not have been able to get the qualifications she did. I cannot tell you how huge and serious her illness was and	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer people with ME/CFS therapies based on the Lightning Process'

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				what it meant to us to see her improve and lead a normal life. She still has to be a bit careful about fatigue and I often think some Perrin treatment would do her good now. I am very disappointed that NICE have chosen not to include osteopathy in their guidelines. This is very short sighted of them as it is needed even more now as so many people are suffering from Long Covid. Please NICE, recommend this invaluable treatment that I can personally vouch for, and save the Long Covid sufferers the years my daughter suffered in bed before discovering the Perrin Technique.	
F.O.R.M.E.	Guideline	028	10	The following comment has been submitted to F.O.R.M.E. by an individual: Osteopaths using the Perrin Technique are helping ME patients to improve and recover but are being discriminated by NICE under their new guidelines. Without any scientific proof they declare that patients should not receive Osteopathic treatment for ME/CFS which so many have been helped by this technique. Please support the patients who disagree with the new guidelines.	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer people with ME/CFS therapies based on the Lightning Process'
F.O.R.M.E.	Guideline	028	10	The following comment has been submitted to F.O.R.M.E. by an individual: As a person with M.E. myself and a daughter with M.E. I don't think any treatment should be ruled out unless it is causing harm. Fund research and find out the efficacy rather than rule it out straight away.	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer people with ME/CFS therapies based on the Lightning Process' The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H)

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F.O.R.M.E.	Guideline	028	10	The following comment has been submitted to F.O.R.M.E. by an individual: Without this (Perrin) Technique I wouldn't have much of a life and wouldn't have my two children. It is a travesty it is been covered up by NICE.	Thank you for your comment. After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. However no evidence was identified to support recommending osteopathy treatments, including the Perrin technique for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy.
F.O.R.M.E.	Guideline	028	10	The following comment has been submitted to F.O.R.M.E. by an individual: I have been having the Perrin treatment for my M.E. and without Dr Perrin and his colleagues I would not be able to function to look after my family. The Perrin treatment works and not an anti-depressant in sight. This treatment should be available to all, bring back the missing people.	Thank you for your comment. After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. However no evidence was identified to support recommending osteopathy treatments, including the Perrin technique for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy.
F.O.R.M.E.	Guideline	028	10	The following comment has been submitted to F.O.R.M.E. by an individual: I feel extremely strongly about the inclusion of the Perrin Technique in NICE guidelines for M.E. I have been unable to work since 2005. I have suffered from multiple debilitating symptoms: fatigue, brain impairment to a level of not being able to work, in particular Dysexecutive Syndrome and working memory issues, non-homeostasis of bodily functions such as having hormonal type symptoms akin to hypothyroidism, adrenal fatigue, low metabolism, prediabetes, excessive weight gain, energy crashes, low body temperature going into hypothermic levels and causing cyanosis of face and extremities, blood pressure ranging from 35-140 daily, postural orthostatic tachycardia symptoms that	Thank you for your comment. After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. However no evidence was identified to support recommending osteopathy treatments, including the Perrin technique for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy.

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				lead to fainting and head injuries. I had lost the ability to sweat and would faint if I got hot. My lung age had deteriorated to plus 36 from my chronological age. I honestly thought I would be dead by 60. For years all the NHS did was fill me with anti-depressants. I lost my career, my health, my life, my pension. My children were brought up in poverty when I had a high flying career and they should have had all that I could give them. Instead I was a dysfunctional mother. After 2 car accidents in 2011, I did not seem to recover and my disabilities worsened. I was not responding to rehabilitation treatment and so was sent for a consultant assessment, where I was diagnosed with M.E. and Fibromyalgia. I also suffer from Costochondritis. As I was suffering from dystonias, in particular oromandibular and hand and foot focal dystonia, I sought cerebral spinal osteopathic treatment and I was also receiving physio for my neck and my physiotherapist did some lymphatic drainage alongside. I noticed my M.E./CFS improve somewhat, I began to sweat again over 30 years of impairment, my lung age improved to plus 31 years from 36, but sadly I made no link and unfortunately I had to stop treatment due to the lack of finance and slowly I regressed. In 2016 I asked to see an NHS neuropsychologist at QMC Nottingham, as I thought I must be getting Alzheimer's or early onset dementia and had physical issues relating to my basal ganglia. The Consultant diagnoses Dysexecutive Syndrome but could not ascertain the cause. In 2018 I was unfortunate to be involved with 2 further whiplash accidents and I spiralled into worsened M.E. again. I then discovered success stories about the Perrin Technique. As soon as I heard about the treatment, I realised the reason	

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				for my respite back in 2015 was likely the coincidental treatment of sacral cranial osteopathy and lymphatic draining that I had accidently had simultaneously from 2 therapists. I began treatment in 2019 with Dr Perrin and one of his licensed practitioners. The results were noticeable very quickly. Initially I had scored a 2-3 on the scale of 0-10 used by Dr Perrin (10 being fully fit). He assessed my sympathetic nervous system was dysfunctional. I had lymphoedema in both breasts, my thoracic spine was flattened. All the hallmark signs of his theory and all the contributory symptoms of M.E. After a year I was at a 5 on the scale. Covid has delayed any further therapy for the present. I am much clearer in my thinking. My breathing has improved. My energy levels have begun to increase after 20 years of suffering. I have also taken my daughter as she has now got signs of M.E., after 2 car accidents. She developed a hypothalamus disorder after the first whiplash: a circadian rhythm disorder and became nocturnal. She developed periodic limb movement disorder: a basal ganglia disorder. She has Asperger's Syndrome and I noticed her impairment of Executive Functioning Skills had increased. Her fatigue levels were excessive. She was struggling to work. I had her assessed. She was at a 6 (on the Perrin scale) and has breast lymphatic draining issues, thoracic spine dysfunction, and sympathetic nervous system dysfunction. I have recommended the Perrin Technique to my sister, who also has M.E. All of my family has joint hypermobility issues. We fit the Perrin diagnostic criteria to the letter. We have so	

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				many issues and the Perrin Technique has been the only successful diagnosis and intervention I have ever had. I feel as though I have my life back, even though I have further to go. Please it is imperative that you do not ignore Dr Perrin's research or his treatment protocol. It could help so many M.E. patients.	
F.O.R.M.E.	Guideline	028	10	The following comment was submitted to F.O.R.M.E. by an individual: My daughter was diagnosed with CFS/ME when she was 11. At first we were offered no treatment at all. Then she was offered CBT through the hospital children's department, who also referred her for physiotherapy. The physiotherapist recommended GET which only made my daughter feel worse. The CBT had not effect on her symptoms and my daughter ended up missing a large amount of schooling. It was only by chance, when my daughter was 15, that a colleague mentioned the Perrin Technique to me. As my daughter had made no improvement since first being diagnoses we decided to give the Perrin Technique a try. Once she started the treatment her symptoms began to improve, so much so that she was able to go to sixth form college and University (being symptom free whilst at University).	Thank you for your comment. After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. However no evidence was identified to support recommending osteopathy treatments, including the Perrin technique for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy.
F.O.R.M.E.	Guideline	028	10	The following comment was submitted to F.O.R.M.E. by an individual: I have really benefitted from having the Perrin Technique over the past year, having been unwell with M.E. for over 15 years. Before lockdown (2020) I was enjoying the best health since being unwell. However, not being able to have the treatment during lockdown had a significant effect on my health.	Thank you for your comment. After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. However no evidence was identified to support recommending osteopathy treatments, including the Perrin technique for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy.

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				I hope that the draft NICE guidelines will be changed, as the Perrin Technique has made a significant improvement to my health.	
F.O.R.M.E.	Guideline	028	10	The following comment was submitted to F.O.R.M.E. by an individual: I have just read the post on Facebook regarding the NICE recommendations and I wanted to offer my support for the use of osteopathy in the treatment of ME/CFS. I was 15 when I was first diagnosed with ME and the first treatment which helped me was when I started the Perrin Technique aged 19. As I also suffer from hypermobility, the treatments helped to align my spine and offer some relief from the pain I was also experiencing in my joints. The lymphatic drainage element of the treatment also made significant contributions to the management of my symptoms. Whilst initially the drainage made me feel worse, once the blockages had been removed in my lymph nodes I began to experience an upsurge in energy and a reduction in symptoms, especially in headaches and the level of fatigue. Now that I am in control of my health, I know that as soon as I begin to experience symptoms again I must go and be treated following the Perrin technique to get me back on an even keel again. I do hope that this information can be of use in your recommendations to NICE. If you require any further detail, please do contact me. Thank you for all the research you are doing into this condition – it has the potential to be life changing for so many.	Thank you for your comment. After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. However no evidence was identified to support recommending osteopathy treatments, including the Perrin technique for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy.

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F.O.R.M.E.	Guideline	028	10	The following comment has been submitted to F.O.R.M.E. by an individual: Having seen the latest draft of the NICE guidelines I would like to register my disappointment in their dismissive action towards Osteopathic treatment for M.E. I was diagnosed at 11 years old and had 7 years of NHS Paediatric M.E. 'treatment' which left me wheelchair bound, unable to stand and in incredible pain all the time. By age 18 I was classed as having extremely severe M.E. and needed 24 hour care – I honestly thought I was going to die. I found the Perrin Technique by chance and it changed my life. I went from being in awful pain, unable to move or look after myself to walking, driving and having a job in a year. The Perrin Technique not only saved my life, but it gave me a life for the first time since I was 11 years old. It allowed me to meet my husband and have my beautiful sons. I am appalled that this treatment is being discriminated against and tarred with the same brush as the Lightning Process.	Thank you for your comment. After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. However no evidence was identified to support recommending osteopathy treatments, including the Perrin technique for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy.
F.O.R.M.E.	Guideline	028	17	This statement goes against NICE's own guidance of not discriminating against different members of the Allied Health Profession, by singling out treatment from physiotherapists and occupational therapists only. We ask that this be rectified to include osteopaths. Osteopathy aims to improve overall joint mobility, muscle flexibility and postural and positional support – all of which are included in the management plan detailed in these draft guidelines.	Thank you for your comment. After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. However no evidence was identified to support recommending treatments and osteopathy services for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy.
Faculty of Occupational Medicine	Guideline	027 - 28	Section 1.11.6	We do not agree with this statement: Advise people with ME/CFS to reduce their activity if increasing it triggers symptoms, or if they have fluctuations in their daily energy levels.	Thank you for your comment. After considering the stakeholder comments this has been edited to,' Advise people with ME/CFS how to manage flare-ups and

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				When returning to work it is important that health care professionals give reassurance that an increase in symptoms on return to work is unlikely to mean harm in most people. Reference: Waddell G, Burton AK. Concepts of rehabilitation for the management of common health problems: The Stationery Office; 2004.	relapses (see the section on managing flare-ups in symptoms and relapse).'
Faculty of Occupational Medicine	Guideline	021	Section 1.9.1	We are concerned that this recommendation may increase fear avoidance beliefs about returning to work. We would prefer NICE to give ME/ CFS sufferers the following guidance: • Work is generally good for health. • Work provides purpose, boosts self-esteem and enables financial independence. • Worklessness is associated with poor physical and mental health and increased risk of self-harm • Ask the person what they believe are the main factors impeding their return to work. • Ask them if they can identify solutions to their return to work obstacles • Do they need adjustments to their work to enable them to return (e.g. flexible hours/ working from home/special equipment)? • Encourage them to liaise with their employer to see if the adjustments could be facilitated • If they need assistance with paying for any adjustments, they or their employer may be eligible for financial assistance from Access to Work (https://www.gov.uk/access-to-work)	Thank you for your comment and information. After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support. ' and discuss with' has been added to the recommendation. The discussion points you have raised have been summarised and added to the committee discussion in evidence review A.

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				- Ask if they have access to occupational health advice via their work; if they do encourage them to make contact with their occupational health department References - Black C. Working for a healthier tomorrow. Dame Carol Black's Review of the health of Britain's working age population. Norwich UK: TSO (The Stationary Office); 2008. - Health matters: health and work. PHE, 2019	
Faculty of Sport and Exercise Medicine (UK)	Guideline	General	General	We welcome this guideline review as the management of these cases is both complex and challenging. As with most complex illness the keys to successful management are the use of an appropriately trained multi-disciplinary team working with the patient to achieve their personalised goals. However, we are concerned that the approach advocated in this guidance is largely negative - disproportionately advocating rest and inactivity and abandoning an approach for which there is evidence. In particular, physical activity GET and CBT are dismissed – or down-graded in their importance. Instead, there is a tendency to refer to committee members 'personal experience' as a source of evidence. It is inappropriate to replace evidence from RCTs – however limited - with personal opinion. This clearly exposes the review to significant bias, not least confirmation bias, if the view	Thank you for your comment. The committee agree that the keys to successful management are the use of an appropriately trained multi-disciplinary team working with the patient in developing and implementing a personalised care and support plan and this has been recommended in the guideline. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations included the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.)

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				comes from sufferers who have not responded to interventions in the last NICE guidance and the views of those who have are not consulted. The removal of GET, and physical activity in general, leads to fundamental problems in treating this group of patients	The guideline is clear that there is no current cure for ME/CFS but there are strategies and treatments available to support symptom management, including specialist support for physical activity and exercise. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception and no evidence was exclude that fitted the protocol inclusion criteria. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee. For further information on GRADE see the methods chapter. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee included members with clinical and personal experience of children and young people with ME/CFS. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See

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					Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). This guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS.
Faculty of Sport and Exercise Medicine (UK)	Guideline	General	General	*Which areas will have the biggest impact on practice and be challenging to implement*?' The guidance focuses on what not to do – it does not give clear guidance on what can be done. It excludes physical activity and provides only rest as an alternative. This approach is known to be ineffective and often highly dangerous in every other disease state – why should it be different in this illness alone? These recommendations are contrary to those of the WHO guidance on physical activity in relation to heath and chronic conditions (World Health Organization 2020 guidelines on physical activity and sedentary behaviour)	Thank you for your comment. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The four symptoms (debilitating fatigue, PEM, unrefreshing sleep and cognitive difficulties) were agreed by the committee as the best basis for identifying people with ME/CFS and as essential to a diagnosis of ME/CFS. The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). The definition on physical activity references the World Health Organisation advice on physical health and notes that in people with ME/CFS physical activity may make their symptoms worsen. The management sections of the guideline include recommendations:

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					• to support people with energy management • to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or programme into the management of their ME/CFS. and are options for the management plan where appropriate. To accompany this the committee have made recommendations that set out how strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. See evidence reviews G and H for the evidence and the committee discussion on these recommendations. After considering the stakeholder comments about the lack of clarity around what the guideline recommends on energy management and physical activity and exercise the committee made the following edits: • on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. • the section on physical activity now includes exercise • Made clear that a personalised collaborative physical activity or exercise programme includes making flexible adjustments to their physical activity (up and down as needed). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity

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					and exercise programmes. This guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Faculty of Sport and Exercise Medicine (UK)	Guideline	General	General	The sole justification for this approach appears to be that the condition is wholly different to every other – including fatigue after other illness and injury, chronic pain, cancer, cardiovascular disease, brain injury and stroke etc For any group attempting to treat these patients there are now no logical approaches available. If there was no evidence for treatment in any other condition, we would revert to best practice and the standard approaches used in similar conditions. We would adopt therapies such as GET and CBT but this guidance constrains their use for no clear, evidence-based reason. Fundamentally, this guidance abandons the first principles of rehabilitation and advocates that we do nothing other than try to prevent decline. However, it restricts the fundamental tools	Thank you for your comment. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The four symptoms (debilitating fatigue, PEM, unrefreshing sleep and cognitive difficulties) were agreed by the committee as the best basis for identifying people with ME/CFS and as essential to a diagnosis of ME/CFS. The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail).

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				which we use to prevent decline in every other condition – mainly physical activity.	
Faculty of Sport and Exercise Medicine (UK)	Guideline	General	General	The implication in the guidance is that the prognosis is poor – although no data is produced to support this. It is clear that it is poor if untreated and these guidelines essentially advocate support rather than treatment.	Thank you for your comment. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations included the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.) The guideline is clear that there is no current cure for ME/CFS but there are strategies and treatments available to support symptom management.
Faculty of Sport and Exercise Medicine (UK)	Guideline	General	General	This is of particularly vital importance following the consequences of the Covid pandemic – as many cases of post viral fatigue are presenting. This guidance will constrain even experimental approaches to the management and rehabilitation of these cases and could have a significant detrimental effect to large groups of the population. The potential detrimental effects of this new guidance could be significant.	Thank you for your comment. The guideline states it was developed before the COVID-19 pandemic. The committee review the evidence relevant to the key areas of the scope and the recommendations were developed based on evidence reviewed before the COVID-19 pandemic. The committee have not reviewed the evidence on COVID-19 and are not in a position to comment or make recommendations in this area either about the long term recovery from COVID-19.
Faculty of Sport and Exercise Medicine (UK)	Guideline	General	General	The language used to describe the concepts of physical activity, exercise GET etc are not those commonly in exercise physiology, exercise medicine or rehabilitation and are – at times – archaic.	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms.

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				Terms such as 'exercise envelope' and post-exercise malaise are consequently unhelpful and express unscientific concepts.	• *Energy envelope to energy limits*. The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms. • *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS. The definition of physical activity is referenced using the [World Health Organization advice on physical activity](). Graded exercise therapy is used in reference to the intervention called graded exercise therapy that has been implemented with people with ME/CFS.
Faculty of Sport and Exercise Medicine (UK)	Guideline	General	General	Fatigue is a normal response to physical activity – it is not a pathological consequence. That fatigue is worsened after illness of any nature is well recognised. Inactivity usually worsens that sense of fatigue. Gradual progressive activity usually improves it. The key to prescribing physical activity is that it needs to be individualised, it needs to be recognised that physiological adaptation is specific to the activity, requires to be progressive and use the principle of overload (increasing resistance/time/intensity). There needs to be appropriate recovery time and that if you don't keep exercising the effects are reversible and lead to deconditioning. There are no references in this guidance to these – basic – principles and	Thank you for your comment. Although it is widely accepted that fatigue is a normal consequence of physical activity in many people, the response to activity in people with ME/CFS is different, out of proportion to the precipitating activity and characterised by PEM. PEM is not, as you suggest in another comment, an archaic term, but is widely accepted in the specialist ME/CFS literature as a characteristic feature of ME/CFS. The four symptoms (debilitating fatigue, PEM, unrefreshing sleep and cognitive difficulties) are recognised throughout the literature and were agreed by the committee as both the best basis for identifying people with ME/CFS and as essential to a diagnosis of ME/CFS. The committee emphasised it is the combination and

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				no suggestion of an understanding of them. Indeed, this illness appears to be the only condition to which these principles do not apply. And again	interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). The committee also agree that a physical activity needs to be individualised and have recommended a personalised collaborative physical activity or exercise programme for people with ME/CFS who:. • feel are ready to progress their physical activity beyond their current activities of daily living or • would like to incorporate physical activity or exercise into managing their ME/CFS. However they specifically rejected the use of programmes based on deconditioning as the cause of ME/CFS.
Faculty of Sport and Exercise Medicine (UK)	Guideline	007	26	Whereas we recognise the importance of a holistic approach to the diagnosis and management of patients with this condition assertions such as; '*Common themes across the qualitative evidence showed a lack of belief about ME/CFS as a real condition by health and social care professionals, and a lack of understanding about what it is and the impact it has. The committee used this evidence to make recommendations to raise awareness about ME/CFS*.' - need to be more clearly evidenced and placed in the context in which they are expressed. Is this a group in which their treatment approach has been inappropriate and ineffective or is it a universal response – indicative of all sufferers. We accept this has been the case for some, but we do not accept that this is been universally so, for example those who	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of

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				have recovered, either spontaneously or with help from CFS services? NICE has not included any service evaluation data but relied on surveys from membership organisations, a methodology which NICE agrees over represents those who have not improved either with or without treatment. This opening statement should be contextualised	the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). *Inclusion of evidence* All evidence that met the inclusion criteria in the protocols has been included. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach before the data is collected. See [Developing NICE guidelines: The manual]for more detail on review methods.
Faculty of Sport and Exercise Medicine (UK)	Guideline	008	17	*Post-exertional symptom exacerbation. The worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated.* *also referred to as post-exertional malaise* As stated previously fatigue is a normal consequence of physical activity. The key in any exercise-based rehabilitation programme is not to avoid fatigue but work within the limits of fatigue to gradually increase exercise tolerance and physical conditioning.	Thank you for your comment. PEM* is not the same as fatigue and there are definitions of PEM and(debilitating) fatigue in the terms used in the guideline. It is commonly agreed that people with ME/CFS can experience post exertional malaise (PEM) after activity. PEM is a worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated. It is in this context, and recognising the evidence from people with ME/CFS indicating that misunderstanding of the impact of PEM and inappropriate advice on how to incorporate physical activity (and exercise) into their lives has resulted for some in a deterioration of their condition, this guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility

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					• feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. **Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.
Faculty of Sport and Exercise Medicine (UK)	Guideline	009	21	*When ME/CFS is suspected, continue with any tests needed to exclude other conditions and explain to people that this does not affect their provisional diagnosis of ME/CFS.* There is a lack of clarity over the diagnostic criteria for ME/CFS. What is missing is any reference to mental health issues and particularly depression. In addition, the approach advocated above suggest that the diagnosis should be assumed prior to excluding other conditions which is counter intuitive and contrary to good medical practice.	Thank you for your comment. After considering the stakeholder comments on early diagnostic labels the committee have amended the wording to remove the recommendation on making a provisional diagnosis of ME/CFS. Diagnosis is now introduced at 3 months.

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Faculty of Sport and Exercise Medicine (UK)	Guideline	010	17-20	Patients are advised '*….not to use more energy than they perceive they have − they should plan their daily activity to stay within their energy envelope and not push through activity to rest as they need to'* The concept of the energy envelope is not one used out with a particular section of the CFS/ME literature. We are unaware of what the physiological basis of this concept is. We are concerned by the frequent reference to it being a fixed quantity. The principle of physiological adaptation to exercise is that by a process of progression and 'overload' exercise tolerance and physical performance increases. It is true that progression needs to be carefully monitored and the programme adjusted in accordance with the patient's response, to avoid overtraining and subsequent underperformance. However, the concept advocated will, at best, lead to a failure progress their exercise tolerance and at worse lead to a deterioration	Thank you for your comment. After considering the stakeholder comments the committee agreed that this concept and energy envelope* might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. The committee agreed that people should be given personalised advice about managing their symptoms and recommend this in the advice for people with suspected ME/CFS section of the guideline. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit Energy envelope to use energy limits.
Faculty of Sport and Exercise Medicine (UK)	Guideline	014	19	*'..often involves periods of remission and relapse, although it is less common to have long periods of remission (see the section on managing flares and relapse)'* What is the evidence behind this statement?	Thank you for your comment. After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS. See evidence review A for the committee discussion on information about the long term outlook for people with ME/CFS
Faculty of Sport and Exercise Medicine (UK)	Guideline	016	6	The Faculty has considerable concern over the safeguarding guidance, which in many places are contrary to good practice in safeguarding and the training which clinicians and non-clinicians currently receive. The additional comments made on	Thank you for your comment. The committee agreed that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the

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				safeguarding are unhelpful and potentially risky for vulnerable adults and children. *'Safeguarding assessments in people with confirmed or suspected ME/CFS should be carried out or overseen by health and social care professionals who have training and experience in ME/CFS.'* The principles of safeguarding are that **anyone** with concerns should raise them to the appropriate authority. This guidance suggests that only specialists can be concerned, which is inaccurate and dangerous. It might discourage people from speaking up.	recommendations in the training for health and social care professionals section of the guideline. With regard to Safegaurding the importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The NICE guidelines on child maltreatment and child abuse and neglect should be followed. This is clear that if a professional has concerns they should be addressed in the same way as with any child or young person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
Faculty of Sport and Exercise Medicine (UK)	Guideline	016	9	*'Recognise that people with ME/CFS, particularly those with severe or very severe ME/CFS, are at risk of their symptoms being confused with signs of abuse or neglect.'* Are we to infer that these cases should not have the same high standard of safeguarding principles applied to them that other patients have?	Thank you for your comment. This recommendation raises awareness about the difficulties that some people with ME/CFS have experienced where safeguarding concerns have been raised. The committee agree that people with ME/CFS should have the same high standard of safeguarding principles applied to them that other patients have.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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Faculty of Sport and Exercise Medicine (UK)	Guideline	017	8	*'Recognise that the following are not necessarily a sign of abuse or neglect in children and young people with confirmed or suspected ME/CFS:* • *physical symptoms that do not fit a commonly recognised illness pattern* • *more than 1 child or family member having ME/CFS* • *disagreeing with, declining or withdrawing from any part of their* • *management plan, either by the child or young person or by their* • *parents or carers on their behalf* • *parents or carers acting as an advocate and communicating on behalf* • *of the child or young person* • *reduced or non-attendance at school'* But they may be and the presence of ME/CFS should not allow genuine concerns to be dismissed.	Thank you for your comment. The importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The principle applies to adults. This is clear that if a professional has concerns they should be addressed in the same way as with any person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
Faculty of Sport and Exercise Medicine (UK)	Guideline	017	8	'*No evidence was identified on safeguarding in ME/CFS, but the committee agreed it was very important to make.... recommendations based on consensus.'* Without evidence there is no reason to produce different guidance from the standard. These are likely to be interpreted as being contrary to good safeguarding practice and training.	Thank you for your comment. These recommendations are to raise awareness about the difficulties that some children and young people and their families have experienced when safeguarding concerns have been raised. The importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative

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					consequences particularly for children and young people, and their families. The committee disagree they are likely to be interpreted as contrary to safeguarding practice and training. Recommendation 1.7.5 is 'that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability.' The NICE guidelines on child maltreatment and child abuse and neglect are cross referred to. This is clear that if a professional has concerns they should be addressed in the same way as with any person Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
Faculty of Sport and Exercise Medicine (UK)	Guideline	022	17	*'self-management strategies, including energy management* *A self-management strategy that involves managing a person's activities to stay within their energy envelope'* This is not an established concept in exercise physiology or exercise medicine	After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
Faculty of Sport and Exercise Medicine (UK)	Guideline	024	4	*'Be aware there is no current treatment or cure (non-pharmacological or pharmacological) for ME/CFS.'* Evidence for this?	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a

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					range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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					However the committee agree there currently isn't a cure for ME/CFS and it is important that people with ME/CFS are aware of this. As you note the rationale provides further information about avoiding claims that interventions will cure ME/CFS. For this reason, the committee have not further edited the recommendation.
Faculty of Sport and Exercise Medicine (UK)	Guideline	024	7	*'Energy management'* This appears to advocate reducing the patient's activity to fit with their tolerance – which is counter to the approach we use in every other condition, whereby we careful tailor their activity to gradually increase their exercise tolerance and self-management. This is not easy and requires expertise, which also engages the principles of pacing, but is the standard treatment in all other diseases	*Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). The approach is to reach stabilisation and then increase after periods of stability where possible. Energy management is part of the care and support plan and developed with a ME/CFS specialist team.
Faculty of Sport and Exercise Medicine (UK)	Guideline	024	21	*'uses a flexible, tailored approach so that activity is never automatically increased but is progressed during periods when*	Thank you for your comment.

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				symptoms are improved and allows for the need to pull back when symptoms are worse' It is important that physical activity should be tailored to the individual and progressed accordingly. Automatically increasing the physiological demand, without reference to the patient's condition is unlikely to be effective. However, the rest of the sentence abandons the principle of pacing – which is key to the management of this and many other chronic conditions requiring rehabilitation	After considering the stakeholder comments this bullet point has been edited to,' uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse).
Faculty of Sport and Exercise Medicine (UK)	Guideline	025	3	*'does not assume that deconditioning is the cause of ME/CFS'* But this approach – encouraging inactivity - will inevitably lead to deconditioning and harm; from other diseases such as diabetes, CV disease, accelerated sarcopenia and osteoporosis	Thank you for your comment. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility. In the physical functioning and mobility section of the guideline the committee recommend that strategies to maintain and prevent the deterioration of physical functioning and mobility should be included in the care and support plans for people with ME/CFS. Areas for consideration include cardiovascular health and bone health.
Faculty of Sport and Exercise Medicine (UK)	Guideline	025	18	*'reduce activity as the first step'* Why – usually the first step would be a reassessment of the situation? This would be followed by adjustment of the programme which might lead to a temporary reduction in activity of it might not.	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to, agree a sustainable level of activity as the first step, which may mean reducing activity.'

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Faculty of Sport and Exercise Medicine (UK)	Guideline	026	9	*'Refer people with ME/CFS to a specialist ME/CFS physiotherapy or occupational therapy service.'* Access is a significant issue also. If this guidance is published they will have no treatment modalities available to use on these patients	The management sections of the guideline include recommendations: • to support people with energy management • to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or programme into the management of their ME/CFS. • to offer CBT to help people manage their symptoms and to reduce the distress associated with having a chronic illness and are options for inclusions in the care and support plan where appropriate and chosen by the person with ME/CFS. To accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. See evidence reviews G and H for the evidence and the committee discussion on these recommendations.
Faculty of Sport and Exercise Medicine (UK)	Guideline	027	3	*'Assess people with severe or very severe ME/CFS at every contact for:* • *areas at risk of pressure ulcers* • *deep vein thrombosis* • *risk of contractures.'* The uncritical advocating of rest and inactivity will increase these risks	Thank you for your comment. The committee note that this recommendation refers to people with severe or severe ME/CFS with very limited mobility.
Faculty of Sport and Exercise Medicine (UK)	Guideline	027	21	*'Do not advise people with ME/CFS to undertake unstructured exercise that is not part of a supervised programme, such as telling them to go to the gym or exercise more, because this may worsen their symptoms.'*	Thank you for your comment. The committee agree there is little dispute amongst clinicians working with people with ME/CFS that they should not undertake

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				The principles of rehabilitation are that we empower people to take responsibility for their recovery and the other elements of their lives. Part of an appropriate rehabilitation plan is the direction of physical activity by those expert in exercise-based rehabilitation. But a significant part is to equip patients to take responsibility for their own programme through self-management. Provided this is done at the right time with the right guidance it is safe and effective. This piece of guidance is disempowering and potentially harmful and lacks any evidence base.	exercise that is not part of a programme overseen by a ME/CFS specialist team, such as telling them to go to the gym or exercise more. It is commonly agreed that people with ME/CFS experience post exertional malaise (PEM) after activity. PEM is a worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated. It is in this context, and recognising the evidence from people with ME/CFS indicating that misunderstanding of the impact of PEM and inappropriate advice on how to incorporate physical activity (and exercise) into their lives has resulted for some in a deterioration of their condition, that this guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS.
Faculty of Sport and Exercise Medicine (UK)	Guideline	027	24	*'Do not offer people with ME/CFS: any therapy based on physical activity or exercise as a treatment or cure for ME/CFS generalised physical activity or exercise programmes – this*	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations.

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				includes programmes developed for healthy people or people with other illnesses, any programme based on fixed incremental increases in physical activity or exercise, for example graded exercise therapy structured activity or exercise programmes that are based on deconditioning as the cause of ME/CFS, therapies derived from osteopathy, life coaching and neurolinguistic programming (for example the Lightning Process).' This judgment appears to have been made by excluding most of the RCTs supporting physical activity Previous NICE guidelines included the significant benefits gained from Graded Exercise Therapy. However, in this review 28 out of 30 CBT and GET trials were excluded which has limited the use of this evidence, frequently replaced by 'personal opinion'. Much of the evidence in review G, despite being graded highly in 2007, was graded as poor quality this time. The explanation for this is not clear. The PACE RCT Lancet trial in 2011 showed benefits of both CBT and GET. The study end point was at 52 weeks where there was a clear benefit. When followed at 135 weeks there was no difference in the groups because after 52 weeks people were free to take up the alternative treatments. The paper concluded that the gains of GET and CBT were maintained, but the two other groups caught up. However, this information has been excluded. Furthermore, by mandating in the Methods section that the outcomes should be taken from the longest period of follow up, the actual finding	Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about

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				of the trial, the one year endpoints, is excluded. This cannot be justified.	experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that

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					may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *Methods* This guideline has updated the 2007 guideline using Developing NICE guidelines: the manual Process and methods [PMG20] Published: 31 October 2014 Last updated: 15 October 2020. The process for quality rating now used in NICE guidance is an internationally agreed process (see the methods chapter for information on GRADE and CERQual). *Data excluded* *No study was excluded that met the review protocols. We think your point refers to* the decision by the committee to downgrade evidence that did not use a diagnostic criteria that includes post exertional malaise (PEM) as essential. PEM is widely acknowledged in ME/CFS specialist practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just do not know how many if the information is not reported. Where this is the case, the trial population could include people that do not have ME/CFS and this makes it difficult for the

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					committee to be confident of the benefits and risks of the interventions on people with ME/CFS. Using GRADE and CERQual the committee agreed that evidence without this information would be 'indirect' (relevance in CERQual) acknowledging this uncertainty about the population. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and CERQual. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative and qualitative evidence and the application of indirectness and relevance. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) *Follow up* Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.

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Faculty of Sport and Exercise Medicine (UK)	Guideline	028	5	There is frequent reference ME/CFS not being caused by deconditioning. No one claims that it is, so this is misleading and should be dropped. On the other hand no mention is made as to how deconditioning can and does occur as a consequence of ME/CFS. The strong advocacy of rest as the mainstay of management will inevitably lead to it. Furthermore, inactivity leads to significant - possibly life-threatening - consequences such as sarcopenia, osteoporosis and pressure sores.	Thank you for your comment. The committee have concluded that therapies based on deconditioning and exercise avoidance theories of chronic fatigue syndrome should not be offered to people with ME/CFS. These therapies assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. The committee recommended that strategies to maintain and prevent deterioration of physical functioning and mobility be included in support plans for people with ME/CFS . To note after considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.
Faculty of Sport and Exercise Medicine (UK)	Guideline	028	16	*'A physical activity programme, if offered, should only be delivered or overseen by a physiotherapist or occupational therapist with training and expertise in ME/CFS.'* This is impractical and contrary to the principles of rehabilitation, patient empowerment and ownership of their own goals	Thank you for your comment. Based on the quantitative and qualitative evidence * and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed

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					that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
Faculty of Sport and Exercise Medicine (UK)	Guideline	028	23	*'If a physical activity programme..... start by reducing the person's activity to within their energy envelope be possible to maintain it successfully before attempting to increase physical ability'* It is not logical to place a blanket direction on people's activity levels. It may be appropriate to regress activity and reassess their programme but there is no reason reduce the activity without appropriate assessment	Thank you for your comment. This is the recommendation for the personalised collaborative physical activity or exercise programme and the assessment will have been done for this by a physiotherapist of occupational therapist within a specialist ME/CFS team.
Faculty of Sport and Exercise Medicine (UK)	Guideline	034	2	*'Do not offer CBT as a treatment or cure for ME/CFS'* CBT is not offered as a cure but can be a very important factor in the management of this and other chronic conditions CBT helps some of the core symptoms of ME/CFS, so why should it not be considered a treatment?.	Thank you for your comment. To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative.

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					CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.
Faculty of Sport and Exercise Medicine (UK)	Guideline	044	14	*'Physical maintenance* *For some people with ME/CFS it can include physical activity which additionally assists bone health, posture and muscle strength. Such activity is undertaken within the person's energy envelope and avoids pushing through boundaries of tolerance'* Not a widely accepted concept in exercise-based rehabilitation. It is contrary to the established principles of physical training.	Thank you for your comment. *Physical maintenance* After considering the range of stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility. The committee agreed this was very important for people with ME/CFS with prolonged limited mobility.
Faculty of Sport and Exercise Medicine (UK)	Guideline	056	1	*'The recommendations will improve consistency of best practice and do not need any additional resources to deliver.'* To the contrary, they are inconsistent with standard practice and will hence cause confusion and possibly harm	Thank you for your comment. These recommendations are to raise awareness about the difficulties that some children and young people and their families have experienced when safeguarding concerns have been raised. The importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. The committee disagree these recommendations will cause confusion and harm. Recommendation 1.7.5 is 'that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected

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					ME/CFS as with any child with a chronic illness or disability.' The NICE guidelines on child maltreatment and child abuse and neglect are cross referred to. This is clear that if a professional has concerns they should be addressed in the same way as with any person Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
Faculty of Sport and Exercise Medicine (UK)	Guideline	063	1	'*Because of the harms reported in the qualitative evidence*' No evidence of serious adverse effects have been proven in the quantitative evidence, and the harm of inactivity in this context is not being reported or considered. There needs to be a recognition of the difference between true lasting harm being caused and the temporary exacerbation of symptoms – which is a common consequence of any rehabilitation programme. The latter will not lead to long-term harm and is an example of a side effect of treatment which would be tolerated if this was a pharmacological intervention.	Thank you for your comment. The effectiveness of an intervention is usually best answered by a RCT because a well-conducted RCT is most likely to give an unbiased estimate of effects. The committee agreed there needs to be better reporting and long-term data collection of harms in RCTs. The difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials is not disputed (for example see https://bmjopen.bmj.com/content/9/2/e024537). Notwithstanding this, it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. Ideally this takes both a quantitative and qualitative approach and includes the experiences and opinions of all people who have had the intervention, patient experience is invaluable. In recognition that the views of people with ME/CFS who had experienced the interventions was important a qualitative review was done with an accompanying call for evidence to identify any unpublished evidence. People with ME/CFS reported harms in the qualitative evidence.

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					As with all NICE guidelines the committee uses its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation.
Faculty of Sport and Exercise Medicine (UK)	Guideline	063	1	*'as well as the **committee's experience** of the effects when people exceed the limits, the committee recommended that people with ME/CFS should not undertake a physical activity or exercise programme unless it is delivered or overseen by a physiotherapist or occupational therapist who has training and expertise in ME/CFS. The **committee reinforced there is no therapy based on physical activity or exercise that is effective as a treatment or cure for ME/CFS.*** This is an opinion	Thank you for your comment. It is acknowledged that people with ME/CFS experience post exertional malaise (PEM) after activity. PEM is a worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated. It is in this context, and recognising the evidence from people with ME/CFS indicating that misunderstanding of the impact of PEM and inappropriate advice on how to incorporate physical activity (and exercise) into their lives has resulted for some in a deterioration of their condition, that this guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they wish to explore a physical activity or exercise programme. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS.
Faculty of Sport and Exercise Medicine (UK)	Guideline	063	1	*'In developing more specific recommendations on the content, approach and delivery of physical activity management, the committee **considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their own experiences** of these types of interventions.*	Thank you for your comment. The effectiveness of an intervention is usually best answered by a RCT because a well-conducted RCT is most likely to give an unbiased estimate of effects. The committee agreed there needs to be better reporting and long-term data collection of harms in RCTs. The difficulties with

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				This is no evidence of harm	the collection, analysis and reporting of adverse events in randomised controlled trials is not disputed (for example see https://bmjopen.bmj.com/content/9/2/e024537). Notwithstanding this, it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. Ideally this takes both a quantitative and qualitative approach and includes the experiences and opinions of all people who have had the intervention, patient experience is invaluable. In recognition that the views of people with ME/CFS who had experienced the interventions was important a qualitative review was done with an accompanying call for evidence to identify any unpublished evidence. People with ME/CFS reported harms in the qualitative evidence. As with all NICE guidelines the committee uses its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation.
Faculty of Sport and Exercise Medicine (UK)	Guideline	063	1	***They recommended not to offer any programme based on fixed incremental physical activity or exercise,*** *for example graded exercise therapy or structured activity or exercise programmes that are based on deconditioning as the cause of ME/CFS.* *In the* ***committee's experience****, people with ME/CFS have had varying results from physical activity programmes and they thought it was important to discuss this with people with ME/CFS and talk to them about the possible risks and benefits. The*	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that

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				committee outlined what a personalised physical activity plan should look like based *on **their experience.'*** In all the areas highlighted it would appear that personal opinion and 'experience' is the sole ground for recommendations which is unusual and potentially controversial for NICE guidance.	were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This, when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.)

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Faculty of Sport and Exercise Medicine (UK)	Guideline	063	21	*'a specialist physiotherapist or occupational therapy service may need increase resources; however, this should not impose a significant cost on the NHS and if it leads to fewer people with deteriorating symptoms, it will be highly cost effective.'* New therapy resources will inevitably impose costs on the NHS – particularly when therapy services are under pressure It is a step too far to say that this will highly cost effective as, patient numbers and the benefits have not been described, nor the costs itemised – therefore any measure of cost utility is purely speculation. Particularly when any therapist will have limited therapeutic tools if this guidance is put in place. The proposed shortening of the duration criteria for the diagnosis of ME/CFS will clearly increase numbers and costs.	Thank you for your comment. The reason that we have stated that this will not impose a significant cost to the NHS is that this is in the context of graded exercise therapy no longer being recommended. We agree that it is speculative to say that this will be highly cost effective, but that is why it is contained within a conditional statement. The diagnostic criteria are slightly stricter than in the previous guideline, although the duration of symptoms in adults has been reduced by one month to be consistent with children. Since the committee have now removed reference to a provisional diagnosis and made recommendations about testing for alternative conditions, the demand on services should not be so great.
Healthwatch Bolton	Guideline	General	General	We welcome the long overdue replacement of the 2007guidelines.We recognise and are thankful for the hard work put in by the committee and others (especially during the pandemic), and the willingness to critically examine inappropriate and harmful advice in the previous guidelines. We are particularly heartened to see the acknowledgement that so much of the evidence for Graded exercise therapy and cognitive behavioural therapy is of low or very low quality. We hope the new guideline will offer all sufferers more protection from the harm caused by current damaging regimens, to all sufferers, especially the vulnerable and children.	Thank you for your comments. Terms used in the guideline After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms. *Pacing*

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				Finally, we feel that the patient community is being listened to. That medical research can progress forward without being restricted by previous harmful psychiatric/ psychological domination and bias. We are particularly pleased that graded exercise therapy has been removed, and that cognitive behavioural therapy has been acknowledged as non-curative.We just hope that the spectre of graded exercise therapy does not rear it's ugly head under the guise of sleep management regimens, exposure to light and noise and graded school attendance for example. That and there is no misappropriation of the terminology activity or energy management to be used as graded exercise therapy as a wolf in sheep's clothing. We recommend that the non evidence based physical activity management, energy management and Cognitive Behavioural Therapy be removed from the guideline. We are concerned that there is no use of the term pacing. The terminology of a 'flare' suggests a momentary short lived event, of worsening. Energy envelope is confusing and unfamiliar, some sufferers have no energy and exist on what seems to be constant over expenditure with no energy contained in any such 'envelope' at all. We would also like to see accountability for those who do not follow the science based recommendations and thus help prevent harm.	The committee discussed the use of the term pacing agreed that it means something different to different people with many versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it. *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes

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					of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G.The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case, the committee agreed it was important people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage

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					their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Healthwatch Bolton	Guideline	General	General	We agree that the World Health Organisation classification of ME/CFS as a neurological condition, should stand. There is supportive evidence of perineural cysts, ganglionitis at post mortem and involvement of the nervous system. We ask that the term ME myalgic encephalomyelitis is used exclusively, the term CFS holds such bad stigma, does not represent the true context of an illness affecting multiple bodily systems. ME/CFS is not simply long term fatigue which the CFS nomenclature suggests.	Thank you for your comment. To note that the text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3)' has been added to the context section of the guideline.
Healthwatch Bolton	Guideline	General	General	Severe We do not agree with the description of severe classification. Having to stop work or education and with limited social, daily activity is severe classification and not moderate. All levels of severity	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The committee note that definitions of severity are not clear cut.

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				should be considered when discussing care plans as symptoms may worsen to more severe.	
Healthwatch Bolton	Guideline	General	General	Specialist Teams We are concerned about the emphasis on specialist teams. This is because: Current specialist teams are not fit for purpose. Many are led by Psychiatrists or Psychologists instead of Physicians, Paediatricians or General Practitioners. Since ME/CFS is a complex, multi-system, chronic medical condition, this is inappropriate. Current specialist clinics work on the theory of de-conditioning and promote outdated and harmful treatments (GET and CBT). They do not provide adequate ongoing care, and none at all to the very severely affected ME/CFS patients who need them the most. Patients struggle physically, financially and cognitively to get to appointments and need a lot of their care and assessment at home. Such patients are discharged without any alternative provision. They cannot handle the volume of ME/CFS patients. Their existence dis empowers General Practitioners and local Physicians/Paediatricians, many of whom have disengaged from their ME/CFS patients.	Thank you for your comment. Based on the evidence (Evidence reviews A.B,C,D and I) and the committee's experience referral to ME/CFS specialist care was recommended for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. ME/CFS specialist teams where seen as the most appropriate place for people with ME/CFS to access support with GPs providing ongoing support and review. The committee recognised certain parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.
Healthwatch Bolton	Guideline	General	General	Infection We are concerned that no effort at all is made in this guideline to address the fact that ME/CFS is often triggered by a viral or	Thank you for your comment.

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				other infection, and the importance of identifying and treating these infections quickly. For best, effect treatment needs to be started within the first 6 weeks, yet the NHS currently neither tests for nor treats infections in suspected ME/CFS. Comprehensive testing to identify viral and other infections should not wait until the diagnosis of ME/CFS is confirmed after 3 months of symptoms, but should be done immediately. With effective treatment, long term sequelae might be greatly reduced, or avoided altogether.	Throughout the guideline the committee have recommended the importance of carrying out investigations to identify other conditions or exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
Healthwatch Bolton	Guideline	008 - 009	Line 17 Box1	Post exertional symptom exacerbation- Worsening and exacerbation of symptoms can occur immediately after or even during activity thus not allowing completion. Increased symptom worsening can occur immediately and also peak afterwards even at 72 hours.Some people have a second peak after initial worsening that may be predictable. We are all different. By putting limitations and exclusions implied by wording tends to lead to errors in diagnosis. Out of kilter symptoms may be implied if the patient does not fit the specified documented mould, which clinicians may do, hence excluding a diagnosis, with detrimental consequence. Unrefreshing sleep-this seems to include exhaustion flu like symptoms, feeling stiff under this bullet point. It is implied that these symptoms are a result of unrefreshing sleep. This is not the case exhaustion can result from mitochondrial dysfunction, stiffness from arthralgia, myalgia, neuralgia, autoimmune, and flu like symptoms from immune disturbances, toxins and inflammatory cytokines. These symptoms should not be listed under this heading. If it is implied that they are the result of unrefreshng sleep then there may be a tendency to try to correct sleep patterns with harmful regimens that are usually prescribed in ME/CFS clinics. Waking up, getting dressed, not	Thank you for your comment. See Evidence review D – diagnosis for the evidence on diagnostic criteria and the committee discussion section explaining why the committee recommended that all four criteria should be present. This includes your point about including cognitive difficulties or orthostatic intolerance. In summary the committee maintain that cognitive difficulties are a key symptom in suspecting ME/CFS and are commonly reported in people with ME/CFS. They note that cognitive difficulties (such as brain fog) are described in most of the criteria (7 of the 9) criteria) reviewed in Evidence review D in contrast with orthostatic intolerance (4 of the 9 criteria) supporting further their experience and expertise and this has been clarified in the discussion section of the report. *PESE/PEM* The committee note that post exertional malaise is usually described as delayed in onset with it typically delayed 12-48 hours after activity, but recognised that some people with ME/CFS report PEM in a reduced (or later) time and have added 'can typically' to the definition.

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				allowing naps and putting to bed later can be very harmful. This is graded exercise not sleep management. The unrefreshing sleep may be the result of pathology within the limbic system which cannot be corrected as aforementioned. In addition to unrefreshing sleep many experience difficulty getting to sleep, difficulty maintaining sleep, sleep reversal, 25 hour patterns , insomnia. Having all 4 symptom criteria to fit before diagnosis will cause exclusion of a diagnosis.This also may delay diagnosis until more symptoms have developed with severity and worsening. This does not favour early diagnosis. Again not fitting tightly into criteria boxes leads to clinics using the term out of kilter which is especially damaging in children as they do not get a diagnosis and are so easily disbelieved, called lazy, school refuser and generally abused by persons who feel they should be in school if they are not ill enough to be in hospital. Parents may wrongly send children to school, that may cause worsening. Some may continue to work as they are financially unsupported otherwise. **The last bullet point in Box 1 should therefore read,** At least one of: **Cognitive difficulties** (often described as "brain fog") including problems finding words, temporary dyslexia or dyscalculia, slurred speech, slowed responsiveness, short-term memory problems, confusion, disorientation and difficulty concentrating or multitasking. **Orthostatic Intolerance (OI)** with symptoms such as dizziness, fatigue, brain fog, palpitations, pallor, nausea and fainting on standing or sitting upright from a reclining position.	To note after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM). The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS. *Unrefreshing sleep* After considering the stakeholder comments on the description of sleep symptoms the committee edited the bullet points to, 'unrefreshing sleep and /or sleep disturbance, which may include: • feeling exhausted, feeling flu-like and stiff on waking • broken or shallow sleep, altered sleep pattern or hypersomnia. The committee have also edited the definition in the terms used in the guideline section. The committee hope this has added some clarity for readers.

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Healthwatch Bolton	Guideline	004	5-6 7	**Change to:** "…is a chronic medical condition affecting multiple body systems, in which mitochondrial dysfunction affecting cellular energy production is present. Exact pathophysiology is still being elucidated." Change 'can' to 'does'… impact	Thank you for your comment. This bullet point has been edited to,' and its pathophysiology remains under investigation' to clarify that there is not enough evidence to make any conclusions about the pathophysiology of ME/CFS and this is an active area of research. The committee agree that for everyone with ME/CFS there is an impact on their lives. However, there is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes.. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS.

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Healthwatch Bolton	Guideline	004	10-11	**Add:** " – in its most severe form it can lead to substantial incapacity and even death…	Thank you for your comment. After taking into consideration the range of stakeholder comments about the tone of the guideline and the potential to be frightening for people with ME/CFS the committee have not included this suggestion. However, the committee note the severity of the impact of ME/CFS has been recognised throughout the development of this guideline. The scope included people with severe and very severe ME/FCS as a population for special consideration and each review highlighted any relevant evidence. In addition recognising the lack of evidence NICE commissioned a report to ensure the views of people with severe and very severe ME/CFS were include in the guideline (Appendix 2_People with severe ME/CFS) and this was considered alongside the other evidence by the committee. When making the recommendations the committee considered people with severe and very severe ME/CFS separately and made additional recommendations where relevant. After considering the stakeholder comments the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline and had more emphasis.
Healthwatch Bolton	Guideline	004	13-14	Add -sometimes to 'change unpredictably'. This suggests variation in severity, when some may remain within one severity level.	Thank you for your comment. The recommendation states that symptoms *can* change, this implies that symptoms may not change and remain the same.

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				Fluctuations in the condition can change over the course of a few hours, ADD-'also within a day'. This worsening is important when considering safeguarding of children. Teachers and others may report that the child was much better when they saw them compared to how the child had reportedly worsened at home. This leads to suspicion and the wrongful damaging criminal accusation of FII and child protection. Children are removed from parents to be observed in their care, usually into psychiatric units, causing irreparable damage to the child and entire family. Disbelieved, a child will be subjected to inappropriate and harmful care, negating their right to be supported with their illness. 'ranging from being able to carry out most daily activities to severe debilitation' gives the impression that a person with ME/CFS may range between being able to carry out most daily activities to severe debilitation, which is not the case.	The committee agreed that fluctuations can occur within a day and have added' over a day'. 'ranging from being able to carry out most daily activities to severe debilitation' - this has been removed from the end of the bullet point.
Healthwatch Bolton	Guideline	004	After 21	**Insert new point:** 1.1.3 The Biopsychosocial (BPS) Theory: The BPS theory has proved extremely damaging in ME/CFS and should be discarded. It has played a central role in perpetuating disbelief in ME/CFS as an organic entity, and is responsible for much of the neglect, disbelief and mismanagement to which the ME/CFS patient community has been subjected over the years. That ME/CFS does not really exist, but instead is a non-disease caused by a combination of faulty illness beliefs on the part of the patient, combined with deconditioning. Thus the patient is not managed as having a physical disease and thus no contraindication to cause harm is placed upon management regimens. The patient is neglected in their care as no further investigation is considered nor any appropriate management such as pain management. GP's paediatricians and	Thank you for your comment. The committee agree that it is important to have raise awareness and have clear statements about the reality and seriousness of ME/CFS. The recommendations in the principles for care section do this, the first recommendation states the reality and seriousness of ME/CFS as a medical condition. The second recommendation acknowledges that people with ME/CFS have experienced disbelief and stigma. Management of ME/CFS and the management of symptoms is addressed in detail later in the guideline. For these reasons your suggestion has not been added.

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				professionals consider that und evidence r these specialist services their patient is receiving all the necessary management, the clinics fail to communicate that they are not actually providing pain and other medications etc.	
Healthwatch Bolton	Guideline	005	Line 3	Add- add awareness of chronicity and likelihood of life long illness.	Thank you for your comment. Long term outlook is addressed in the section on information and support.
Healthwatch Bolton	Guideline	005	10	'..early accurate diagnosis…' as GP's are usually the first contact for the patient, it is important that they are educated in ME/CFS. That a diagnosis appropriate advice and support to rest may protect against worsening whilst other physical investigations such as blood sampling is undertaken.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. .
Healthwatch Bolton	Guideline	005	12	It should be established who is doing the monitoring of the patient and undertaking review and what that actually consists of. Appropriate blood sampling, assessments for co morbidities, or investigations for other conditions that may arise which may be unrelated to the ME/CFS.	Thank you for your comment. Review is addressed in detail in the review in primary care section of the guideline and includes the points you make.
Healthwatch Bolton	Guideline	005	15	Emphasise that the patient is always in complete charge of decision making about choices regarding their care. Patients and families should not be the coerced into inappropriate and harmful management, including school attendance, by involving educational welfare, child safeguarding, child protection and care orders at court. Specialists should not tell social workers that without treatment patients will get worse, eliciting forced incarceration. Some paediatric ME/CFS clinics have a form they fill in as to how likely the patient is to engage	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment

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				in treatment. Some children and families that wish to withdraw from clinics are fearful they will trigger child protection proceedings, as this does happen. Some children and families remain at clinics in the hope they will get some component of support such as educational provision, as they are so desperate, yet they disagree with the management approach, they feel they have little alternative support. Again, due to the lack of education doctors and paediatricians often know little about ME/CFS and many still think it is psychological. Patients and families should be informed of their rights to withdraw from any component of their care without consequence. We prefer the use of the term care plan to management.	and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.).
Healthwatch Bolton	Guideline	005	23	Include - ME/CFS specialists in the list of those causing prejudice an disbelief by lack of understanding.	Thank you for your comment. The recommendation includes examples and is not meant to be exhaustive for this reason your suggestion has not been added.
Healthwatch Bolton	Guideline	005	23	**Change to:** "health and social care professionals, teachers, schools, education authorities"	Thank you for your comment. The recommendation includes examples and is not meant to be exhaustive for this reason your suggestion has not been added.
Healthwatch Bolton	Guideline	006	20-22	**Add a symptom:** Insomnia and sleep reversal -under sleep disturbance "gastrointestinal difficulties such as abdominal pain, gastroparesis, constipation, diarrhoea, reflux, nausea…	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Healthwatch Bolton	Guideline	006	24-25	**Complete the symptom list:** "neurological symptoms such as "brain fog", headaches, photophobia, dizziness, ataxia, in-coordination, double vision and other visual disorders, fasciculation, tremors, buzzing, blepharospasm." Also add Orthostatic intolerance	Thank you for your comment. The list of examples is based on the committee's knowledge of the symptoms that people with severe and very severe ME/CFS can experience but is not intended to be an exhaustive list. Examples of orthostatic intolerance are included and this has been edited to add clarity.

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Healthwatch Bolton	Guideline	006	4	Be aware that the child may not be be ale to understand a doctor if they speak indistinctly and the clinician may also wrongly document the child comments, ensure that the child and clinician have both understood what is being said.	Thank you for your comment. The information and support section of the guideline provides further recommendations on communication.
Healthwatch Bolton	Guideline	006	7	Change 'severe and very severe' to include everyone with ME/CFS as they can all experience these symptoms at all levels of severity.	Thank you for your comment. The committee agree that any of the symptoms included here can affect anyone with ME/CFS, the aim of this section is to highlight symptoms can occur with such severity that they significantly affect the lives of people with severe or very severe ME/CFS
Healthwatch Bolton	Guideline	006	16	**Complete the sentence:** "extreme weakness, with severely reduced movement, even paralysis or near paralysis."	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Healthwatch Bolton	Guideline	007	7	**Complete the sentence:** "taking into account possible sensitivity to touch, the need to speak softly and/or work in dimmed light, and the need to avoid perfumes or other strong smells	Thank you for your comment. Hypersensitivity and the examples you mention are included in the previous recommendations on symptoms people with ME/CFS may experience. These are examples in the recommendations and as with any examples these cannot be exhaustive for this reason your suggestions have not been added.
Healthwatch Bolton	Guideline	007	008	**Elaborate:** "need aids such as manual or electric wheelchairs, reclining wheelchairs, mobility scooters, hoists, stair lifts, hospital beds and/or pressure-relieving mattresses, dark glasses, noise protection. Aids should be implemented and made available without delay	Thank you for your comment. After considering the range of stakeholder comments this has been edited to, 'are housebound or bed-bound and may need support with all activities of daily living, including aids and adaptions to assist mobility and independence in activities of daily living (for example wheelchairs)' The section on aids and adaptions provides further information.

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					These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Healthwatch Bolton	Guideline	008	14-15	'the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' This diagnostic criterion of significant reduction in activity puts the patient at the level of moderate to severe in their severity. If NICE aims to recognise and make early diagnosis see page 1 then mild symptoms need to be recognised. If a person developing ME/CFS has mild onset will they only achieve a diagnosis when they have worsened and progressed in severity? This is harmful. Many patients who start with ME/CFS continue to push through their illness and they remain motivation to get on with things but it is this continuity of activity, as we know, that causes worsening and damage. This too is why CBT is so harmful that illness beliefs were implicated in reduced activity and were a negative influence when indeed patients know that increasing and pushing through is harmful and that the harmful thing to do is to actually ignore this learned experience and try to override It by pushing through and continuing activity. There is a vast array of symptoms that can arise with ME/CFS and these may be present in reduced number and severity in mild or early onset. Earlier this guideline page 4 line 14-15 states that symptoms range from being able to carry out most daily activities to severe debilitation.If a patient presents as being able to do most daily activities will they get a diagnosis of ME/CFS as their activities are not significantly reduced. This is unclear definition	Thank you for your comment. The committee note that it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important when suspecting and in the diagnosis of ME/CFS. It is anticipated that over the period of 6 weeks and then at 3 months this would result in a significant reduction in a person's ability compared to the pre-illness levels and this is generally accepted description of the impact. The IOM 2015 describes, 'a substantial reduction or impairment in the ability…'.

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Healthwatch Bolton	Guideline	00 8	7	Elaborate on physical examination to include joint hyper-mobility considerations, skin elasticity, pooling of blood in the feet on standing. Using the study by Hives L. et al 2017 physical palpation of tender points.These signs are not being evaluated as an alternative to the standard clinic methods but as an adjunct and a cost effective, easy to use and effective aid to screening for ME/CFS which has been shown to be effective in that study but are currently not being taken account in the draft guidelines. The control group being healthy group in this study should not take away the strengths of the study as it showed that if all the signs are not present then the clinician will have to reassess their diagnosis of ME/CFS which will hopefully avoid unnecessary treatment and /or management, We ask the committee to review the paper and consider that these signs are not forgotten and are explored further as a screening tool when clinically assessing patients with suspected ME/CFS/CFS.	Thank you for your comment and information. The committee have not included specific assessments in the physical examination as these are based on clinical judgement and individual to the person's symptoms. In addition any list could not be exhaustive and there is the risk that the examples given are seen as the only assessments to do. For this reason the committee did not add your suggestion.
Healthwatch Bolton	Guideline	008	9	**Add to the sentence:** "baseline investigations to exclude other diagnoses such as those listed in the Chronic Fatigue Syndrome Myalgic Encephalomyelitis Primer for Clinical Practitioners 2014 Edition" at: http://bit.ly/IACFS-ME-primer-2014 **Rationale:** Current understanding is so poor, doctors need more guidance. The IACFS Primer does this very well. Include tests, blood tests and investigations for other co morbidities which commonly occur, have significant cumulative impact and are extremey important to acknowledge and diagnose at the same time.	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.

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Healthwatch Bolton	Guideline	008	16	**Change bullet point:** "symptoms are new and had a specific onset" to ' New OR specific onset' **Rationale:** Not all ME/CFS patients have a sudden onset of symptoms, many have a gradual onset. Yet others have struggled for many years before diagnosis, and may not be able to pinpoint when their symptoms started. Furthermore, a gradual onset can be mistaken for a sudden onset when patients erroneously perceive their illness to originate from an event that was in actual fact just the proverbial last straw, in a person who was already ill but still managing to cope.	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the symptoms have developed and have not always been present covering that the symptoms are not lifelong. This now includes the cohort of people who develop symptoms gradually sometimes over months or even years.
Healthwatch Bolton	Guideline	009	17-20	**Change to:** "Do not delay making a provisional diagnosis of ME/CFS if a person meets the criteria set out above. ME/CFS should be regarded as a positive clinical diagnosis based on the taking of a careful and thorough history. It is not a "diagnosis of exclusion", although other conditions need to be excluded. Post-exertional worsening is a cardinal symptom. As soon as ME/CFS/CFS is suspected, give the patient advice to avoid over-exertion."	Thank you for your comment. Your points on careful clinical assessment, the importance of excluding and identifying other diagnosis, PEM as a key symptom and giving advice to people with suspected ME/CFS are addressed in this section in other recommendations. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestions have not been added to the recommendation.
Healthwatch Bolton	Guideline	009	15	Insert- allodynia	Thank you for your comment. These are examples of types of pain that people may experience and the committee note that any list of examples is not intended to be exhaustive.
Healthwatch Bolton	Guideline	009	21	Add- also include continue with tests and investigations to recognise any comorbidities which commonly occur with ME/CFS (Ehlers Danlos SyndroME/CFS- joint hypermobility, Hashimotos, Mast Cell Activation Syndrome, IBS coeliac,	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried

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				fibromyalgia Postural Othostatic Tachycardia Syndrom etc) and which may add to symptom number and symptom exacerbation with cumulative impact, and for which some alternative management may be available.	out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. The discussion section of Evidence review D includes lists of common differential and co- existing diagnoses. The conditions you mention are included.
Healthwatch Bolton	Guideline	010	9-10	Some children may not be able to attend school at all, or in a very reduced capacity. The local authority usually require medical evidence before they put provision in place such as home tuition or online learning. The education welfare officer needs to be informed that the child is ill and to authorise absences. The school should be made aware that fluctuations occur in children and that they may appear healthy one minute and become ill very quickly, that this may only occur when they are at home, when the adrenalin has worn off, and to allay suspicion of FII.	Thank you for your comment and information. There is further information in the section 1.9 of the guideline on how to support children and young people in education.
Healthwatch Bolton	Guideline	010	5	Early symptom onset in a child may be misinterpreted as lazy or school refuser and expose the child to abuse and neglect from professionals. The diagnostic criteria set out in this guideline is too strict. Symptoms should not have reached a stage at which the child has significantly reduced activity, early diagnosis is essential and mild symptom severity has to be considered paramount. Fitting the child into all the diagnostic symptoms may not yet have been established and will hinder a diagnosis. For example slow writing or out put may not be seen as cognitive difficulty but laziness. Writing inability or confusion	Thank you for your comment and information.

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				misdiagnosed as dyslexia. The inability to focus to get dressed in a certain order after PE not seen as cognitive problems. Keep looking at the clock is loss of concentration and focus not boredom. Children often have to battle through the system to get a diagnosis and then they end up at clinics which do not manage ME/CFS in line with NICE .Clinics may push children into school so the clinic can be seen as having been successful in outcome measures. They do not usually provide pain medication and the referring doctors imagine that this will be provided leaving the child without pain medication. More harm than good may be done by children's clinic not only in their harmful regimens but also in the way in which they are imposed upon a child. Fear of reproach if withdrawing when the clinic blame lack of patient engagement and involves safeguarding. Clinic myths need to be dispelled- say children are too young, that you are unlikely to have more than one family member affected and do not recognise familial links. That improvement should have been made after 2 years.	
Healthwatch Bolton	Guideline	010	17	They should only do half of what they feel they are able to do.	Thank you for your comment. The committee have recommended that people do not use more energy than they perceive they have, this may vary from person to person. The committee agreed that people should be given personalised advice about managing their symptoms and recommend this in the advice for people with suspected ME/CFS section of the guideline. Your suggestion is very specific and for this reason has not been added.

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Healthwatch Bolton	Guideline	010	20	Rest as they need to.. unless the person has had ME/CFS for sometime they will not realise that harmful effects of not resting and that rest should be taken in advance of feeling the need to rest.	Thank you for your comment. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term. The committee agreed it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and this advice should not result in harm to anyone. As you note the committee recommend a personalised approach and this would include discussing with the person with suspected ME/CFS about how much rest is appropriate.
Healthwatch Bolton	Guideline	010	22	Perhaps a diagnosis could be given earlier than 3 months if the ME/CFS is familial, and obviously so.	Thank you for your comment. The genetics of ME/CFS was not identified as a priority area in the scope and not explored in a review as such the committee are unable to make recommendations on this topic.
Healthwatch Bolton	Guideline	011	9-12	• Many of the current specialist paediatric clinics are not fit for purpose and have caused harm. Unless new clinicians are employed that are going to treat children with ME/CFS as having real physical symptoms and not manage clinics as they have previously then I would suggest that a paediatrician manages the child and symptoms and as their patient. They have a duty of care to each patient to have a knowledge and understanding of their condition by continued practice development.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section).

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				Instead of specialist teams, ME/CFS should be managed locally by General Practitioners, Physicians and Paediatricians, who are best placed to provide ongoing care. All Physicians, Paediatricians and General Practitioners should be educated in and made competent in diagnosing and managing ME/CFS. They already have the knowledge, expertise and educational materials to be able to roll out basic information very quickly, with the right institutional support. Existing specialist teams should be abolished and General Practitioners and local Physicians/ Paediatricians should take ownership of their ME/CFS patients. Local General Practitioners, Physicians and Paediatricians are responsible for co-ordinating care, providing regular reviews, home visits, responding to patients' concerns, and advising other agencies as necessary such as social welfare, employment and education. Only a few select specialist centres should remain. These should be led by Physicians, Paediatricians or General Practitioners and serve an advisory, training and educational role only, or be developed to provide specialised inpatient services for ME/CFS patients. The performance of local ME/CFS services be regularly audited. Use the term medical care plan not management plan	The committee highlight where access to a ME/CFS specialist services is required. They have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. The committee discuss further access to ME/CFS specialist teams in Evidence review I-Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.

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					Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Healthwatch Bolton	Guideline	011	5-6	Note finding no abnormalities on routine investigations is usual for ME/CFS and ME/CFS is **NOT** Functional Neurological Disorder (FND). A diagnosis of ME/CFS explicitly excludes the diagnosis of FND for symptoms that relate to the ME/CFS	Thank you for your comment and information.
Healthwatch Bolton	Guideline	011	7	**Insert additional points after 1.4.1, before 1.4.2:** 1.4.2 Important exclusionary conditions (alternative diagnoses important not to miss): Anaemias Autoimmune diseases such as rheumatoid arthritis, lupus Cardiac disease Endocrine disorders such as diabetes, Addison's disease, thyroid disease, menopause Infectious diseases such as tuberculosis, HIV/AIDS, chronic hepatitis, Lyme disease Intestinal diseases such as Coeliac or Crohn's disease Malignancies Mitochondrial Diseases Neurological disorders such as multiple sclerosis, Parkinson's disease, myasthenia gravis Primary psychiatric disorders and substance abuse (but not clinical depression) Significant pulmonary disease Primary sleep disorders such as sleep apnoea 1.4.3 Non-exclusionary conditions:	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude and identify other diagnoses. The committee have now included examples of investigations that might be carried out when ME/CFS is suspected. The discussion section of Evidence review D- Diagnosis includes a list of differential diagnosis and conditions that commonly occur in people with ME/CFS. These include many of the examples you list. **The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.**

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				Entities that commonly occur in association with ME/CFS such as allergies, fibromyalgia, irritable bowel syndrome, multiple chemical sensitivities, hypermobility and Ehlers Danlos Syndrome. Any medical condition that has been adequately treated and is under control Any isolated physical abnormality or laboratory test that is insufficient to diagnose an exclusionary condition 1.4.4 For more information on the pathophysiology and diagnosis of ME/CFS, see: http://bit.ly/IntConsPrimerME2012 **Rationale:** Current understanding is so poor, doctors need more detailed guidance. The Chronic Fatigue Syndrome Myalgic Encephalomyelitis Primer for Clinical Practitioners does this very well. http://bit.ly/IACFS-ME-primer-2014	
Healthwatch Bolton	Guideline	012	10 1.5.2	**1.5.2** Local ME/CFS services should be led by Physicians, Paediatricians or General Practitioners with appropriate training in ME/CFS. not Psychiatrists. Services should be community based, and at a minimum include Doctor(s), Occupational Therapists and Social Workers. Early Occupational Therapy assessment and support is essential, within a month of diagnosis, and patients often also need: district or community nurse input to enable procedures to be carried out at home, social care, physiotherapy, dietetic support, psychological support and home visits by their doctor, optician and dentist All of these should be available at home should the patient require it. Every patient should have a designated case	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the

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				worker from the local ME/CFS service responsible for co-ordinating all their health and social care needs. The case worker is their first point of contact. Shared care arrangements between Physician/Paediatrician and Primary Care can be useful. **1.5.3** As ME/CFS is a chronic, debilitating and currently incurable condition, Occupational Therapy is a key part of management. Occupational therapists are trained in both physical and mental health care, in the social and medical model. They are trained to assess and implement support for those whose health impact their ability to participate in activities of daily living, including sleep, cognitive, sensory and physical tasks. The word "occupational" here refers to any activity that one engages time in. This includes personal care, productivity (for example education, parenting, employment, home making duties), leisure and social activities. Occupational therapists have core skills in: Activity analysis. Activity management. Adaptive strategies including rest, energy conservation and pacing. Environmental assessment and home modification. Equipment prescription, including seating, beds, hoists and wheelchairs, scooters, stair lifts Ability to advise and signpost on for care support. Ability to write reports for benefit applications. Work place assessment and guidance, including the allied health professional (AHP) fitness for work report to support people to remain in employment, and employers with advice on phased return to work.	committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. The multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse.

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				Allied Health care professionals also include osteopath who are capable of being involved in care plans, can be funded by NHS CCG's and can be part of the patient choice in their own care plan - Page 12 line 4- Change psychosocial term and do not routinely undertake a psychological assessment	
Healthwatch Bolton	Guideline	014	016	This daily fluctuation must be conveyed to all professionals involved with the child to allay any suspicion of FII.	Thank you for your comment.
Healthwatch Bolton	Guideline	015	1	The child and family should not be deceived about possible chronicity. Importance should be placed upon harm and long term worsening if rest and pacing are not undertaken immediately and that health surpasses educational need. What evidence is there to support this statement but that of committee members. This may impact negatively upon benefit claims and perception of professionals that illness is transient and short lived when it may be life changing.	Thank you for your comment. This recommendation was based on the qualitative reviews exploring the experiences of people with ME/CFS and the committee's experience. See evidence review A for the committee discussion on further information about the long-term outlook for people with ME/CFS.
Healthwatch Bolton	Guideline	015	8	Provide reports to support benefits and insurance claims. Doctors need to be aware that being on benefits is a need and entitlement and does not prevent recovery due to malingering behaviour.	Thank you for your comment. It is not within NICE'S remit to make recommendations about healthcare professionals providing medical reports to supporting applications for benefits.
Healthwatch Bolton	Guideline	016	6-8	**Change to:** "If Safeguarding assessments are required for people with confirmed or suspected ME/CFS, they should be carried out or overseen by health and social care professionals who have training and experience in ME/CFS." Not all ME/CFS patients should be safeguarded as the comment may suggest. Safeguarding assessment will	Thank you for your comment and information. After considering the stakeholder comments this recommendation has been edited to,' *If* a person with confirmed or suspected ME/CFS needs to be assessed'.

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				negatively impact upon the child causing worsening of symptoms due to stress. Sudden fluctuations in severity, multiple family members being affected, age of the child, inability to recover or worsening may elicit damaging FII allegations and child protection proceedings. That people with ME/CFS run the risk of being confused with depression and mental health problems and should be protected from such wrongful misdiagnosis. Patients should have the right to request second or first opinions about their diagnosis and comorbidities via the NHS or privately fund without this being seen as medical shopping behaviour, but as a patient that is probably being failed by current services.	
Healthwatch Bolton	Guideline	018	19	This advice should apply to include moderate or any level of patient symptom severity depending on their individual need	Thank you for your comment The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms and is addressed in the first recommendation in this section.
Healthwatch Bolton	Guideline	019	9-21	Patients should not be hospitalised or managed in an psychiatric ward, bed or unit Exposure to light and noise to 'normalise' a patient with ME/CFS is barbaric and cruel and specialist should not harm patients in such a way especially when they have no control and are in hospital, for example.	Thank you for your comment. This recommendation considers how the hospital environment could be adapted and not where people should be admitted for this reason your suggestion has not been added. Noise has been edited to sound and 'strong' has been removed.

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				Change noise to sound Change strong smells to smells	
Healthwatch Bolton	Guideline	020	Line 26-30	**Change to:** For people with moderate, severe or very severe ME/CFS, consider providing or recommending aids and adaptations such as: For mobility – a manual or electric wheelchair, mobility scooter, automatic or adapted car, blue badge, sunflower lanyard, stair lift, walking aids, grab rails. Daily living – reclining chair, hoist, hospital bed, pressure relieving mattress, shower or kitchen stool, blender, feeding cup or straw, speech to text software. Environmental adaptations – blackout blinds, extra dark sunglasses, sound proofed windows, special light bulbs (daylight white), dimmable switches, blue light blocking glasses for screens, ear plugs, ear defenders, noise cancelling headphones. Remember that aids and adaptations do not just maintain independence and improve quality of life, they help people with ME/CFS conserve energy and stay within their energy envelope, thus maintaining their level of health and function. **Rationale:** Patients' needs must be explicitly stated as they are currently largely neglected and left to struggle on their own. For example, wheelchairs are only provided if patients are completely unable to mobilise within their homes. Difficulties mobilising outside of the home is not taken into account, nor is the need to conserve energy in order to preserve function. Hospital beds are only provided in hospice situations which is grossly inadequate, given that people with ME/CFS can be mostly or completely bed-bound for many	Thank you for your comment and information.. These are examples in the recommendation and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.

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				years or decades. No support at all is given for sensory hypersensitivities. Explain mobility aids such as wheelchairs or mobility scooters are a means of maintaining independence, not a cause of further dependence, is not giving in, detrimental but facilitates quality of life. Children's ME/CFS services wrongly fail to recommend their use. They enable not disable	
Healthwatch Bolton	Guideline	020	Line 12	Also provide voice to type software.	Thank you for your comment These are examples in the recommendation and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Healthwatch Bolton	Guideline	021	Line 10	Including ' Access to Work '	Thank you for your comment. Additional text on work has been added to the committee discussion in evidence review A and includes that adaptions and adjustments should be discussed and gives examples including flexible working and reference to the Access to work scheme.
Healthwatch Bolton	Guideline	021	Line 15	**Insert additional point between 1.9.2 and 1.9.3:** "Adjustments at work or education could include home schooling, online education, exams taken at home, extra time in exams, reduced timetable, working from home, flexible or reduced hours, providing transport, designated parking space, a quieter work area with lower light settings, speech to text software, text to speech software, audio books, ergonomic assessment, or a place to rest when needed	Thank you for your comment. Further information in types of adaptions and adjustments are included further in this section and in the committee discussion in evidence review A and the points your raise are highlighted there. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.
Healthwatch Bolton	Guideline	022	Line 11	ADD- Some children may not be well enough to engage in any education at all and should not be pushed to do so. Some may only able to manage some elements of simple daily living even with help	Thank you for your comment. When writing recommendations there is a judgment to be made about how much information is included in a recommendation.

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				such as eating, brushing teeth. If a child only has energy to do this they cannot spare energy for education, socialise etc. Education should not be prioritised before the ability to socialise, mobilise, play and have a family life. It should be last on the list after the best quality of life possible has been achieved with the small amount of energy available.	Too much information in a recommendation results in a guideline becoming unwieldy and unusable. Evidence review A includes more detail on education and the balance of activities.
Healthwatch Bolton	Guideline	022	Line 14	Involve health and social care only with the patients consent Line 22- no evidence that all ME/CFS patients have an emotional need	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. Line 22 The committee disagree emotional wellbeing is an important part of a holistic health approach. People with ME/CFS should have access to people with this expertise if required
Healthwatch Bolton	Guideline	023	Line 12	Have a named paediatrician for advice not a specialist team	Thank you for your comment. This has been edited to clarify it is the paediatric ME/CFS specialist team.
Healthwatch Bolton	Guideline	024	Line 22	Disagree with this -'Progressed during periods when symptoms are improved' this can be misinterpreted or used as a form of graded exercise . If is is implied that this	Thank you for your comment.

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				management is effective then it will be imposed at clinics and especially in children to increase school attendance. We do not agree with Energy management plans as they are orientated towards forward planning of activities and progression/ increases.	After considering the stakeholder comments this bullet point has been edited to,' uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse).
Healthwatch Bolton	Guideline	025	Line 1-2	There is no evidence to support the effectiveness of energy management such that that persons with ME/CFS ' reach stabilisation or to increase tolerance or activity' WE disagree with this theory of being able to somehow stabilise ME/CFS, increase tolerance or increase activity. No evidence just experience of the committee. There is potential to cause harm in all levels of severity	Thank you for your comment. After considering the stakeholder comments tolerance has been deleted. This guideline applies to all people with ME/CFS and the committee noted that in their experience some people with ME/CFS where appropriate and with the appropriate support can increase their activity levels.
Healthwatch Bolton	Guideline	025	Line 3	Change to ' Deconditioning is not the cause of ME//CFS'	Thank you for your comment. The committee deleted the bullet point on deconditioning noting that this recommendation was about providing advice to people with ME/CFS about the approaches to implement energy management and this point was not useful in this context.
Healthwatch Bolton	Guideline	026	Line	Change ' a physical activity programmes' to ' some physical activity'	Thank you for your comment. This recommendation refers to a physical activity programme not generally to physical activity.
Healthwatch Bolton	Guideline	027	Line 23	Change- '… may worsen their symptoms to' ' May worsen their symptoms, causing relapse and long term damage and overall severity'	Thank you for your comment. The impact of symptoms worsening and how to manage this is addressed throughout the guideline. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.
Healthwatch Bolton	Guideline	028	Line 12-14	We have concern over the continued use of non evidence based physical activity programme. This can easily be	Thank you for your comment.

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				misinterpreted and manipulated into a Graded exercise therapy regimen. Only clear evidence based therapy should be used. Remove… '… who are ready to progress their physical activity beyond their current activities of daily living, or…'	The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy 'based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed it was important people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.

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Healthwatch Bolton	Guideline	028	Line 16-18	Should be guided by the patient at all times	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Healthwatch Bolton	Guideline	028	Line 10-11	Remove the term ' therapies derived from osteopathy' It is important to stress the need to warn against NLP and the Lightning Process and the false belief that symptoms can be alleviated by such manipulations of thought processes and the harm this causes. We ask that the committee to review the section 1.11.16 and omit the words "derived from osteopathy" in the 'do not offer section' of the guidance. Also with reference to section 1.11.11 (page 26) offering treatment and gentle techniques that aim to improve overall joint mobility, muscle flexibility, postural and positional support, muscle strength and endurance, cardiovascular health should remain as in the draft and not mention specific disciplines or professions in the final version of guidance to maintain health equality. These aims are all part of what the Allied Health Professionals attempt to achieve with	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer people with ME/CFS therapies based on the Lightning Process'.

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				the application of some forms of manual therapy, as for example in The Perrin Technique.	
Healthwatch Bolton	Guideline	028	Line 19-20	'Tell people about the possible benefits, show the evidence, emphasise the risks…. If risk is involved there is potential to cause harm. We do not recommend physical activity as it is not evidence based. Change 'some' to 'many'	Thank you for your comment. Any discussion of a person's care and management of symptoms should include the possible risks and benefits. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).

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					Based on the evidence* and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). The committee agreed not to change some to many, this point was to illustrate that the impact of a physical activity or exercise programme can vary.
Healthwatch Bolton	Guideline	028	Line 21-22	Patient evidence documented here states that activity management programmes can cause worsening and harm. We do not advocate Activity management programmes.	Thank you for your comment.

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				Insert- "A physical activity programme will not cure their ME/CFS. If not approached with great caution, it can easily provoke a relapse."	Any discussion of a person's care and management of symptoms should include the possible risks and benefits. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Based on the evidence* and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where

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					appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
Healthwatch Bolton	Guideline	028	Line 28-29	'…attempting to increase physical ability' What evidence and rationale is there that physical ability can be increased. This is just deconditioning theorising.	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review

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					quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Based on the evidence* and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise

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					interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
Healthwatch Bolton	Guideline	028	Line 25	Establish a baseline with the use of apps and monitors. We do not agree with the theory of a baseline, it is too difficult to achieve.	Thank you for your comment. The committee agree the terminology is varied to describe some one's lower energy limit. This point is that the level should not worsen someone's symptoms. The use of apps would be according to the individual.
Healthwatch Bolton	Guideline	029	Line 1-2	Remove this advice here. There is no evidence is there that small increments increase improve physical ability. This is deconditioning theory or is this just graded exercise therapy?	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.)

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					The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. With regard to you comment, the committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed it was important people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F

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					and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Healthwatch Bolton	Guideline	029	Line 11	**Insert third bullet point:** "incorporating extra periods of rest and sleep, listening to their bodies, stopping all activity and resting or sleeping as much as they need to."	Thank you for your comment. The following section on symptom management includes sleep and rest. The committee noted that there was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice. This applies here and advice on rest and sleep should be part of the personalised collaborative physical activity or exercise programme.
Healthwatch Bolton	Guideline	029	Line 19	Explain The role of rest- not specific enough ADD- the importance of rest Restriction should not be placed on rest Dispel the myth that too much rest is counter productive and harmful If your body tells you to rest then rest Take rest breaks actually before you feel a need to Define rest- laid down horizontally, no stimulus, sitting can be classed as activity, noise , light etc can be activity to some. The way that rest is managed in clinics currently can be harmful. Current 'sleep hygiene' regimens in clinics is graded exercise. Waking is extremely harmful. You cannot correct such symptoms by attempting to enforce a routine	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual.

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Healthwatch Bolton	Guideline	030	Line 2-3	**Insert additional point: 1.11.24 Sleep:** Sleep patterns are often disordered in ME/CFS. Patients should try to go with the flow if possible, and learn to live with their natural rhythm, even if their sleep times are very abnormal or variable. Getting sleep is more important than when they sleep. In the early stages of the illness, hypersomnia is common. It is important that people with ME/CFS listen to their bodies and sleep as much as they need to. This gives the best chance of recovery and functional improvement in the long term. Hypersomnia can also happen during flares and relapses. As always, patients should listen to their bodies in order to get out of the flares or relapses. Standard "sleep hygiene" practices may not be appropriate in ME/CFS, such as strictly limiting daytime sleep. Education should be provided flexibly to enable children and young people with ME/CFS to get the sleep they need. Where it is necessary to adjust a patient's sleep pattern, e.g. to fit around work hours, melatonin or other sedatives can be tried. Changes should be made gradually in small increments. Insomnia is a common problem. melatonin, phenergan, low dose amitriptyline or other sedatives can be tried. Start low and go slow – ME/CFS patients are very sensitive to medication and prone to side effects. Formal sleep studies may be required in some patients to diagnose concomitant sleep disorders.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice. *Orthostatic intolerance* In the suspecting ME/CFS section of the guideline orthostatic intolerance is identified as one of the symptoms that are commonly associated with ME/CFS. The committee made a consensus recommendation to raise awareness about this. The guideline is about the diagnosis and management of ME/CFS and for this reason the committee was unable to make more detailed recommendations on the causes or diagnosis of orthostatic intolerance. The committee did not make any recommendations on the management of orthostatic intolerance noting that although this can be straightforward it this can involve advice on diet, carrying out daily activities and activity support and should be tailored to the person taking into account their other ME/CFS symptoms. The committee noted medicines usually prescribed for OI can worsen other symptoms in people with ME/CFS and should only be prescribed or overseen by a clinician with expertise in orthostatic intolerance. (see evidence review G).

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				On waking, patients often experience a period of profound weakness or paralysis, subjectively experienced as "heaviness" or "dead weight", in which they are unable to move. This takes a variable amount of time (hours) to wear off completely, and may be felt to some degree even after patients manage to get out of bed . Orthostatic intolerance should be assessed in all patients with ME/CFS. , and a good understanding of this common symptom appreciated and supported.	
Healthwatch Bolton	Guideline	030	Line 14	If clinics are not managing pain (like some paediatric ME/CFS clinics) they should inform the referring clinician that this symptom will not be managed so that the patient is not left suffering without appropriate pain management.	Thank you for your comments. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate.
Healthwatch Bolton	Guideline	033	Line 2	**Insert additional point after line 2:** 1.11.40 Consider Mast Cell Activation Syndrome and Coeliac Disease in patients with multiple food intolerances.	Thank you for your comment. Throughout the guideline the committee have recommended the importance of being aware of differential diagnoses and coexisting conditions, a coeliac screen is included in the list of investigations that might be considered in section 1.2. The committee hope that the recommendation to refer people with ME/CFS with a restrictive diet for a dietetic assessment will improve the identification and management of complications that people with ME/CFS can experience and they decided not to refer to any one particular condition.

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Healthwatch Bolton	Guideline	034	Line 17-18	Remove-…'but recognises that thoughts, feelings, behaviours and physiology interact with each other.'	Thank you for your comment. The committee specifically rejected the assumption that people with ME/CFS have 'abnormal' illness beliefs and behaviours as an underlying cause of their ME/CFS and wanted this highlighted in the recommendations on CBT. There was concern, particularly from the lay members of the committee, about the wording of CBT manuals that make suppositions about 'wrong' cognitions. The committee considered that the narrative around fear avoidance and false illness beliefs can deny patient experience, as fears can be completely rational and protective against harm. Therefore, the committee decided to specify in the recommendations that CBT does not assume people with ME/CFS have 'abnormal' illness beliefs and behaviours as an underlying cause of ME/CFS, but recognises thoughts, feelings, behaviours and physiology and how they interact with each other.(See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Healthwatch Bolton	Guideline	034	Line 2-5 and Line 7	**Change to:** "Psychological therapy, including CBT, is not a treatment or cure for ME/CFS. Only offer formal psychological support to people with ME/CFS who would like to use it to support them in living with chronic illness and to reduce the psychological distress associated with this. Do not offer CBT as a treatment or cure for ME/CFS Instead of CBT, psychological support can include various modalities of psychotherapy and supportive counselling." This should be monitored.	Thank you for your comment. After considering the range of stakeholder comments the first recommendation in this section has been edited to remove the word treatment. The committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.

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					The recommendation now starts with, 'explain to people with ME/CFS that cognitive behavioural therapy (CBT) may help them to manage their symptoms but it is not curative' After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).
Healthwatch Bolton	Guideline	035	Line 15	Children should not be offered CBT. There is an identified risk. There is no evidence to support it's use. Close and careful monitoring and auditing of what CBT is being dispensed to the child and family is essential. The feedback forms should go direct to the auditing of the clinic and not taken at the time of review, the family and child should not feel under obligation to give good feedback.if they feel this is not the case.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. This also applies to children and young people where there was some evidence of benefit in the quantitative and qualitative evidence. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Healthwatch Bolton	Guideline	036	General	Depression and anxiety should be seen as a secondary factor to the ME/CFS Importantly the ME/CFS patient should not be managed on a psychiatric ward or bed or unit. Do Not refer a person with ME/CFS to mental health services unless they	Thank you for your comment.

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				show a serious deterioration in their mental health which does not derive from their ME/CFS. Indeed,the correct diagnosis, coupled with sensitive help in managing symptoms, and practical advice, can often alleviate any depression or anxiety.The ME/CFS diagnosis needs to be embraced and supported with understanding that their anxiety symptom is a s a result of the ME/CFS and manage them thus so.	
Healthwatch Bolton	Guideline	037	Line 9	Add- and rest	Thank you for your comment. The recommendation includes general strategies for people with ME/CFS, specific strategies would be individual to the person with ME/CFS and discussed as part of their care and support plan. The risk of including examples in a recommendation is that they cannot be exhaustive and there is the risk these are taken as the only options available.
Healthwatch Bolton	Guideline	039	Line 8-12	ADD- Take blood tests at the review and check for co morbidities and any new illnesses. ADD that the review undertaken at home should be offered in those who are severe, or offer telephone or remote online service.	Thank you for your comment. The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a change in symptoms are investigated. This should ensure that changing or new symptoms are not overlooked and appropriate blood tests are done. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home

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					visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The committee note that the review here is based in primary care and this would reduce the need for travelling to specialist centres.
Healthwatch Bolton	Guideline	040	Line 17-18	**Change to:** "provide evidence-based content developed by and in collaboration with: Practicing ME/CFS Physicians and Paediatricians who take a biomedical approach towards ME/CFS. medical professionals who have ME/CFS, especially those who also have expertise in medical Education. ME/CFS patient organisations." **Rationale:** Training programmes must be developed by the right people in order that the programmes reflect the new, accurate and scientific narrative of illness.	Thank you for your comment. This recommendation has been edited to,' ME/CFS' specialist services.
Healthwatch Bolton	Guideline	040	Line 12	ME/CFS should be taught in medical school as a neurological disease as per World Health Organisation of complexity of need, care and support. That recognition in children is important to prevent them being abused and neglected by educational, social and medical persons in their wrongful accusations and beliefs.This is so damaging. **Insert additional points before 1.15.1:** 1.15.1 ME/CFS should be included in the undergraduate medical curriculum, and postgraduate Physician, Paediatric and General Practice curriculae. All doctors should understand that ME/CFS is a complex, multi-system, chronic	Thank you for your comment and information. It is beyond the remit of NICE to recommend what should be included in medical curricula and part of GMC revalidation. After considering the stakeholder comments the committee have made some edits to the recommendations including that health and social care providers should ensure that all staff delivering care to people with ME/CFS maintain CPD relevant to their role in line with this guideline.

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				medical illness, not a psychological or psychiatric condition. It is classified by the World Health Organisation and by SNOMED-CT as Neurological. All Physicians, Paediatricians and General Practitioners must be competent diagnosing and managing ME/CFS **Rationale:** For ME/CFS patients' needs to be met, doctors must be properly educated. Current understanding is extremely poor and most doctors believe ME/CFS is psychological. See: https://bit.ly/2yFAtY8 1.5.2 medical education should begin immediately, given the current poor state of knowledge and attitudes. medical Schools must incorporate ME/CFS into the curriculum by the next intake in September 2021, and all doctors graduating from July 2022 onwards must: Understand that ME/CFS is a complex, multi-system, chronic medical illness, not a psychological or psychiatric condition. Know the most common symptoms of ME/CFS (debilitating fatigue, post-exertional symptom exacerbation, sleep disturbance, cognitive difficulties, orthostatic intolerance, myalgia). Know who to ask for help if they suspect ME/CFS (General Practitioner, Physician, Paediatrician). Know that Graded Exercise Therapy and CBT based on the deconditioning theory is harmful in M/CFS, and that any exercise or physical activity programme requires great caution. **Rationale:** The need for medical education is urgent. There is no reason for any delay as we already have the knowledge,	To note the text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) has been added to the context.

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				expertise and educational materials to be able to roll out basic information very quickly, with the right institutional support. 1.5.3 Health Education England, its equivalents in devolved nations and medical Royal Colleges must incorporate ME/CFS into the postgraduate Physician, Paediatric and General Practice curriculums immediately, with the following initial learning objectives (to be updated as scientific knowledge on ME/CFS grows): Be able to diagnose ME/CFS. Be able to exclude other alternative diagnoses as appropriate. Understand the biological nature of ME/CFS– that it is not a psychological or psychiatric condition. Understand the long term nature of ME/CFS, the level of disability it can cause, and its impact on patients and their families. Know the common symptoms of ME/CFS and commonly associated conditions. Be willing to take a patient centred approach to management. Know that Graded Exercise Therapy and CBT based on the deconditioning theory is harmful in ME/CFS and reject their use as treatments for ME/CFS. Know that any exercise or physical activity programme requires great caution in line with this guideline. Be able to provide medical evidence as needed to enable patients to obtain financial and social support, or adjustments to work, education and training. Be familiar with this guideline	

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				Competencies in these learning objectives must be demonstrated as a requirement for Certificate of Completion of Training (CCT) from 1/1/2022. **Rationale:** The need for medical education is urgent. There is no reason for any delay as we already have the knowledge, expertise and educational materials to be able to roll out basic information very quickly, with the right institutional support. 1.5.4 Physicians, Paediatricians and GPs who have achieved CCT before 1/1/2022 must undertake continuous professional development in ME/CFS to bring themselves up-to-date. Their compliance with this must be reviewed at their next appraisal and their next GMC revalidation.	
Healthwatch Bolton	Guideline	041	Line 5	**Insert new section: "1.16 Audit"** The performance of ME/CFS services must be audited. Data such as these must be collected annually: Time between initial presentation and diagnosis Length of symptoms before patients present. Whether patients are managed by a formal community based ME/CFS service, existing generic local services, a Psychiatrist or Psychologist led specialist clinic, or a Physician/Paediatrician/GP led specialist clinic. Whether patients have a designated case worker and who this is (OT, social worker, ME/CFS nurse, etc.) Severity category – mild, moderate, severe, very severe.	Thank you for your comment. The committee agree that audit is an important part of measuring performance in services but this guideline focused on clinical recommendations, the development of audit systems was not included as an area in the scope and the committee are unable to make recommendations in this area. Your comments will also be considered by NICE where relevant support activity is being planned. NICE – quality standard?

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				Severity category in the previous year and at initial presentation/diagnosis. Time between diagnosis and first OT assessment. Whether this was done at home Whether patients received their regular review (annually for adults, 6 monthly for children). If not, why not. Whether patients are in employment, education or training. Full time or part time Were patients or their families the subject of Safeguarding investigations. The outcome of the investigations. The effect on the patients' health. Sample of patients' views of the services. Diagnostic process for ME/CFS including timeliness. Are their health care needs being met, what needs to change. Are their social care needs being met, what needs to change. Are health services accessible, e.g. blood tests, patient transport, scans, appointments? Are social services accessible, any barriers to access? Do they feel supported and understood. If not, which part of the service is falling short **Rationale:** The care of people with ME/CFS has been grossly inadequate to date. It is imperative we make sure the situation is improving, and learn from where it's not working	

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Healthwatch Bolton	Guideline	041	Line 12	It is good to have an advocate where appropriate but they must be listened to. Damage can be done during care proceedings undertaken by social services when they are making assessments placing families under suspicion allegation. Children and vulnerable need protection from cruel and barbaric processes, which arise as a result of ignorance, lack of understanding and false beliefs, even from specialist ME/CFS clinics and this has to stop.The child and family should always be believed and supported.	Thank you for your comment.
Healthwatch Bolton	Guideline	043	general	Management We do not agree with the proposal for the guideline Management plan, under it's definition. The ME/CFS patient should have an agreed and informed care plan . It does not have to be developed by a specialist team but that of a well trained clinician. A holistic assessment need not take place as undertaking a diagnosis already requires assessment. The term holistic has alternative meanings and implications and should not be used. Only evidence based care should be offered .Energy management, physical maintenance, physical activity, cognitive behavioural therapy are not evidence based. Energy management is based on the experience of the committee. (Page 61 line 1) All these strategies can cause worsening and harm in all levels of severity. They cannot safely be applied to patients with ME/CFS that have unquantifiable energy availability, unpredictable and individual fatiguability and post exertional malaise severity duration and intensity.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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Healthwatch Bolton	Guideline	043	Line 3	Management should include pain management, sleep medication, vitamin levels. If these are not undertaken as part of the plan the GP or person managing the patient needs to be fully aware so that these needs can be met elsewhere.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans. https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) The definition is a summary and includes an overview of what is within the care and support plan, it is not meant to be exhaustive. For this reason you suggestions have not been added.
Healthwatch Bolton	Guideline	044	Line27-28	**Change to sentence:** "The person's symptoms and level of disability may be similar to or worse than at illness onset."	Thank you for your comment. This sentence has been removed.
Healthwatch Bolton	Guideline	044	Line 21	Change to -' worsen 12 to 72 hours after activity and can last for days , weeks or even months '	Thank you for your comment. The committee note that post exertional malaise is usually described as delayed in onset with it typically delayed 12-48 hours after activity, but recognised that some people with ME/CFS report PEM in a reduced (or later) time and have added 'can typically' to the definition.
Healthwatch Bolton	Guideline	055	Line 18	Change noise to sound	Thank you for your comment. This has been edited to sound.
Healthwatch Bolton	Guideline	055	Line 28	The outlook for children should be evidence based population data and not that of the committee members. Children may no longer wish to attend the clinics, not because they are recovered, but that they do not wish to continue with inappropriate care. There is no evidence for comparison as clinics do not have this data nor do they follow this up long term , later in life, or any such comparison to adults.There is little standardisation of successfully measuring improvement or recovery. Success may be based upon school attendance which is often at the expense of other activities and quality of life measures.	Thank you for your comment and information.

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Healthwatch Bolton	Guideline	057	Line 22	Inpatient stay for ME/CFS management should not be done in a psychiatric, bed,ward , hospital or unit and a separate room should be provided not a ward.	Thank you for your comment.
Healthwatch Bolton	Guideline	061	Line 15	Add mild and moderate- Inappropriate energy management can also cause worsening in mild and moderate cases	Thank you for your comment. This refers specifically to people with severe ME/CFS or very severe ME/CFS.
Healthwatch Bolton	Guideline	068	Line 12	As some current CBT ME/ CFS specialist practitioners do not recognise any harm from current CBT uses how are they going to portray them to families and children and 'inform' them of harm. There is no evidence to support the use of CBT.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Healthwatch Bolton	Guideline	069	Line 1	As many co-morbidities are common with ME/CFS we feel that they should be managed better by clinics, some do not explore the possibility of their existence, as they are not told to do so in the guidelines. Some may wrongly dismiss a diagnosis of ME/CFS if they believe there is a co-morbidity involved and do not link them. Experience shows that some ME/CFS	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to identify co-existing conditions and to exclude other diagnoses. The committee have now included examples of investigations that might be carried out.

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				specialists do not know what POTS is and believe that all children are hyper-mobile when discussing the possibility of EDS joint hyper-mobility, even where there is abdominal involvement such as constipation, reflux. Education of clinicians in both ME/CFS and associated co-morbidities is essential as the enormous overlap in cellular involvement and causation continues to be explored	The discussion section of Evidence review D- Diagnosis includes lists of differential and conditions that commonly occur in people with ME/CFS and has the examples you have listed
Inhealth Pain Management	Guideline	General	General	There is no mention of the role of social prescribing. Social prescribing might be very useful for many people with a range of conditions no less in the case of people living with Chronic Fatigue syndrome. It might be helpful to signpost clinicians or commissioners reading this material to existing social prescribing intiatives.	Thank you for your comment. No evidence was identified for social prescribing and the committee decided they could not make recommendations in this area.
Inhealth Pain Management	Guideline	General	General	Energy Envelope: This seems overly emphasised within the document and unfortunately is not great science: There is no set amount of 'energy' that is available in the day. Whilst the rationale for energy envelope is explained there are dangers with this model, and I am concerned that its over emphasis in what will effectively be taken as a commissioning and therapy document will leave people trapped in a spiral of lessening activity. Some dangers, outlined: There is no mention of engaged activity leading to 'energy generation' and improved wellbeing, as opposed to rest which naturally leads to sluggishness and fatigue. Please adjust the emphasis on rest within the document and stress the importance of learning 'energy generation' activities. Likewise, issues associated with homeostatic control – there does not seem to be a strong suggestion of clinically challenging these problems. Trying to rest one's way out of	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or

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				homeostatic problems will not address the issue and may indeed increase the bodies intolerance to movement, blood pressure changes, etc. Please include some form of mention of challenge and gentle/timely increase of challenge within the document. Sleep needs activity to be restful/restorative. Over rest will probably lead to a reduced adenosine level which will ensure the sleep pressure is low and therefore deep sleep will be unattainable. Hence over-resting can lead to deep-sleep starvation, fatigue, and poor memory, etc. The emphasis on the rest will not help the attainment of deep sleep. Structure, activity and the appropriate understanding of sleep science will help with sleep as will appropriate activity challenges. Also, internal stressors (see below) are common in people with chronic fatigue, and this inability to 'switch off' also ensures poor depth of sleep – see note on psychological Approaches.	downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). *Energy envelope* After considering the stakeholder comments the committee agreed that this concept might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *To note energy envelope has been edited to energy limits There is a section on rest and sleep in the symptom management for people with ME/CFS part of the guideline.
Inhealth Pain Management	Guideline	General	General	Psychological Approaches: The emphasis of CBT on purely managing and coping with the condition does not take into account the role of excessive thought processes, poor emotional regulation and other internal stressors on the general allostatic loading that in turn gives rise to increased fatigue/flareup. Whilst it is understandable that we would wish to avoid using CBT, neurolinguistic programming and other cognitive processes to 'fix' the fatigue issue it is important to acknowledge that stressors come in many forms and include cognitive, emotional, physical, infective, and immune processes and that there are ways of a mediating some, if not all, of these stressors.	Thank you for your comment. The committee agree that activity is not just about physical activity. Activity is defined in the guideline as any effort that uses energy, which and includes cognitive, emotional and social activity, as well as physical activity. Different activities combine and interact to cause a cumulative impact for the individual.

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				Clinically, I have seen numerous patients who are less affected by physical activity than cognitive, emotional, and sensory activity. This means that CBT, mindfulness, and ACT may well be helpful in the management of fatigue. Whilst I may baulk at a the discussion of Transactional Analysis and drivers due to it being incredibly old school; discussions and techniques to reduce internal stressors still clinically seem to be helpful for people with chronic fatigue.	
Inhealth Pain Management	Guideline	General	General	Graded Exercise Therapy: Whilst the politics of graded exercise has a long history within the management of chronic fatigue, it may be helpful to define graded exercise properly within these guidelines rather than throwing the baby out with the bathwater. The development of graded exercise from psychological graded exposure takes into account the self-directed nature of increasing activity and allows gentle increase in activity without the automated incrementation/increase wrongly ascribed to this technique. Explanation of 'proper' graded exercise as a development from graded exposure may go some way to overcoming the misunderstanding and misapplication of exercise as applied to chronic fatigue. It will also help the inclusion and reading of evidence - as it appears historically within research	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and

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					application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. A definition of GET has been included in the guideline.
Inhealth Pain Management	Guideline	General	General	Knowledge and Skills: The frequent advice to refer to clinician's with experience in managing ME/CFS may not be helpful. The potential for enough clinicians with ongoing expertise and experience of ME/CFS has yet to be realised and frankly may not be a priority. Unfortunately, our service has seen NICE guidelines used in commissioning to remove services and justify sub-optimal clinical practice. If a set of usefully experienced clinicians do not exist in a local area, time and effort from Commissioners will probably move on to something that can be (more easily) done. I would suggest a framework of knowledge and skills and reference to freely and easily	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should be trained in ME/CFS and so they can deliver care relevant to their role and in line with this guideline. Evidence review B includes the committee discussion on the development of training materials. This guideline focused on clinical recommendations and the committee did not comment on the delivery of services, which can be determined locally. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS.

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				available training material be suggested by the guidelines – as this gives people something to do in their locality.	
Inhealth Pain Management	Guideline	004	16	We wondered if in addition to feelings of mistrust there should also be comment on the feelings of grief and loss that people experience. Recognise people with ME will often be grieving for the life they had and the person they knew themselves, so they will also display the symptoms of grief.	Thank you for your comment. While the committee agree that people with ME/CFS may experience feelings of grief and loss for the life they had this recommendation has a different focus raising awareness about the prejudice and stigma that people with ME/CFS have experienced from other people. For this reason your suggestion has not been added to the recommendation.
Inhealth Pain Management	Guideline	024	4	The statement: "Be aware there is no current treatment or cure (non-pharmacological or 4 pharmacological) for ME/CFS." This statement is quite definitive and does not reflect that people can reach a state that they consider themselves to have recovered. Whilst there is a clear need to be clear on this difficult issue it might be useful to reflect that some do see improvement over time?	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. However while the committee agree there are people who recover there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. For this reason, the committee have not further edited the recommendation.
Inhealth Pain Management	Guideline	024	6	The section on energy management is large and detailed. The evidence review on Non-Pharmacological Management did not identify many studies that could comment on this topic. As a result much of this guidance seems to be based on the Committee's understanding of the topic. Given the limited volume of evidence this is not surprising and reasonable to involve the experiences of experts and people with lived expertise. However, it would also seem appropriate to reflect that the advice on Energy Management is based on this level	*Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening

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				of understanding and ongoing best practice. Perhaps a recommendation for research would be a suitable outcome as it seems a fruitful area of potential enquiry.	their symptoms by exceeding their limits. This is included in the rationale for the energy management section. The research recommendation on self-monitoring techniques has been edited to include research into establishing and then maintaining energy limits.
Inhealth Pain Management	Guideline	025	18	The line "reduce activity as the first step" could be replaced by the more flexible approach of "analyse the activity the first step and reduce or activity as appropriate". This would allow people to tailor their changes as appropriate for them. It may not be that people need to reduce activity rather change their approach to it?	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to, agree a sustainable level of activity as the first step, which may mean reducing activity.'
Inhealth Pain Management	Guideline	026	1	Could the following phrase be added as a reason for referral into a specialist CFS/ME service "require a holistic assessment to empower engagement in meaningful occupations such as work/ leisure/ hobbies". This also addresses psychosocial aspects of reasons to seek allied health professional advice.	Thank you for your comment. This section refers to referral for physical activity, earlier in the guideline in section 1.5 there are recommendations on a holistic assessment and developing a care and support plan. This includes the points you make.
Inhealth Pain Management	Guideline	027	21	Advising not to tell people to make use of unstructured exercise seems very limiting for many people. There is not high levels of availability for specialist supervised exercise programs or activity programs, many of the ones that exist are likely to be limited to the duration of a referral into a service. The great range of severity of CFS/ME is recognised within the guideline and as a result some people may very much value their involvement with self-directed exercise or community activity when they have carefully considered and adjusted it's role within their lifestyle. We would suggest that a person-centred approach to exercise is taken where healthcare professionals work with the individual to work out what form of activity or exercise is suitable and attractive to them.	Thank you for your comment. The committee agree there is little dispute amongst clinicians working with people with ME/CFS that they should not undertake exercise that is not part of a programme overseen by a ME/CFS specialist team, such as telling them to go to the gym or exercise more. It is commonly agreed that people with ME/CFS experience post exertional malaise (PEM) after activity. PEM is a worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated. It is in this context, and recognising the evidence from people with ME/CFS indicating that misunderstanding of the impact of PEM

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				Recognising the response to a definition of the term "Graded exercise therapy" we felt that there is avoidance of any comment on scope for healthcare to support people to make values or goals based changes to their lifestyle and activity levels within their own abilities and tolerance. The variability and fluctuation seen in symptoms of CFS/ME make this challenging but not impossible with close working with the individual dealing with this condition. It would also seem approach is within the committee advocated approach of energy conservation and enveloping.	and inappropriate advice on how to incorporate physical activity (and exercise) into their lives has resulted for some in a deterioration of their condition, that this guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS.
Inhealth Pain Management	Guideline	029	8	Given recognition of the role of Occupational Therapy in supporting people perhaps this line should read: "providing access to support from the specialist ME/CFS physiotherapy/occupational therapy service". We also wanted to highlight the role of Occupational Therapists in delivering these guidelines. It seems from reading them that Occupational Therapists are excellently placed and skilled to deliver this care.	Thank you for your comment. The committee agreed where a physical activity or exercise programme is offered, it should be overseen by a physiotherapist in a ME/CFS specialist team. The committee agree that occupational therapists have an important role in the guideline.
Inhealth Pain Management	Guideline	030	14	The only comments on pain management are on the use of pharmacology and refers to the medications on the management of neuropathic pain. This seems surprising given that NICE is concurrently developing a guideline on the	Thank you for your comments. Although pain relief was included in the protocol for pharmacological interventions no evidence was identified and the

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				management of Chronic Pain which includes guidance on pharmacology. Since the development of the NICE guidance on the Management of Neuropathic Pain there have been greater comment on the negative societal effects and high levels of prescription of Tramadol, Gabapentin and Pregabalin. Perhaps the CFS/ME guideline could refer to the NICE guidance on the management of Chronic Pain rather than Neuropathic Pain? We would also raise that there is no comment on non-pharmacological aspects of management of pain. This formed a majority of guidance in the NICE guidance on the management of Chronic Pain. This could be commented on in the CFS guidance then refer to the Chronic Pain guidance for greater detail?	committee agreed they were unable to make any recommendations for specific medications. The committee linked to NICE guidance that was relevant to people with ME/CFS, the committee acknowledged that this does not address all the type of pain that people with ME/CFS may experience. *Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. As such the difference between the guidelines is not a problem. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that any when managing any co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate. The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS

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Inhealth Pain Management	Guideline	034	1	CBT is mentioned but there is not recognition of other psychological approaches. The evidence review didn't identify any relevant studies and perhaps this should be commented on as an area for further research? For instance: Stress management, Relaxation techniques, Mindfulness and Mindful Breathing, Practice Desensitisation, Practice Positive Psychology	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	General	General	We applaud the Committee's withdrawal of graded exercise therapy (GET) and cognitive behavioral therapy (CBT) as recommended treatments for myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS). We also applaud the Committee's revocation of deconditioning and abnormal/ distorted beliefs as the cause of ME/CFS. This is a major, positive change for patients in the UK and beyond as NICE Guidelines are reviewed and followed around the world. Our organization and our members have never recommended GET or CBT as treatments for ME/CFS and believe, while deconditioning may be present in ME/CFS, the underlying cause of the disease originate from other physiological mechanisms that are not yet fully understood.	Thank you for your comment. To note after considering the range of stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
International Association for Chronic Fatigue Syndrome/ Myalgic	Guideline	General	General	Question 1: Because of the major shift away from GET/ CBT and the theories behind them, many health professionals, institutions, and organizations will need to change their beliefs and attitudes about ME/CFS. Some have estimated that it takes as long as 17 years for evidence to translate into patient care. Additional time, funds, and staff may be needed to implement	Thank you for your comment and information. The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and then in more detail in the discussion of the

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Encephalomyelitis (IACFS/ME)				these changes. There are actions the Committee can take to accelerate this process. Research on persuasion demonstrates that people are more likely to change their beliefs or actions when they are provided with the rationale. Therefore, the Committee should consider briefly providing the rationale for this shift in the Guidelines itself. Even though evidence is documented in the Appendices, our experience has been busy healthcare professionals often do not have the time or interest to read supplements/ appendices and may focus only on the Guideline, Furthermore, healthcare professionals are not starting from a blank slate but rather may already have some knowledge and, unfortunately, misconceptions about ME/CFS. For example, some UK-based physicians and groups have already publicly expressed that this major shift was prompted by undue pressure from a small group of patients. While there may be advocacy from patients, we feel their activities have been appropriate given GET and CBT were not effective and even harmful for many. Issues with CBT/ GET were not confined to the UK: surveys of thousands of patients across countries and across more than a decade showed that a median of 50% of patients reported worsening from GET-type programs. Questions 3: There have also been many scientific studies in the last 2 decades showing objective, biologically based abnormalities in patients that may explain their symptoms. Citing or summarizing some of these studies in the Guidelines would help health professionals understand why GET and CBT are no longer recommended. Below are some examples of reviews that could be cited.	evidence sections in the review chapters. The context section to the guideline provides a concise background to the guideline. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. Your comments will also be considered by NICE where relevant support activity is being planned. All of the references you provide have been checked for their inclusion in the guideline reviews, none meet the inclusion criteria for the guideline reviews.

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				a. Stevens S, Snell C, Stevens J, et al. Cardiopulmonary Exercise Test Methodology for Assessing Exertion Intolerance in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Front Pediatr*; 6. Epub ahead of print 2018. DOI: 10.3389/fped.2018.00242. b. Tomas C, Newton J. Metabolic abnormalities in chronic fatigue syndrome/myalgic encephalomyelitis: a mini-review. *Biochem Soc Trans* 2018; 46: 547–553. c. Rutherford G, Manning P, Newton JL. Understanding Muscle Dysfunction in Chronic Fatigue Syndrome. *J Aging Res* 2016; 2016: 2497348. d. Cockshell SJ, Mathias JL. Cognitive functioning in chronic fatigue syndrome: a meta-analysis. *Psychol Med* 2010; 40: 1253–1267. e. Jackson ML, Bruck D. Sleep abnormalities in chronic fatigue syndrome/myalgic encephalomyelitis: a review. *J Clin Sleep Med*. 2012;8(6):719-728. Published 2012 Dec 15. doi:10.5664/jcsm.2276 Finally, many medical and scientific professionals have pointed out the limitation and flaws in PACE and other trials. Two examples are cited below. a. Journal of Health Psychology Special Issue August 2017 https://journals.sagepub.com/toc/hpqa/22/9 b. sasusa. PACE: The research that sparked a patient rebellion and challenged medicine. *Sense About Science USA*,	

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				https://senseaboutscienceusa.org/pace-research-sparked-patient-rebellion-challenged-medicine/ (2016, accessed 19 December 2020).	
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	005	001	Question 1: For the section on "Approach to Delivering Care", the shift away from CBT and GET should be mentioned here, at the beginning of the document. This major change should be mentioned at the Guideline's beginning since it is a major change from previous practice and some readers may not read the whole document or focus only on early sections of the Guideline.	Thank you for your comment. The focus of this section is to raise awareness about ME/CFS. These recommendations are supported by the evidence. Lack of belief in ME/CFS and understanding about the impact of their symptoms was reported by people with ME/CFS in Evidence review A, Appendices 1 and 2 and supported by the committee's experience. These recommendations supports good clinical practice in building relationships between healthcare professionals and people with ME/CFS. The management of ME/CFS and symptom management is addressed in detail later in the guideline for this reason your suggestion has not been added.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	005	019	Question 1, Question 3: For the section on "Additional principals" for children and young people, consider including information about safeguarding here, at the beginning of this Guideline, instead of delaying until page 16-17 to mention this topic. Families and children in the UK have not only been met with doubts and disbelief by health professionals, they have been subjected to social service investigations and legal proceedings when they have disagreed with treatments like CBT/ GET. Consider citing Jane Colby's 2014 study on this issue, which showed out of 121 cases, none were found to be guilty of child abuse/ neglect. The article is entitled ""False Allegations of Child Abuse in Cases of Childhood Myalgic Encephalomyelitis (ME)" and is located on the Tymes Trust website. This may help convince professionals who persist with previous ideas about paediatric ME/CFS.	Thank you for your comment. The committee agree that safeguarding is an important topic in this guideline. After considering the stakeholder comments on the order of the guideline the committee agreed to keep safeguarding later in the guideline after the diagnosis and assessment and care planning sections of the guideline.

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International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	006	007	For section 1.1.8, consider deleting "sleep disturbance" point since these issues affect even mildly/ moderately affected ME/CFS patients and adding problems with chewing, abdominal pain, diarrhoea, and bladder issues to this list. Interstitial cystitis and irritable bowel syndrome may also be more common in ME/CFS than the general population.	Thank you for your comment. The committee agree that any of the symptoms included here can affect anyone with ME/CFS, the aim of this section is to highlight symptoms can occur with such severity that they significantly affect the lives of people with severe or very severe ME/CFS. As such the committee disagree that sleep disturbance should be deleted. The committee discussed whether interstitial cystitis is more common in people with ME/CFS and agreed that that this wasn't their clinical experience case and did not add this (or urinary symptoms) to the list of symptoms. The NICE guideline on Irritable bowel syndrome has been added to the guidelines listed in the coexisting conditions section of the guideline to signpost people with ME/CFS for support with these gastrointestinal symptoms. The committee have noted at the beginning of the managing ME/CFS section and 'managing coexisting conditions that the recommendations in the section on principles of care for people with ME/CFS and section on access to care and energy management should be taken into account when managing symptoms and coexisting conditions in people with ME/CFS.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	006	028	Address bowel/ bladder continence issues in this section. For example, severely affected patients may benefit from a bedside commode, voiding schedule, intermittent catherization, adult diapers, etc. Incontinence also increases moisture and thus, the risk for pressure ulcers.	Thank you for your comment. Personal care is included in the second bullet point,' may need help with all activities of daily living'. As with any list the examples given are not meant to be exhaustive.

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International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	008	002	Question 1: While it is true that there is no specific diagnostic test for ME/CFS yet and diagnosis is made primarily on clinical grounds, it is also important to explain to health professionals and patients that studies have shown consistent, biological abnormalities in patients. The problem with only stating the first part is many people – including health professionals, patients, the family members, their friends, employers, the public, etc. - often then jump to the conclusion that ME/CFS is based only on subjective symptoms, that is, there is no biological basis for ME/CFS. That jump may be why ME/CFS patients have been inappropriately labelled as work-shy, "complainers', etc. or misdiagnosed with depression and anxiety. Question 3: In the United States Institute of Medicine report, abnormal results from cardiopulmonary exercise testing, natural killer cell activity, tilt table testing, and neuropsychological batteries were cited even as none of these tests alone or in combination can currently make a definitive diagnosis of ME/CFS. However, they provide objective evidence supporting subjective symptoms and can help health professionals narrow down the diagnosis. Institute of Medicine. *Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness*. Epub ahead of print 10 February 2015. DOI: 10.17226/19012. https://www.nap.edu/catalog/19012/beyond-myalgic-encephalomyelitischronic-fatigue-syndrome-redefining-an-illness	Thank you for your comment and information. The first recommendation in the guideline states, 'Be aware that ME/CFS is a complex, chronic medical condition affecting multiple body systems and its pathophysiology is unclear is still being under investigated. This is again noted in the context section of the guideline. Based on this and that no evidence was identified in evidence review D to support this recommendation your suggestion has not been added. The principles of care section at the front of the guideline make it clear that ME/CFS is a medical condition and people with ME/CFS have experience have experienced prejudice and disbelief.

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International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	008	010	Suspecting ME/CFS at 6 weeks for adults and 4 weeks for children may be too early. While patients affected by ME/CFS should be diagnosed in a timely manner, the shorter duration of time may mean premature diagnosis of ME/CFS before some conditions have a chance to resolve (e.g., Epstein-Barr virus infectious mononucleosis) spontaneously or with treatment and premature termination of necessary evaluations. For example, anchoring biases may affect a physician who decides a provisional diagnosis is the final diagnosis and orders no further testing.	Thank you for your comment. The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. However after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted. The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. • Further investigation/differential diagnoses. The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have added examples of investigations to be done when suspecting ME/CFS and have added that ME/CFS should be suspected if the 'symptoms are not explained by another condition.'
International Association for Chronic Fatigue Syndrome/ Myalgic	Guideline	008	017	For Box 1, the description of post-exertional symptom exacerbation onset should allow immediate onset also. Patients report that immediate onset can occur in some situations. It would also be helpful to health professionals to describe the symptoms because post-exertional fatigue and musculoskeletal	Thank you for your comment. The committee note that post exertional malaise is usually described as delayed in onset with it typically delayed 12-48 hours after activity, but recognised that some people with

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Encephalomyelitis (IACFS/ME)				pain are common even in healthy people and people with other conditions (e.g., after a long hike or in someone with osteoarthritis) whereas post-exertional flu-like feelings, sore throat, headaches, insomnia, and cognitive dysfunction are not. a. Chu L, Valencia IJ, Garvert DW, Montoya JG. Deconstructing post-exertional malaise in myalgic encephalomyelitis/ chronic fatigue syndrome: A patient-centred, cross-sectional survey. PLoS One. 2018 Jun 1;13(6): e0197811. doi: 10.1371/journal.pone.0197811. PMID: 29856774; PMCID: PMC5983853. b. Stussman B, Williams A, Snow J, et al. Characterization of Post–exertional Malaise in Patients With Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Front Neurol*; 11. Epub ahead of print 2020. DOI: 10.3389/fneur.2020.01025.	ME/CFS report PEM in a reduced (or later) time and have added 'can typically be delayed 12- 48 hours…' to the definition. To note after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM). The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	009	004	Regarding orthostatic intolerance (OI), the Committee may want to consider including this symptom as part of diagnostic criteria or highlighting it in some way. Since the US Institute of Medicine report in 2015, more evidence has accumulated about OI and ME/CFS. For example, the Visser/ van Campen/ Rowe group have published studies reinforcing the high prevalence (up to 95%) of OI symptoms in ME/CFS patients and also demonstrating objectively that up to 90% of ME/CFS patients suffer from a mean 25% decline in cerebral blood flow on standing up. This latter finding occurred regardless of the severity of illness, whether overt heart rate/ blood pressure changes were seen, and whether a patient already carried an OI-related diagnosis or not. Additionally, include the more subtle symptoms of OI - such as cognitive confusion, fatigue, feeling sicker in general, etc. –	Thank you for your comment. The decision not to include orthostatic intolerance was based on the evidence of the criteria reviewed in evidence review D .They note that orthostatic intolerance is only described in 4 of the 9 criteria. The four symptoms (debilitating fatigue, PEM, unrefreshing sleep and sleep disturbance (or both), and cognitive difficulties) were agreed by the committee as the best basis for identifying people with ME/CFS and as essential to a diagnosis of ME/CFS. The committee emphasised it is the combination and interaction of the symptoms that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail).

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				as feelings of dizziness/ near syncope are on the extreme end of OI symptoms. Finally, remind health professionals that OI is often misdiagnosed as anxiety since symptoms such as dizziness, hyperventilation, and palpitations are common to both conditions. Similar to ME/CFS, OI-related syndromes are often not taught in medical schools. a. van Campen CLMC, Verheugt FWA, Rowe PC, Visser FC. Cerebral blood flow is reduced in ME/CFS during head-up tilt testing even in the absence of hypotension or tachycardia: A quantitative, controlled study using Doppler echography. *Clin Neurophysiol Pract*. 2020;5:50-58. Published 2020 Feb 8. doi:10.1016/j.cnp.2020.01.003 b. Schmidt LL, Karabin BL, Malone AC. Postural Orthostatic Tachycardia Syndrome (POTS): Assess, Diagnose, and Evaluate for POTS Treatment (ADEPT). *IMI* 2017; 4: 142–153.	
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	010	017	Health professionals should advise patients with a provisional diagnosis to keep a diary of symptoms and activities. This can help the patient and professional determine a baseline, identify post-exertional symptom exacerbation, and plan/ modify activities. It may be helpful to educate professionals that this step has minimal risk even for patients who eventually recover or are diagnosed with another condition.	Thank you for your comment. After considering the stakeholder comments the committee agreed that this concept and energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on PEM and energy limits* may not be helpful. At such keeping a diary at this stage may not be appropriate. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits.

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International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	010	023	The 3 months requirement for diagnosis may be premature. Previously, the 3-month duration was used only for children and most criteria for adults used 6 months. While patients affected by ME/CFS should be diagnosed in a timely manner, the shorter duration of time may mean premature diagnosis of ME/CFS before some conditions have a chance to resolve (e.g., Epstein-Barr virus infectious mononucleosis) spontaneously or with treatment and premature termination of necessary evaluations. For example, anchoring biases may affect a physician who decides a provisional diagnosis is the final diagnosis and does no further testing. Question 1, Question 2: On p. 52, line 2, the Committee suggested patients be referred to specialist clinics at 3 months. While this may guard against mis- and overdiagnosis, the duration may also be affected by the availability and accessibility of specialty referrals for a patient. Does the Committee have data on how accessible specialty services currently are? Can they handle a potential increase in referrals? Since no study has tracked prospectively in detail how patients are or ideally can be diagnosed (including which alternative diagnoses are found and when/ how they are found), this data should be collected and examined first before making a final decision about duration.	Thank you for your comment. *Reduction in timeline* After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. Based on the evidence and their clinical experience the committee found no reason why the time to diagnosis should be different in adults compared to children and young people noting that 5 of the 7 diagnostic criteria reviewed in Evidence review D do not have separate time referrals. People with ME/CFS do experience delays in diagnosis and the committee recognised that referral to a specialist team for confirmation of diagnosis can take months, taking this into account it is important that this process is started at 3 months and people are given appropriate advice until they are seen by a ME/CFS specialist team. *Further investigation/differential diagnoses.* The committee have similar experience of people being referred and having another diagnosis and throughout the section on suspecting ME/CFS the committee have recommended that investigations should be done to exclude other diagnoses and this should continue where ME/CFS is suspected. If in any doubt specialist advice should be sought. The committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'. *Capacity of current services* The committee do not have detailed data on the capacity of existing services but accept that they won't have capacity for a

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					large increase in extra referrals. Since the committee have now removed reference to a provisional diagnosis and made recommendations about testing for alternative conditions, the demand on specialist services should not be so great. Although the duration of symptoms in adults has been reduced by one month to be consistent with children, the diagnostic criteria are slightly stricter than in the previous guideline,
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	011	004	Remind health professionals to validate the patients' experience when diagnosing ME/CFS. Since most health professionals have not been educated well about this condition, patients may have faced physicians, nurses, and other professionals who have attributed their symptoms to deconditioning, depression, malingering, etc. Patients may also have encountered family members, friends, employers, and others who doubt that their symptoms are due to a medical condition. Communicating to patients, and especially their family, that their symptoms and experiences are real can be healing.	Thank you for your comment. Validation of the person's experience and the prejudice people have encountered is addressed at the beginning of the guideline in the principles of care section. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	012	003	During initial assessment for ME/CFS, health professionals should consider taking a complete function and social history. Because cognitive functioning may be more disabling even than physical functioning, cognition should be assessed. Functioning in different spheres – e.g., work, school, personal care, familial obligations – should also be evaluated. Social history can include where the patient lives, who they live with, financial resources, work/ education history, and who they can count on for support.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
International Association for Chronic Fatigue Syndrome/ Myalgic	Guideline	017	013	Studies suggest there may be a genetic component to ME/CFS. In the past, children of affected parents or siblings have had their ME/CFS attributed to the home environment or parental upbringing rather than genetic reasons. Here is one example:	Thank you for your comment and information.

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Encephalomyelitis (IACFS/ME)				Albright F, Light K, Light A, Bateman L, Cannon-Albright LA. Evidence for a heritable predisposition to Chronic Fatigue Syndrome. *BMC Neurol*. 2011;11:62. Published 2011 May 27. doi:10.1186/1471-2377-11-62	
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	017	014	Families and children in the UK have not only been met with doubts and disbelief by health professionals, they have been subjected to social service investigations and legal proceedings when they have disagreed with treatments like CBT/ GET. Consider citing Jane Colby's 2014 study on this issue, which showed that of 121 families, none were found to be guilty of child abuse/ neglect. The article is entitled ""False Allegations of Child Abuse in Cases of Childhood Myalgic Encephalomyelitis (ME)" and is located on the Tymes Trust website. This may help convince professionals who persist with previous ideas about paediatric ME/CFS.	Thank you for your comment and information. References are not included in NICE recommendations and as such your suggestion not added.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	017	021	Allow recording of visits (e.g., via mobile phone) if providers are informed beforehand. Patients often have cognitive issues affecting attention and memory. Be flexible about allowing caregivers during a visit. If needed and patients/ families can provide equipment, allow caregivers to attend appointments virtually (e.g., via a tablet) if they cannot m accompany a patient in person.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	018	013	Patients may also give up or reduce activities ahead of a visit or rest more/ put up with symptom exacerbation afterwards to attend an appointment.	Thank you for your comment and information.

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International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	019	003	Visiting hours may need to be restricted/ modified. Patients/ families should be encouraged to inform staff of pre-existing activity limitations and staff should heed these when planning mobility efforts.	Thank you for your comment These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	019	008	Question 2: We are happy to see the Committee include suggestions surrounding hospitalization. These suggestions should also be extended to usually mildly or moderately affected patients, as - like many chronic illnesses - hospitalization can exacerbate any existing condition. Although these additional considerations can be more costly and time/ resource-intensive, paying attention to them early on may result in less complicated hospitalizations and decreased length of stay.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments and hospital stays can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. The committee agreed that it was important to raise awareness about the challenges that people with severe and very severe ME/CFS have. We agree that preventing symptom exacerbation should have some resource savings, although we do not think there is evidence that this leads to reduced length of stay.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	021	003	Question 1: We commend the Committee for recognizing that ME/CFS may interfere and even stop a person's occupational and educational trajectory. Consider including a statement that for some affected patients, they may need to stop their education or work entirely and, unfortunately, indefinitely, if doing so severely affects their health. This is the reality for many patients: up to a 66% disability-associated unemployment rate has been reported. It would be helpful for the Committee to acknowledge this reality and advise health professionals, who are often under time and clinical pressures, about how to document disability and its impact on work for both work accommodations and application for disability benefits. Health	Thank you for your comment and information. After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support. ' and discuss with' has been added to the recommendation. Additional text on work has been added to the committee discussion in evidence review A and includes that adaptions and adjustments should be discussed.

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				professionals often have not been educated about this type of documentation during their training and may regard such requests as onerous. However, work accommodations and disability benefits are absolutely vital for many patients' financial survival and access to basic shelter, adequate nutrition, etc. until more effective treatments are found. Question 3: The following examples are drawn from the United States of America and might provide some ideas. a. US Department of Labor Job Accommodation Network ME/CFS webpages https://askjan.org/disabilities/Chronic-Fatigue-Syndrome.cfm b. Comerford BB, Podell R. Medically Documenting Disability in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) Cases. *Front Pediatr*; 7. Epub ahead of print 2019. DOI: 10.3389/fped.2019.00231.	
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	024	006	Question 1, Question 2, Question 3: Consider referring to/ examining a virtual pacing program like cfsselfhelp.org which was designed by a chronic disease self-management expert with a personal history of ME/CFS, an occupational therapist, and a physician specializing in ME/CFS. Although based in the United States, the program has been in existence for over a decade and has coached patients from around the world. Tailoring a pacing program to an individual patient may be time- and staff-intensive, not to mention staff need to be trained about ME/CFS and activity management. Our experience has been besides physicians, nurses, occupational, and physical therapists are also unfamiliar with ME/CFS.	Thank you for your comment. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme

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				In contrast, this program is free/ low-cost, designed by and run by people affected by ME/CFS. In the United States, during medical education sessions, when the website has been brought up (by professionals unaffiliated with the program), patients, caregivers, and health professionals have been enthusiastic about it. For the latter, it saves them time and effort. For the former, it is easily accessible and set up to meet individuals' needs/ preferences by people they can trust to know what living with ME/CFS is like.	
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	025	003	Under 'Energy Management", similar to the statement about deconditioning, consider adding "does not assume that irrational fear/ avoidance of activity is the cause of ME/CFS". From the 2011 Lancet PACE CBT article: "CBT was done on the basis of the fear avoidance theory of chronic fatigue syndrome. This theory regards chronic fatigue syndrome as being reversible and that cognitive responses (fear of engaging in activity) and behavioural responses (avoidance of activity) are linked and interact with physiological processes to perpetuate fatigue." Consequently, health professionals may still believe and treat patients under this premise. It should be explained to patients and health professionals there are physiological limits that may explain why patients cannot exceed a certain level of activity, no matter how much they try. An analogy can be made to patient with asthma or heart disease where patients often have limits to their ability to exercise/ engage in physical activity without medical treatment. Currently ME/CFS does not have a specific medical treatment available and thus patients are further limited.	Thank you for your comment. As you mention this is included in the section on CBT and is relevant in that section as CBT has been implemented on the basis of the fear avoidance theory of chronic fatigue syndrome. This was to clarify this is not the case here for CBT here. The committee deleted the bullet point on deconditioning noting that this recommendation was about providing advice to people with ME/CFS about the approaches to implement energy management and this point was not useful in this context.

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International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	025	072	Acknowledge there are times (e.g., special events) or situations (e.g., work obligations) where a patient may choose to or must exceed their energy limits. However, patients should be aware of possible negative consequences Since we do not understand the roots of all symptom exacerbations currently, it should be noted not all exacerbations can be avoided or reduced by activity management. For example, menstrual cycles and intercurrent infections can also exacerbate symptoms.	Thank you for your comment. The committee agree that part of the energy management plan and reviewing it would include reference to how people can manage changes in their circumstances. In the section of flare ups and relapses the committee have added a recommendation raising awareness that flare-ups and relapses can happen in ME/CFS even if the person's symptoms are well managed.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	027	003	Two other areas that should be assessed regularly in the severely ill are constipation and aspiration risk. Lack of movement and supine positioning around meals are risk factors.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	027	020	Before embarking on a physical activity program, the patient and medical staff may want to consider how additional exercise fits into the patient's overall life. If the patient is already struggling with work, school, housework, etc. they might need to reduce or adjust their other activities to fit in exercise. For some patients, their other life activities may take priority over exercise.	Thank you for your comment and information. The committee agree that it is important that people with ME/CFS take into account all types of activity (cognitive, physical, emotional and social) and the overall level of activity when developing and undertaking any energy management plan, this includes how physical activity might be included.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	027	024	Assess patients for orthostatic intolerance (OI) when planning for a physical activity program. Consider a program that starts with or emphasizes activities that can be done in a supine, half-reclining, or sitting position. For example, swimming, a recumbent instead of upright bike, rowing machine, supine/ seated stretches. Water-based activities where the patient is	Thank you for your comment. Anyone with ME/CFS that wishes to explore a physical activity or exercise programme is referred to physiotherapist in a ME/CFS specialist team, they would then assess the person. The assessment is not included in these recommendations they focus on what a programme should look like. The detail of the

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				entirely or semi-submerged in water also provides hydrostatic pressure to the lower extremities that alleviates OI. .	programme would be personalised to the person undertaking the programme. For these reasons your suggestions have not been added.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	028	008	Similar to the statement about deconditioning, consider adding a statement about NOT offering "programmes that are based on irrational fear/ avoidance of activity as the cause of ME/CFS". From the 2011 Lancet PACE CBT article: "CBT was done on the basis of the fear avoidance theory of chronic fatigue syndrome. This theory regards chronic fatigue syndrome as being reversible and that cognitive responses (fear of engaging in activity) and behavioural responses (avoidance of activity) are linked and interact with physiological processes to perpetuate fatigue." Consequently, health professionals may still believe and treat patients under this premise.	Thank you for your comment. This is included in the section on CBT and is relevant in that section as CBT has been implemented on the basis of the fear avoidance theory of chronic fatigue syndrome. This clarifies this is not the case here for CBT here.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	029	016	The endpoint of activity may not be a normal level of age-appropriate function or exercise for a healthy person. Rather the goal should be to find a level of physical activity the patient can sustain consistently without or with acceptable/ minimal symptom exacerbation. The disease likely has a physiological ceiling beyond which patients cannot expand their activity/ exercise levels safely.	Thank you for your comment. The recommendation is for a reduction to stabilise symptoms. The new physical activity baseline is in reference to the current level. This is a personalised collaborative physical activity or exercise programme and any levels would be agreed with the person and reviewed regularly.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	030	003	Question 1, Question 2: OI (orthostatic intolerance) is often undiagnosed in ME/CFS patients although up to 95% may be affected. It has a significant impact on function and quality of life and effective, low-cost treatments exist for some patients. Besides medications, there are many safe, free low-cost nonpharmacologic measures which a primary care doctor can initiate. The main obstacle is most health professionals are uneducated about OI. Diagnosing and treating OI may decrease cost of care since these patients may become more functional.	Thank you for your comment and information. **In the suspecting ME/CFS section of the guideline orthostatic intolerance is identified as one of the symptoms that are commonly associated with ME/CFS. The committee made a consensus recommendation to raise awareness about this. The guideline is about the diagnosis and management of ME/CFS and for this reason the committee was unable to make more detailed recommendations on the causes or diagnosis of orthostatic intolerance.**

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				Costigan A, Elliott C, McDonald C, Newton JL. Orthostatic symptoms predict functional capacity in chronic fatigue syndrome: implications for management. QJM. 2010 Aug;103(8):589-95. doi: 10.1093/qjmed/hcq094. Epub 2010 Jun 9. PMID: 20534655. Questions 3: For example, patients can be educated about consuming adequate salt/ fluids, using compression stockings, avoiding/ preparing for situations that exacerbate OI (e.g., hot weather, standing still in line), and counteractive measures (e.g., squatting, crossing legs). Dr. Peter Rowe's 2014 document for Dysautonomia International contain more examples and may be found by searching for "Dysautonomia International", "Rowe", and "orthostatic intolerance."	The committee did not make any recommendations on the management of orthostatic intolerance noting that although this can be straightforward it this can involve advice on diet, carrying out daily activities and activity support and should be tailored to the person taking into account their other ME/CFS symptoms. The committee noted medicines usually prescribed for OI can worsen other symptoms in people with ME/CFS and should only be prescribed or overseen by a clinician with expertise in orthostatic intolerance. (see evidence review G).
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	030	013	The most common types of pain in ME/CFS are muscle and non-inflammatory joint pain, although these may vary in severity. For some patients with mild pain, no medication or treatment is needed/ desired while for others, pain is a major disabling symptom and warrants careful assessment. It is important in these cases to examine whether pain might be related to another disorder with specific treatments, e.g., fibromyalgia, migraine headaches, Ehler-Danlos syndrome, irritable bowel syndrome, endometriosis, etc. The latter conditions commonly co-exist with ME/CFS. There is also inadequate research on types of pain and pain treatments in ME/CFS. a. Marshall R, Paul L, McFadyen AK, et al. Pain Characteristics of People with Chronic Fatigue Syndrome. *Journal of Musculoskeletal Pain* 2010; 18: 127–137.	Thank you for your comments and this information. The committee agree it is important to investigate if symptoms are related to another disorder and recommend throughout the guideline that the advice of an appropriate specialist should be sought if there is any uncertainty in interpreting signs and symptoms.

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				b. Chu L, Valencia IJ, Garvert DW, et al. Onset Patterns and Course of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Front Pediatr; 7. Epub ahead of print 2019. DOI: 10.3389/fped.2019.00012.	
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	031	006	Many patients take or try various vitamins, supplements, and herbs. Medical staff should encourage patients to tell them everything they are taking. Patients may not be aware of serious side effects from these substances or dangerous medication interactions.	Thank you for your comment. The committee agree and recommendation 1.12.24 includes advising people with ME/CFS about the lack of evidence to support routinely taking vitamins and supplements as either a cure or to manage symptoms.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	033	006	Irritable bowel syndrome is commonly co-morbid with ME/CFS. Thus, other symptoms that might interfere with maintaining an adequate, nutritious diet include abdominal pain, diarrhea, bloating, and constipation. Medical staff will need to assess and treat these symptoms as the situation warrants. For the severely affected, constipation may be exacerbated by lack of movement. In bedbound patients, severe impaction of stool may manifest as diarrhea (rather than constipation) and can result in poor appetite also.	Thank you for your comment. The NICE guideline on Irritable bowel syndrome has been added to the guidelines listed in the coexisting conditions section of the guideline to signpost people with ME/CFS for support with these gastrointestinal symptoms**.** The committee note that when referring to relevant NICE guidance the recommendations in the sections on principles of care for people with ME/CFS, access to care and energy management should be taken into account.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	033	015	For some patients, they may also benefit from being fed by caregivers. Placing snacks near the patient may allow them to eat/ drink when they feel better between meals. In some cases, patients have placed a cabinet or even small refrigerator near them to hold snacks	Thank you for your comment and information. The list of examples was identified by the committee based on their experience of what can help people and is not intended to be an exhaustive list
International Association for Chronic Fatigue Syndrome/	Guideline	034	001	Since CBT has been emphasized previously in ME/CFS, we are pleased to see the Committee address its use as a means of psychological support for ME/CFS rather than as treatment for it. We are also pleased to see that support groups are no longer	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any

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Myalgic Encephalomyelitis (IACFS/ME)				viewed negatively (e.g., as reinforcing "abnormal" illness beliefs) as noted for example on p. 55, line 6. Because different people respond positively to different types of psychological support, consider mentioning support groups in this section also.	misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	034	002	Although this Guideline concentrates rightfully on ME/CFS and not on co-morbid conditions, since depression and anxiety are common in ME/CFS, perhaps include a note that CBT is established to be effective for depression/ anxiety. This way, clinicians are reminded and patients/ caregivers are educated that in patients with co-morbid mood disorders, CBT is often among the first-line treatments for these conditions. We have encountered patients affected by depression/ anxiety who are reluctant to accept CBT for these diagnoses because they are concerned that their mood disorder will be conflated with their ME/CFS. Clarifying the role of CBT should help.	Thank you for your comment. *Co-existing conditions* The managing co-existing conditions of section of the guideline raises awareness that other conditions may coexist with ME/CFS, including depression and anxiety and these should be investigated and managed in accordance with best practice. This section also lists related NICE guidelines and recommends the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS.
International Association for Chronic Fatigue	Guideline	035	022	Question 1, Question 3: Traditionally, requirements for in-person mental health care has been an obstacle for homebound/ bedbound patients. Psychological help which can	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms

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Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)				be accessed remotely, via telephone or online conferencing programs, may be vital for severely affected patients. Initial in-home visits may also be helpful.	experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	036	007	This section omits several conditions which are commonly known to co-exist with ME/CFS and have specific, effective non-pharmacological and pharmacologic treatments. For example, the incidence of fibromyalgia may be as high as 70% and of orthostatic intolerance syndromes as high as 95%. Other conditions that fall in this category include irritable bowel syndrome, migraine headaches, sleep apnea, and multiple chemical sensitivity. This citation has a table and discussion of common co-morbid conditions. Emphasize that while ME/CFS has no effective disease-modifying treatments, many co-morbid conditions do and treating them can substantially improve patients' lives. Chu L, Valencia IJ, Garvert DW, et al. Onset Patterns and Course of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Front Pediatr*; 7. Epub ahead of print 2019. DOI: 10.3389/fped.2019.00012.	Thank you for your comment. This section links to related NICE guidance on co-existing conditions. Evidence review D- Diagnosis includes comprehensive lists of differential and co-existing conditions that are commonly associated with ME/CFS. After considering the stakeholder comments the committee added the NICE guideline on irritable bowel syndrome in adults.
International Association for Chronic Fatigue Syndrome/ Myalgic	Guideline	043	001	Since data about duration of flares is sparse, it may be better to leave this as "days" without a specific number. Flares can also last weeks and months. Flares can vary in their triggers, symptoms, severity, and duration from patient to patient. They may even vary within a patient at different times or stages of their illness. Readers should be informed in reality, patients,	Thank you for your comment. After considering the range of stakeholder comments the reference to 1-3 days has been removed and 'after a few days' included.' A relapse lasts longer than a flare up' has been added to this definition.

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Encephalomyelitis (IACFS/ME)				caregivers, and clinicians can only identify a flare (vs. permanent worsening) in retrospect, after a patients has recovered to their baseline.	
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	043	020	Symptoms of OI may be more subtle than dizziness/ fainting or near fainting. The definition could include symptoms like nausea, fatigue, confusion, feeling sick overall, etc. when in an upright position which resolves immediately or soon after sitting or lying down.	Thank you for your comment. These are examples in the definition and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	044	001	Explicitly include "personal care" as a physical activity. Personal care includes toileting, feeding oneself, dressing, bathing, etc. For the most severely affected and even some moderately affected patients, self-care is a challenge and should be inquired about by healthcare professionals. 'Household" activities may imply housework and caring for family rather than self-care.	Thank you for your comment. The definition does include that for many people, physical activity has a health benefit but in people with ME/CFS physical activity may make their symptoms worsen. The committee noted that the impact would vary in individuals with ME/CFS and agreed to leave the definition broad.
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	044	021	Onset of worsening can be shorter than 12-48 hours. For example, worsening can occur immediately after or a few hours later depending on the patient's baseline state, type/ intensity/ duration of activity, and environment (e.g., noisy, hot, etc.). Note the type of symptoms patients experience. Although symptoms can vary from patient to patient and even within patients from one post-exertional episode to another, some common post-exertional symptoms are not those most healthcare workers usually associate with exertion. For example, besides post-exertional physical/ cognitive fatigue and muscle/ joint pain, patients can experience appearance or worsening of mental confusion, headaches, sore throats, and problems with sleep.	Thank you for your comment and information. The committee note that post exertional malaise is usually described as delayed in onset with it typically delayed 12-48 hours after activity, but recognised that some people with ME/CFS report PEM in a reduced (or later) time and have added 'can typically' to the definition.

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				a. Dr. Larry Baldwin charts the presence and intensity of symptoms during different post-exertional episodes. https://solvecfs.org/guest-post-dr-larry-baldwin-on-post-exertional-debility-in-mecfs/ b. Stussman B, Williams A, Snow J, et al. Characterization of Post–exertional Malaise in Patients With Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Front Neurol; 11. Epub ahead of print 2020. DOI: 10.3389/fneur.2020.01025. c. Chu L, Valencia IJ, Garvert DW, et al. Deconstructing post-exertional malaise in myalgic encephalomyelitis/ chronic fatigue syndrome: A patient-centered, cross-sectional survey. *PLOS ONE* 2018; 13: e0197811.	
International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	048	012	".. declining a specific treatment should not affect other areas of the person's care." We are pleased that this statement was made and would suggest that it be repeated elsewhere in this document in the physical activity and CBT sections. Previously, we had heard from patients that declining GET or CBT damaged their relationship with healthcare professionals, who would view them as stubborn/ non-compliant/ irrational. This resulted in patients being discharged from a doctor's practice, refused certain testing/ treatments, and facing resistance when requesting assistive devices, caregiver support, or disability benefits.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. Recommendation 1.1.5 in the principles of care section of the guidelines is about this experience of people with ME/CFS.

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International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	049	022	In the United States, the US Institute of Medicine believed that a time shorter than 6 months and definitely 6 weeks would be too early to give a firm diagnosis of ME/CFS. Conditions that present like ME/CFS take time to investigate and may take time to resolve (e.g., Epstein-Barr virus infectious mononucleosis). Furthermore, treatment of some conditions takes time and their resolution/ substantial improvement may help healthcare professionals distinguish these conditions from ME/CFS (which would not resolve or improve much with treatments aimed at other conditions). One potential downside of a "too early" diagnosis is some healthcare professionals may terminate a thorough investigation earlier than warranted, believing they already have the answer. The Committee may also want to consider adding orthostatic intolerance (OI) to the 4 core symptoms. This is because OI symptoms can exist in up to 95% of ME/CFS patients and recent studies show decreased cerebral blood flow in 90% of ME/CFS patients (regardless of severity of illness, overt blood pressure/ heart rate changes, or existing diagnosis of OI), OI can be effectively treated, and successful treatment can significantly impact quality of life/ function. a. van Campen C (Linda) MC, Verheugt FWA, Rowe PC, et al. Cerebral blood flow is reduced in ME/CFS during head-up tilt testing even in the absence of hypotension or tachycardia: A quantitative, controlled study using Doppler echography. *Clin Neurophysiol Pract* 2020; 5: 50–58. b. Costigan A, Elliott C, McDonald C, et al. Orthostatic symptoms predict functional capacity in chronic fatigue syndrome: implications for management. *QJM* 2010; 103: 589–595.	Thank you for your comment. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 6 weeks -'Provisional' diagnosis has been deleted. The committee agreed that the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. • Further investigation/differential diagnoses. Throughout the section on suspecting ME/CFS the committee have recommended that investigations should be done to exclude other diagnoses and this should continue where ME/CFS is suspected. They have now added some examples of tests to be done. If in any doubt specialist advice should be sought. The committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'. *Orthostatic intolerance* The decision not to include orthostatic as a key criteria decision was based on the evidence of the criteria reviewed in evidence review D . They note that orthostatic intolerance is only described in 4 of the 9 criteria compared to cognitive difficulties that is described in 7 out of the 9 criteria reviewed. The committee note there is additional information on orthostatic intolerance in the management of symptoms section of the guideline and in evidence review D.

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International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME)	Guideline	060	009	Question 3: During 2017-2018, the United States National Institutes of Health convened a working group to come up with outcomes measures for ME/CFS across studies. These measures are known as "Common Data Elements." The goals of the project were a) to help researchers save time when selecting outcomes for studies, b) to facilitate comparisons across studies and c) to encourage further data sharing and mining. This website details the results of the working group: https://www.commondataelements.ninds.nih.gov/Myalgic%20Encephalomyelitis/Chronic%20Fatigue%20Syndrome	Thank you for your comment and information.
Invest in ME Research	Evidence review G	347	15-16	Evidence review G re Flares and Relapse on page 347 lines 15 and 16 "The committee noted this was a common part of ME/CFS and had explained in the Information and support section of the guideline that ME/CFS involves periods of remission and relapse." Remission implies that patients are well at times. Many ME/CFS patients never experience remission but adapt to living at a certain level and others have a steady decline no matter what they do.	Thank you for your comment. The committee agree that the long-term outlook of ME/CFS varies from person to person, and that although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS. This section of the guidelines and the recommendations and the recommendations on Information and Support have been amended to reflect this.
Invest in ME Research	Guideline	General	General	As we comment later in this document there must be a section at the beginning of the guidelines that describes the disease. You reference the IOM report – maybe you should use that description and add it to the Context section later in the Guidelines, and then move that section to the beginning.	Thank you for your comment. The introduction section has been replaced with the context section at the back of the guideline and includes background information. The context is not intended to be exhaustive and sets the scene for developing the guideline.
Invest in ME Research	Guideline	General	General	You asked –	Thank you for your comments and suggestions. Implementation

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				In addition to your comments below on our guideline documents, we would like to hear your views on these questions: 1. **Which areas will have the biggest impact on practice and be challenging to implement? Please** say for whom and why. • Providing timely and correct diagnosis o Challenging for both patients and doctors as not enough doctors who understand ME/CFS o The document mentions the word "specialist" numerous times but does not define the specialist or where/how patients are going to be able to access them. There needs to be funding for specialists. This will be extremely challenging in the current environment and history dictates that ME will likely not receive the amount of funding for these specialists that is required. o Challenging for medical education as there is considerable effort needed to get rid of the thinking that ME/CFS is caused by childhood trauma, for example. • Providing ongoing care o Challenging to undo the harm that long-term patients have suffered as a consequence of the 2007 CG53 guideline recommendations and the apathetic approach to ME that governments, the NHS, MRC and NICE have taken toward ME. o Challenging to encourage commissioners to fund specialist care that satisfies the demand	Thank you for your comment. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as training and access to specialist services, to implement some recommendations in the guideline. guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned.

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				o Challenging to healthcare providers to get long-term patients to trust them and reconnect with healthcare as many have not seen a doctor for their ME/CFS for years. o Challenging to NHS to re-educate ME/CFS service providers that followed the information in the 2007 guidelines and the research that the public funders supported. Getting them to acknowledge that their care set ups need to be overhauled. • Providing appropriate care and follow up for the very severely affected patients that have special needs. o Hospitals for example cannot guarantee isolation from noise, light, smells etc. How to accommodate for all the special requests and requirements in practice? o There are not enough knowledgeable healthcare staff to advice on problems with tube feeding and other dietary issues for example. Not enough dieticians in general and even less so those that understand ME/CFS. o Not enough healthcare professionals who do home visits • Treating children with ME/CFS with respect and listening to them o Challenging for social services and paediatricians to understand that ME/CFS is a disease that does not require child protection orders to be implemented just because the child has been diagnosed with ME/CFS	

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				2. **Would implementation of any of the draft recommendations have significant cost implications**? • Medical education on ME/CFS needs to be standardised and updated as required. Needs funding. • GPs need to follow up their ME/CFS patients just as they do any other of their chronically ill patients so that they can provide medical evidence for DWP assessments for example. • ME/CFS services need to connect to research initiatives to foster learning and collaboration. This needs funding. • Very severely ill ME/CFS patients need in-patient facilities and respite care offered to carers that are often family members. Funding is required for this. 3. **What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.)** • There needs to be major investment in all areas of ME/CFS biomedical research to help provide good evidence for policies that guide patient care. • Invest in ME Research has been involved in funding and initiating ME/CFS research at Quadram Institute in Norwich since 2013. The charity initiated partnership involves the local East Coast Community Health ME/CFS clinic and is an example of good collaborative practice	

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				that has been initiated by patients and carers without any support from public funding.	
Invest in ME Research	Guideline	General	General	It would be prudent to produce separate sections of the guidelines for children and for severely affected (maybe even splitting this category into severe and very severe sections). At the moment these groups get lost in the overall text. The specific information concerning children and severe, very severe ME patients should be clearly visible and not imbedded in the overall text. This will aid healthcare staff in understanding and treating the disease better. The draft guidelines are a cumbersome document to read and need more clarity.	Thank you for your comment. After considering the stakeholder comments the committee restructured the guideline placing a separate section for people with severe or very severe ME/CFS after the main of recommendations. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. With reference to children and young people they decide that these recommendations were placed as additional recommendations in the relevant sections.
Invest in ME Research	Guideline	001	5	We commented on terminology used by NICE fourteen years ago when we commented on the draft guidelines and the finalised guidelines CG53. You should not be using Encephalopathy – use the term used by the WHO. The 2007 guidelines (CG53) used the term CFS/ME – so perhaps you need to explain why the old guidelines (the "Gold Standard" as described by NICE director Professor Littlejohn) referred CFS/ME but are now being updated by these draft guidelines to use ME/CFS.	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'*

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Invest in ME Research	Guideline	003	2	An introduction to the disease is required in the Contents, before Recommendations. You need to describe ME here in order to set the scene for GPs and those others for whom this document is intended. (the 2007 guidelines had an introduction of sorts) The guideline needs to include an introduction that gives general information on ME/CFS such as numbers affected, the most common triggers etc. It should also describe the terms being used and the reason for the update – and possibly admit to the flaws in the 2007 guidelines that were rejected by (most) charities. The introduction should mention the WHO ICD-10 classification G93.3 and as well as ICD-11 classification code of 8E49. WHO ICD-10 and ICD-11 both use postviral fatigue syndrome as the lead term and include myalgic encephalomyelitis in ICD-10 with chronic fatigue syndrome in the alphabetical index/indexed to G93.3. ICD-11 includes both myalgic encephalomyelitis and chronic fatigue syndrome under the lead term post viral fatigue syndrome. WHO does not use the term myalgic encephalopathy – neither should you! Even if SNOMED (code 52702003) does accept that term it would make far more sense, and be more responsible of NICE, to use the term that WHO uses as the preferred term in	Thank you for your comment. The introduction section has been replaced with the context section at the back of the guideline and includes this information. The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) has been added to the context.

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				order to reduce the amount of confusion and possibly mistakes. The correct coding and terminology is important for data collection on the incidence and prevalence and healthcare planning and you could aid in this aspect by standardising on the WHO terminology. It would help GPs, commissioners and other healthcare professionals see the category of disease they are dealing with. It should not be left open for speculation. Re-education of healthcare professionals should start here in the introduction. Many of the specialist services that were set up following on from the 2007 guidelines were within mental health services headed by a spectrum of professionals with no one speciality adopting ME/CFS. These guidelines need to describe ME, CFS and the reason for the use of ME/CFS to avoid free for all interpretation happening again.	
Invest in ME Research	Guideline	004	17-18	This should read "…who do not understand this disease". The inference in your terminology is that this is peculiar to the individual. If it affects 250,000 in the UK then it is more serious than other diseases such as MS or HIV/AIDS.	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change condition to disease. Reference to the ICD10 classification has been included in the context section of the guideline.

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Invest in ME Research	Guideline	004	5	As you base these guidelines on the IOM report then why do you not use the same definition for ME? Here it is – " ME/CFS is a serious, chronic, complex, and systemic disease that frequently and dramatically limits the activities of affected patients." reference: Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness Committee on the Diagnostic Criteria for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome; Board on the Health of Select Populations; Institute of Medicine Washington (DC): National Academies Press (US); 2015 Feb 10. The National Academies Collection: Reports funded by National Institutes of Health. PMID: 25695122	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change the terms used.
Invest in ME Research	Guideline	004	16	1.1.2 Recognise that people with ME/CFS may have experienced prejudice This should read 1.1.2 Recognise that **many** people with ME/CFS have experienced prejudice	Thank you for your comment. The current wording is clear that there are people with ME/CFS that have experienced prejudice and your suggestion does not add further clarification. For this reason the recommendation has not been edited.
Invest in ME Research	Guideline	004	16	It might be helpful to mention here that the previous 2007 NICE guideline and its recommendations, and the travel of research and clinical considerations that followed, contributed	Thank you for your comment. The current wording is clear that there are people with ME/CFS that have experienced prejudice and your suggestion does not

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				to the prejudice, stigma and build-up of distrust between patients and healthcare professionals. Maybe it should be mentioned in the introduction rather than here (see our comment 3)?	add further clarification. For this reason the recommendation has not been edited. The context notes that the 2007, 'guideline made recommendations on cognitive behavioural therapy and graded exercise therapy. Both treatments are controversial for this condition, and there are disagreements and uncertainty about their effectiveness among both people with ME/CFS and health providers.'
Invest in ME Research	Guideline	004	20	should read ".. they may have justifiably lost trust..."	Thank you for your comment. This recommendation highlights the reason why people with ME/CFS have lost trust in health and social services, to add justifiably is unnecessary. For this reason the recommendation has not been edited.
Invest in ME Research	Guideline	005	15	Should read "Explain and emphasise to people with ME/CFS ....."	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. For this reason your suggestion has not been added. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.).

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Invest in ME Research	Guideline	005	20	It might be useful to mention here that the 2007 guidelines and the travel of research that followed contributed to this prejudice and disbelief. There is a great deal of re-education that is needed to be arranged and performed in order to change the current thinking of healthcare professionals and social workers.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Invest in ME Research	Guideline	006	1	The most important aspect is that health care and social care professionals truly need to listen to the child and believe in them and learn from them to be able to support them.	Thank you for your comment.
Invest in ME Research	Guideline	008	9	There should be a recommendation for a minimum set of appropriate blood tests as well as most common "red flags"/other conditions to keep in mind for exclusion especially as it is known that there is a high rate of misdiagnosis? In the CG53 guidelines of 2007 NICE did include recommendations under chapter 1.2.2 History, examinations and investigations. What has changed since 2007? You state in the evidence review – "The committee took the view that an exhaustive list of all possible conditions which might be considered was not possible, nor was it appropriate to provide advice on these conditions in this guideline, where there is relevant NICE guidance it is referenced in the recommendations." There is no need for an exhaustive list but some of the most common examples of exclusions to keep in mind would be helpful as misdiagnosis is very common and GP appointments do not allow much time to be spent on each patient.	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and as you say there is no need for one and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.

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Invest in ME Research	Guideline	008	17	Should you mention here that these criteria are modified from the IOM 2015 criteria?	Thank you for your comment. This is referred to in the rationale section of the guideline linked to this recommendation.
Invest in ME Research	Guideline	009	17	How would suspected ME/CFS be coded in healthcare records? Advice to GPs here would be useful.	Thank you for your comment. The coding of conditions in healthcare records is not in the remit of NICE.
Invest in ME Research	Guideline	010	17	To reduce their activities and listen to their bodies (common sense approach) would be the first item to mention	Thank you for your comment. After considering stakeholder comments this bullet point has been edited to ,'advise ..not to use more energy than they perceive they have − they should manage their daily activity within this limit and not push through symptoms'. The committee hopes this clarifies that people should listen to their bodies.
Invest in ME Research	Guideline	011	7	Who are these specialist teams experienced in ME? They do not exist now so where do they come from? What do they consist of? What training and experience do they require? Repeatedly trotting out this term "specialist team" means little when you do not have to define them or identify them.	Thank you for your comment. Based on the evidence (Evidence reviews A.B,C,D and I) and the committee's experience referral to ME/CFS specialist care was recommended for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. ME/CFS specialist teams where seen as the most appropriate place for people with ME/CFS to access support with GPs providing ongoing support and review. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I-Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development

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					of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.
Invest in ME Research	Guideline	011	8	Should this be care plan instead of management plan?	Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Invest in ME Research	Guideline	011	8	Is the diagnosis and care (management) plan taken care of by separate healthcare professionals? Who is in charge/takes responsibility for the overall care?	Thank you for your comment. After considering stakeholder comments the committee agreed to edit this recommendation to,'refer adults directly to a ME/CFS specialist team experienced in managing ME/CFS to confirm their diagnosis and develop a care and support management plan.' And hoped this adds clarity. Evidence review I-multidisciplinary care has further information on ME/CFS specialist teams. The multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Invest in ME Research	Guideline	011	10	This is very precarious as there is no description of a specialist paediatric team.	Thank you for your comment. The committee discuss further access to ME/CFS specialist teams in Evidence review I-Multidisciplinary care, they note that children and young people are likely to be cared for under local

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				We know from experience how badly wrong this can go where a paediatric team is headed by somebody who does not believe in ME. This is where many lives begin to unravel. What are the definitions of specialist teams - who decides?	or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.
Invest in ME Research	Guideline	011	11	Who is in charge of the child's overall care if there are various professionals involved? Why does the paediatrician who diagnoses the child need to refer further to a paediatric ME/CFS specialist team? As you probably know there are paediatric "*ME/CFS specialist teams*" that have considered ME as a problem arising from childhood trauma. How do you ensure that there are specialist paediatric teams available whose approach is in line with the new guidelines?	Thank you for your comment. The multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse. The committee added referral at the 4 week point to a paediatrician in the first instance for further assessment and investigation and then to a ME/CFS specialist for confirmation of a ME/CFS diagnosis to ensure children and young people will have a timely accurate diagnosis of ME/CFS. See Evidence review D- for the evidence and committee discussion. The committee acknowledged that non-specialists may not feel confident in diagnosing ME/CFS and recommended that people with suspected ME/CFS are referred to a ME/CFS specialist service for confirmation of the diagnosis (Evidence review B). In addition, the referral to community paediatricians for further investigations before ME/CFS specialist teams is the experience of committee members of working with children and young people. **The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff**

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					delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Invest in ME Research	Guideline	011	12	Should this be a care plan instead of management plan?	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Invest in ME Research	Guideline	011	13	The make-up of the desired specialist team should be described to give commissioners some direction as, at the moment, there is no national standard.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section).
Invest in ME Research	Guideline	011	16	NICE should recommend standard tools to be used for the assessment.	Thank you for your comment. Symptom assessment questionnaires are discussed in Evidence review D. In summary no validated questionnaires were identified and the committee were not confident in making a recommendation on s standard tool.
Invest in ME Research	Guideline	012	10	Replace management plan with care plan	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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Invest in ME Research	Guideline	012	27	Should that be worsening symptoms?	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
Invest in ME Research	Guideline	013	2	Replace management plan with care plan	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Invest in ME Research	Guideline	013	10	Replace management plan with care plan	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Invest in ME Research	Guideline	013	13	Replace management plan with care plan	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Invest in ME Research	Guideline	014	1	It would be best to learn from the child and provide the information they ask for. Find out what is important to the child.	Thank you for your comment and information.
Invest in ME Research	Guideline	014	8	This is one of the most important aspects of this guideline. If you give all involved (patient, school, employers etc.) the right kind of information at the point of diagnosis then there is no need for all of the extra and unnecessary talk of tailored goal setting and other top down guidance. Patients are just ill and have not lost their intelligence.	Thank you for your comment and information.
Invest in ME Research	Guideline	014	10	What kind of sources would be considered reliable and up-to-date? Just collecting words without definition is irrelevant.	Thank you for your comment. Throughout the guideline various sources of information are referenced, for example ME/CFS specialist services, self-help

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					groups, support groups and other local and national resources for people with ME/CFS.
Invest in ME Research	Guideline	014	19	Replace "often" with "can involve"	Thank you for your comment. After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS. See evidence review A for the committee discussion on information about the long term outlook for people with ME/CFS.
Invest in ME Research	Guideline	014	20	Many patients remain at their baseline and experience no remission at all.	Thank you for your comment and information.
Invest in ME Research	Guideline	014	21	Instead of flares and relapse use worsening of symptoms.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
Invest in ME Research	Guideline	015	4	who decides this information? Giving information on some groups may lead to wrong or distorted information being given	Thank you for your comment. The committee agreed on a broad recommendation on where to access information and not to add examples of organisations. As with any list of examples these cannot be exhaustive and there is the risk these are taken as the only options available.
Invest in ME Research	Guideline	016	7	Who are these - what definition – where? Replace "should be" with "must be". There are few who have training and experience in ME. How should they be trained and by whom?	Thank you for your comment. The committee agreed that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. This applies to this section. Must is used in a recommendation when there is a legal duty to apply a recommendation. This is not the case here and no changes have been made to the recommendation.

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Invest in ME Research	Guideline	016	14	It would be good to have information on where these trained and experienced professionals can be found. Is there a register of such professionals? Do they have training in ME in reality?	Thank you for your recommendation. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline.
Invest in ME Research	Guideline	018	15	It is not the fear that stops ME patients doing anything. They know if they are well enough to leave the house or not.	Thank you for your comment. After considering stakeholder comments about the word fear this recommendation has been edited 'risk that their symptoms will worsen may prevent people from leaving their home'.
Invest in ME Research	Guideline	020	20	Replace management plan with care plan	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Invest in ME Research	Guideline	020	30	Replace management plan with care plan	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Invest in ME Research	Guideline	021	6	Replace "some" with "most" or "many"	Thank you for your comment. This recommendation applies to all people with ME/CFS and the committee agreed that some is appropriate here.
Invest in ME Research	Guideline	022	1	Replace management plan with care plan	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Invest in ME Research	Guideline	022	17	Is not the patient themselves the experts in self- management?	Thank you for your comment.

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					The section on energy management in the guideline explains it is a self-management strategy led by the person themselves but with support from a healthcare professional.
Invest in ME Research	Guideline	022	19	Should this be managing worsening of symptoms? Flares and relapse imply that there has been a period of improved health? For many ME/CFS patients the reality involves maintaining their level of health and avoiding making things worse.	Thank you for your comment. After considering the range of stakeholder comments on the wording of flare the committee edited flare to flare ups. The description of flare up in the terms in the guideline includes that a flare up is a worsening of symptoms.
Invest in ME Research	Guideline	023	6	There are numerous mentions of specialist teams but there is no acknowledgement that there are very few teams in the UK that could be considered specialists. No mention of the training necessary, no mention of the cost of retraining, and in the current economic climate no chance of them being created.	Thank you for your comment. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as improved access to specialist services, to implement some recommendations in the guideline. guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned.
Invest in ME Research	Guideline	023	9	Replace management plan with care plan	Thank you for your comment. Management plan has been edited to care and support plan.
Invest in ME Research	Guideline	023	10	Replace relapse with worsening of symptoms.	Thank you for your comment. After considering the range of stakeholder comments on the wording of flare and relapse the committee edited flare to flare ups and did not edit relapse. The description of flare up and relapse is included in the terms in the guideline and references the worsening and exacerbation of symptoms.
Invest in ME Research	Guideline	024	18-24	Lines 18 to 24 resemble dressed-downgraded exercise programme. It makes it sound as if patients cannot judge their limits themselves.	*Thank you for your comment.* *Energy management*

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				They can if they are informed of the disease in an honest manner and told that one cannot exercise one's way out of ME/CFS.	Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Graded exercise therapy focuses on physical activity and the aims to increase activity. The recommendation is clear that energy management is a self-management strategy led by the person themselves but with support from a healthcare professional within a ME/CFS specialist team.
Invest in ME Research	Guideline	024	1	Should it be caring for ME/CFS?	Thank you for your comment. This section refers to ME/CFS as a condition and not people with ME/CFS as such managing is more appropriate here. To note Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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Invest in ME Research	Guideline	024	4	Perhaps this should be stated in an introduction at the beginning (see our comment 3)	Thank you for your comment. The introduction section has been replaced with the context section at the back of the guideline. This describes the disagreement an uncertainty in the evidence for therapies in ME/CFS and the need to update the 2007 guideline.
Invest in ME Research	Guideline	024	6	This section tries to please everyone and is open to anyone's interpretation. Advice on reducing activities and finding a level that is manageable should be considered as part of standard medical care. If patients feel supported and are allowed/encouraged to find their own limits/ judge their own function and monitored at regular follow-ups by their GP or a relevant specialist then that is all that is required. As there is no evidence for any treatment, management or therapy in ME/CFS then standard medical care principles should be followed.	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits.
Invest in ME Research	Guideline	025	1	This is a meaningless statement.	Thank you for your comment.
Invest in ME Research	Guideline	025	5	There is too much talk of plans and goals etc. It makes it all sound as if patients had lost the skill to live and need to be managed.	Thank you for your comment. The committee agreed that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and

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					support plan without it affecting access to other aspects of their care. The beginning of this section is clear that this is a self-management strategy led by the person themselves with support from a healthcare professional in a ME/CFS specialist team. Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits.
Invest in ME Research	Guideline	025	15	Again why specifically mention an activity plan as though it is an objetive regardless of the disease. The objective is to get well not achieve a text-book goal.	Thank you for your comment. Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits.
Invest in ME Research	Guideline	025	19	Why plan activity? Surely this must be done only of/when the patient can. By definition that means it cannot be planned.	Thank you for your comment. The principles of energy management are set out in recommendation 1.11.2. The aim is to support the person with ME/CFS to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limit. Planning is important to reduce this risk.
Invest in ME Research	Guideline	026	4	again...continued emphasis on physical activity	Thank you for your comment.

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					Based on the quantitative and qualitative evidence (evidence reviews A, G and H) and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Invest in ME Research	Guideline	026	4	Is it sensible to try to establish energy management plans for severe or very severe ME patients? One would think that provision of practical help and aids in managing the demands of daily living is required. You say in your rationale - "The committee agreed that if energy management strategies are inappropriately applied in people with severe or very severe ME/CFS this will increase the potential for harm. To reflect this, they recommended specialist advice and additional care in this group."	Thank you for your comment. Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that all people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity.

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				How confident is the guideline development group that there are enough specialists that can safely provide this advice?	The additional recommendations on people with severe to very severe ME/CFS are to ensure that additional caution is taken. The committee included (if possible) to emphasise that any increases may not be possible and the plan should be developed by a physiotherapist or occupational therapist working in a ME/CFS specialist team. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services , to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS.
Invest in ME Research	Guideline	026	16	This could be considered as part of standard medical care for anyone with a long-term chronic condition and is welcomed.	Thank you for your comment.
Invest in ME Research	Guideline	027	20	The committee justifies this physical activity chapter with their statement – "Because of the harms reported in the qualitative evidence, as well as the committee's experience of the effects when people exceed the limits of their energy envelope, **the committee recommended that people with ME/CFS should not undertake a physical activity or exercise programme unless it is delivered or overseen by a physiotherapist or occupational therapist who has training and**	Thank you for your comment and information. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline.

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				expertise in ME/CFS. The committee reinforced there is no therapy based on physical activity or exercise that is effective as a treatment or cure for ME/CFS." What is the purpose of this physical activity then if it is not a treatment or cure? An evidence based guideline should stick to evidence and this chapter is very confusing as it tries to cover all bases and leaves it open to anyone's interpretation. It tries to shoehorn exercise into the guideline whilst saying there is no evidence to support it and leaves the door open for out-dated and discredited models to continue. The previous chapters of energy management and physical maintenance should suffice. As and when patients feel their energy envelope limits increase they start to do more intuitively. It does not need to be made up into another "management" plan. We make the observation that this guideline seemingly tries to overturn the 2007 guideline by addressing the same therapies in a more "patient friendly" way instead of starting from a blank page and just going by the evidence. If there is no evidence of any treatment then we feel it would be best to follow standard medical care principles until more evidence is established.	When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.

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				In 2017 IiMER representatives met the deputy CMO of England and what was said then still applies we feel: "In Practical terms: we need physician led services (very few of which currently exist) which provide help and continued surveillance. ME is an identifiable problem due to the characteristic of post exertional malaise (PEM). Surveillance is needed as other diseases such as lymphoma can be hidden in that cohort." https://investinme.org/IIME-Newslet-1701-01.shtml	*See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *Treatment or cure* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS.
Invest in ME Research	Guideline	028	16	In 1.11.16 you instructed **not to offer** – • any therapy based on physical activity or exercise as a treatment or cure for ME/CFS • generalised physical activity or exercise programmes – this includes programmes developed for healthy people or people with other illnesses Now in this 1.11.18 you state " • A physical activity programme, if offered, should …."	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by

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				Conflicting and dangerous statements. What a mess! In any case, most of the physiotherapists and OTs that have specialised in ME/CFS in the past 13 years need to be retrained.	physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Invest in ME Research	Guideline	028	19	The same thing could be said about almost anything including GET so why not just stay with the evidence and remove this whole chapter of physical activity.	Thank you for your comment. Based on the quantitative and qualitative evidence * and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with

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					ME/CFS. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
Invest in ME Research	Guideline	028	20	This sort of statement is meaningless. How does the physiotherapist or OT judge who benefits, is made worse or experiences no difference? It is only by trial and error.	Thank you for your comment. The risk and benefits refers to the risks and benefits of a physical activity programme and not a judgment about who benefits.
Invest in ME Research	Guideline	029	20-22	In the NICE guidelines of 2007 advised against sleep in the day. In CG53 from 2007 it was stated – "1.4.2.3 Sleep management strategies should not include encouraging daytime sleeping and naps. People with CFS/ME should be advised that excessive sleep does not generally improve physical	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people

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				or mental functioning, and excessive periods of daytime sleep or frequent napping may further disrupt the sleep–wake cycle." Now the 2020 draft guidelines state – " • how to introduce rest periods into their daily routine, including how often and for how long, as appropriate for each person" How strange that NICE took 13 years to agree with us that patient should do what they need to when they need to – despite there being no new research evidence. Only properly conducted sleep investigations can determine what is appropriate for each person.	should be given advice on the role of rest and sleep and personalised sleep management advice.
Invest in ME Research	Guideline	032	8	Are there enough dietitians who specialise in ME/CFS to fulfil this recommendation? What is NICE's solution if not?	Thank you for your comment. The committee agree there is a lack of dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The recommendation has been reworded to describe dietician as a 'dietician who has a special interest in ME/CFS', the committee recognised that currently dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better. The implementation of this recommendation should …..

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Invest in ME Research	Guideline	032	22	Are there enough paediatric dietitians who specialise in ME/CFS to cover the demand?	Thank you for your comment. The committee agree there is a lack of paediatric dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS. The recommendation has been reworded to describe paediatric dietician as a 'paediatric dietician who has a special interest in ME/CFS', the committee recognised that currently paediatric dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are paediatric dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better. The implementation of this recommendation should …..
Invest in ME Research	Guideline	033	44	Are there enough dietitians who specialise in ME/CFS to fulfil this recommendation?	Thank you for your comment. The committee agree there is a lack of dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The recommendation has been reworded to describe dietician as a 'dietician who has a special interest in ME/CFS', the committee recognised that currently dieticians are not solely based in

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					ME/CFS services (specialising in ME/CFS) but there are dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better.
Invest in ME Research	Guideline	034	16-20	All of the history behind CBT and the funding awards for research using CBT and the practices of vested interests pushing this have been predicated on assuming ME patients have abnormal illness beliefes. This is blatant falsehod from NICE and we are surprised that members of the committee have agreed to leave this in guidelines. It is unfit and a a waste of NHS resources This applies to the whole section which should be removed.	Thank you for your comments. **The committee specifically rejected the assumption that people with ME/CFS have 'abnormal' illness beliefs and behaviours as an underlying cause of their ME/CFS.** Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT **as described in the guideline** could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Invest in ME Research	Guideline	034	6-8	Instead of general psychological therapies it appears that you have chosen to highlight CBT only simply because the current specialist services offer it. That is not a good reason to justify this or to continue to promote this therapy especially as you already admit that the evidence base is poor. Referencing your own words – "CBT is currently provided for people with ME/CFS in specialist services. These recommendations clarify when CBT should be offered to people with ME/CFS".	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).

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					CBT Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). The committee agreed that it is important that CBT should be only delivered by a healthcare professional with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS.
Invest in ME Research	Guideline	034	1	In your evidence summary you state that there is no evidence for non-pharmacological or pharmacological therapies. You should stick to that evidence and not hang on to remnants of the past guideline. There is no need specifically to mention CBT here as your evidence review found CBT research into ME/CFS to be of low or very low quality. The Royal College of Psychiatrists say: "When does CBT help? CBT has been shown to help with many different types of problems. These include: anxiety, depression, panic, phobias (including agoraphobia and social phobia), stress, bulimia, obsessive-	Thank you for your comment. *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).

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				compulsive disorder, post-traumatic stress disorder, bipolar disorder and psychosis. CBT may also help if you have difficulties with anger, a low opinion of yourself or physical health problems, like pain or fatigue." Based on the above description this topic is already covered in the section "Managing coexisting conditions" on page 36 lines 12 to 20 with links to relevant NICE guidelines. "For recommendations on identifying and treating associated or comorbid 13 anxiety, depression or mood disorders see the: 14 • NICE guideline on depression in adults 15 • NICE guideline on depression in adults with a chronic physical health 16 problem 17 • NICE guideline on depression in children and young people 18 • NICE guideline on generalised anxiety disorder and panic disorder in 19 adults 20 • NICE guideline on common mental health problems." Coping with symptoms of ME/CFS is covered by earlier sections of energy management. "1.11.2 Discuss with people with ME/CFS the principles of energy management, its role in supporting them to live with their symptoms, the potential benefits and risks and what they should expect."	
Invest in ME Research	Guideline	034	30	The lines 1 to 13 do not offer any assurance that the CBT described here is any different from the current practice.	Thank you for your comment.

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				It talks about meaningful goals, priorities, sleep, activity and rest. This whole section gives too much credence to a talking therapy that you have found to have a low or very low evidence base for ME/CFS.	Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Invest in ME Research	Guideline	035	15-17	There is no evidence of efficacy of CBT for children with ME/CFS. Why even mention it here? If children feel supported and listened to all the way through the investigations/diagnosis/follow- up then there is less likely to occur any problems that need psychological intervention. Any such interventions should be addressed separately by professionals trained to deal with such problems and not by healthcare professionals who have had a weekend course in CBT or not plugged by a compromised national institute that ought to be concerned with clinical excellence.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. This also applies to children and young people where there was some evidence of benefit in the quantitative and qualitative evidence. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline.

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					To note the training recommendations have been edited. In this section it is clear that CBT should be only delivered by a healthcare professional with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. This applies to children and young people.
Invest in ME Research	Guideline	035	25	Severe or very severely ill patients surely do not have excess capacity to engage in any therapy needing cognition. All their energies are taken by basic needs Remove this.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). The committee agreed that it was important that CBT should be available for all people with ME/CFS but that is was important to highlight the additional caution needed for people with severe or very severe ME/CFS.

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					The recommendations on the awareness of severe or very severe ME/CFS and its impact include that interactions should be risk assessed in advance to ensure its benefits will outweigh the risks to the person.
Invest in ME Research	Guideline	037	1	Should the title be Managing worsening of symptoms? Many patients adapt to living within their limits and flares or relapse imply that patients are normally ok but flares and relapse happen at times and can be managed by following some agreed plan. There is too much talk of a plan. It should be very simple such as increase activity when possible, decrease when necessary. The patient must be in charge. Knowledgeable healthcare professionals can be sought for advice if necessary.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse. The committee agree care should be personalised, including that of the management of flare ups and relapses. This is recommended in the assessment and care planning section of the guideline. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Invest in ME Research	Guideline	037	9	Remove word "temporarily".	Thank you for your comment. This section is about managing a flare up* and relapse and the strategies to address this. Temporarily reducing activity levels is an appropriate response to a flare up and would be reviewed after the flare up has resolved.

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Invest in ME Research	Guideline	037	18	The most important aspect here should be assessing the patient and not reviewing a management plan.	Thank you for your comment. The committee agree and the review of the care and support plan is carried out and discussed with the person.
Invest in ME Research	Guideline	037	23	If the patient's condition worsens for years then the most important thing is to monitor the patient.	Thank you for your comment. The committee agree that review and monitoring is important. The review section of the guideline recommends regular review that takes into account the person's circumstances.
Invest in ME Research	Guideline	038	3	Things should not be more complicated than necessary. Simply, Increase activity when possible, decrease when necessary. The patient must be in charge with knowledgeable healthcare professionals giving input if necessary/available/needed.	Thank you for your comment. The committee agree and have recommend general advice to reduce activity, rest and reassess energy limits to stabilise symptoms. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Invest in ME Research	Guideline	038	18	What strategies might there be that can overturn decisions by insurance companies and corporate parasites employed by the DWP to oversee benefits assessments that coerce patients into following NICE guidelines - as has previously been the case for thirteen years since the last flawed NICE guidelines were published.	Thank you for your comment and information.

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				There should be no nuances in NICE guidelines that only NICE Directors are aware.	
Invest in ME Research	Guideline	038	21	First link did not work	Thank you for your comment. This has been amended.
Invest in ME Research	Guideline	039	1	This is far more important than any management plan. A regular review of the patient, just like in any other chronic illness, should be part of ME/CFS patient's care. Many other illnesses can hide in this patient group. Misdiagnosis is common.	Thank you for your comment.
Invest in ME Research	Guideline	039	14	Is this not the wrong emphasis and terminology? Patients with ME are ill - they are not in some contest where achievement is the aim. This is about health.	Thank you for your comment. 'Achieved' here describes to the impact of symptoms on someone's life and does not refer to achieving as in a contest.
Invest in ME Research	Guideline	039	16	Why does self management have to concentrate on activity?	Thank you for your comment. Activity has been edited to energy management plan.
Invest in ME Research	Guideline	040	17	Most of the current specialist services need to be educated themselves first before they can be trusted to educate others. Invest in ME Research and many of our supporters have consistently campaigned for CBT and GET to be removed from the NICE guidelines since they first were introduced in 2007. For thirteen years, Invest in ME Research has provided education to counter the official misinformation. Our cpd-accredited international ME conferences has provided education from a round the world - how much has been used by "specialist services" that you assume exist?	Thank you for your comment and information. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme
Invest in ME Research	Guideline	041	4	First link did not work	Thank you, this has been corrected.

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Invest in ME Research	Guideline	043	8	Why is CBT mentioned here specifically rather than a general term? Instead refer to psychological therapies if you need to. Again shows the bias by NICE to retain CBT despite lack of evidence of efficacy.	Thank you for your comment. CBT is included as it can be part of someone's care and support plan if they have chosen to use it in supporting them in managing their symptoms.
Invest in ME Research	Guideline	044	18	Is it necessary to introduce yet another term (PESE) when the term PEM is well established in the literature and used in research criteria? Of course, there is no need. There should be some basis in the literature for changes like this to be used in NICE guidelines. Otherwise, we will end up using various terms as and when people choose to do so. Terminology within ME is already a mess – NICE are just further complicating the picture. Is this done on purpose?	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.
Invest in ME Research	Guideline	044	21	Remove the word "also" as post exertional malaise (PEM) is the most commonly used term. It may not exactly describe what patients experience but NICE consensus guidelines cannot just decide to use yet another term. This is so negligent of NICE. Evidence review Diagnosis page 44 Table 4 - "Post-exertional symptom exacerbation (PESE) Note: the committee's preferred term is PESE"	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.

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Invest in ME Research	Guideline	045	21	All of the recommendations seem too general and without any proper explanation or thought behind them that it is impossible to make any comment on them. If the recommendations were meant to be based on the content of the NICE guidelines then collecting information on patients using standardised and validated tools would be a good starting point.	Thank you for your comment. There is more detailed information in the research recommendations in Evidence reviews D and H**.**
Invest in ME Research	Guideline	047	13-14	What caused this? Surely it was partly due to poor NICE guidance in the past. Perhaps that should be recognised. In any case this needs to be stated in an introduction at the beginning of the guidelines (see our comment 3 above).	Thank you for your comment. E**vidence reviews A and C explore the** evidence assessing **why there is a lack of belief about ME/CFS and the committee discussion sections have further detail.** The context section provides a concise summary of the topic and is not intended to be exhaustive, as this is explored in detail elsewhere it has not been added.
Invest in ME Research	Guideline	047	2	Rather study the underlying sleep issues with ME in a proper sleep clinic fashion	Thank you for your comment. The recommendations on sleep include to think about the possibility of an underlying sleep disorder or dysfunction and whether to refer to an appropriate specialist.
Invest in ME Research	Guideline	048	1-6	This does not just apply to ME - it would be the same for all diseases where a patient has had a bad experience. The real issue is that these bad experiences are based on the fact that healthcare professionals have been fed misinformation and false beliefs - which has then in turn affected their perception and treatment of ME patients. Again, NICE ducking the real issue.	Thank you for your comment. The aim of the recommendation was to raise awareness that people with ME/CFS have experienced prejudice and stigma and is based on the evidence identified in the Evidence reviews A and C and the committee's experience.
Invest in ME Research	Guideline	048	23-24	The document talks about specialist services and multidisciplinary teams throughout the document. There are very few specialists or multidisciplinary teams in the UK.	Thank you for your comment. Thank you for your comment. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment,

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				It is quite obvious to us that there needs to be more resources for providing the care outlined in this document. Of course additional resources are required to overcome discriminatory practices which have been built up from erroneous guidelines in the past. Early diagnosis is going to demand more resources especially as the current ME/CFS services tend only to operate part-time. Proper diagnostic criteria are required to be standardised. This document will not in itself change much for patients	such as access to specialist services, to implement some recommendations in the guideline. guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas.
Invest in ME Research	Guideline	052	26	Current practice recommends a set of basic blood tests and lists some "red flags". Would it be prudent to retain these basic blood test from the current guideline?	Thank you for your comment. After considering the stakeholder comments examples of tests have been included in the guideline.
Invest in ME Research	Guideline	053	3	What course of action or treatment would you think could be offered at an earlier stage to prevent disease progression when not enough research has been funded to identify what might prevent such progression. **But thank you for finally admitting that ME is a disease.**	Thank you for your comment. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that advice prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and it would not cause harm to anyone.
Invest in ME Research	Guideline	053	5	It would be good to define the specialist team. What is the minimum staffing requirement for such a team?	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS

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					results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The scope of the guideline did not include service specifications and cannot make recommendations on staffing requirements.
Invest in ME Research	Guideline	054	10-12	It is therefore important not to offer any form of therapy that has no evidence base. It is better to use the principles of standard medical care, offer common sense advice, and explain the current state of knowledge in an honest and straightforward manner.	Thank you for your comment.
Invest in ME Research	Guideline	055	3	NICE should organise a publicity campaign to expel the myths that have permeated all levels of public policy about ME/CFS.	Thank you for your comment.
Invest in ME Research	Guideline	056	8 – 9	We doubt this very much. Of course it will require more resources as existing social services staff need to be re-educated and there is little knowledge of ME at present.	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. This applies to this section on safeguarding.
Invest in ME Research	Guideline	056	26 – 29	There needs to be some practical solution offered here. We need to establish places around UK that have experience and knowledge about severe or very severe ME/CFS and can provide advice as necessary.	Thank you for your response. Your comments will be considered by NICE where relevant support activity is being planned.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
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Invest in ME Research	Guideline	058	3-4	It is not just "leaving school" - but being excluded from school. This should be specifically stated - often children are excluded because of the illness with schools making little effort to assist in adjusting to the child's needs – both short and long term.	Thank you for your comment. Leaving school in this context does not have any meaning other than not in school. For this reason you suggestion has not been added.
Invest in ME Research	Guideline	058	16	This is doubtful. It will require adjustment from school teachers and possibly classes – possibly re-training.	Thank you for your comment.
Invest in ME Research	Guideline	059	21-24	This almost inevtiably will lead to addition of new staff in the current climate where resources are already limited - if the intent is really to improve the care of people with ME. It will require re-training.	Thank you for your comment. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as training and access to ME/CFS specialist services , to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS.
Invest in ME Research	Guideline	060	2	You state there was limited evidence for any intervention to manage ME/CFS and this was supported by the committee's experience yet you go on to assess some interventions in detail. This does not make sense. In practice, you can only recommend standard medical care.	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review

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					quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Taking all these considerations into account, including the evidence that people with ME/CFS report receiving a lack of information and support (Evidence review A) the committee decided it was important to make recommendations to support people with ME/CFS to manage their symptoms.
Invest in ME Research	Guideline	060	25	Not confusion - NICE were told that GET should not be recommended for people with ME when the 2007 guidelines recommended it. NICE did not listen. Stop obfuscating the lack of responsibility shown by NICE in flawed recommendations. Therehas been no confusion from patients.	Thank you for your comment.
Invest in ME Research	Guideline	061	13	What specific circumstances? Please define.	Thank you for your comment. This refers to recommendation 1.11.8.
Invest in ME Research	Guideline	062	2	It is worth noting that there is no clinical trial evidence to justify recommendation of energy management.	Thank you for your comment. Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms

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				There is only patient experience and patients do this because it is common sense and guided by their instinct rather than some proven intervention.	(Evidence review A) and their experience the committee concluded that all people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity.
Invest in ME Research	Guideline	063	7	Interesting that nothing has changed since 2007 in terms of research and now you admit what patients have been saying since 2007. What a waste of 13 years where the lives of people with ME have been compromised by poor NICE guidelines. Maybe you need to include an apology.	Thank you for your comment.
Invest in ME Research	Guideline	067	23-29	CBT should not be offered in this guideline The Royal College of Psychiatrists say: "When does CBT help? CBT has been shown to help with many different types of problems. These include: anxiety, depression, panic, phobias (including agoraphobia and social phobia), stress, bulimia, obsessive-compulsive disorder, post-traumatic stress disorder, bipolar disorder and psychosis. CBT may also help if you have difficulties with anger, a low opinion of	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).

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				yourself or physical health problems, like pain or fatigue." Based on the above description this topic is already covered in the section "Managing coexisting conditions" on page 36 lines 12 to 20 with links to relevant NICE guidelines. There is no good evidence of efficacy of CBT and it needs to be removed.	
Invest in ME Research	Guideline	071	11-12	It is not in NICE's remit to discuss or amend the name myalgic encephalomyelitis. You should remove this. Names of diseases are not always accurate and there is no value in cherry-picking symptoms to discuss.debate at this point. Chronic Fatigue Syndrome is not necessarily accurate either. Research will eventually decide the name once credible evidence is found to satisfy everything. Until then NICE should not dabble in name changing. WHO recognises myalgic encepgalomyelitis. It does not recognise encephalopathy. Use the WHO classification.	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'* The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3)' has been added to this section.
Invest in ME Research	Guideline	071	9	We feel that this section needs to be expanded upon and should be relocated to the beginiing of this document in order to set the scene before reading whatever final guidelines are produced.	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.

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					The format of NICE guidelines is now to have the context at the end of the guideline. This section is clearly labelled and easily accessed on the guideline website page.
Invest in ME Research	Guideline	072	12	You may menion that patients challenged the NICE guidelines of 2007 and took NICE to a judicial review..	Thank you for your comment. We note that the subsequent text in this section acknowledges the controversy regarding the previously recommended treatments.
Invest in ME Research	Guideline	72	19	What are these major studies? This is important in order to determine what triggers a review of guidelines. Previously NICE have been tardy in complying with patients' wishes to review the flawed 2007 guidelines.	Thank you for your comment. This sentence has been removed in case it adds confusions. The updating of the guideline will follow NICE processes for updating guidelines.
LDN Research Trust	Equality Impact Assessment C C C C	General 71 75 35-51 75	General 46 33 General 38-39	**<u>Equality Impact Assessment</u>** In light of the disparate infection and death rates in different ethnic communities from COVID-19, it is surprising that the Equality Impact Assessment saw no need for additional guidance for ethnic minority populations. It is known that occupation as well as factors such as poverty and multi-occupancy or multigenerational homes are responsible for some of the differences in COVID-19 infection rates, and these factors may well be responsible for some of the increased prevalence of ME/CFS in ethnic minority groups (64–66). However, without adequate research such factors will not be teased out or addressed. "Language" "Focus on physical symptoms" Evidence review C the narrative summary of review findings found several issues specific to ethnic minority people, listed in	Thank you for your comments. An equality impact assessment (EIA) has been completed for this guideline and is available on the guideline webpage. When evaluating all the evidence the committee considered all the groups identified in the EIA, the applicability and generalisability of the evidence was considered by the committee in their discussion of the evidence. Very little specific evidence was identified for any of the groups and the committee agreed that the recommendations should equally apply to all groups and did not discriminate against any particular group and separate recommendations were not thought necessary for any of these groups. The committee agree these factors need to be considered when delivering care and have added, 'Be sensitive to the person's socioeconomic, cultural and ethnic background, and faith group, and think about how these might influence their symptoms,

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				review findings, 3, 4, 6, 9, 10, 11, 12, 13, 15, 16. The summary of the data analysis reduced these to two points, language barriers, and focus on physical symptoms with the addition of the high turnover of inner city G.P.s commented on in the discussions. It gave a low confidence in the findings due to them coming from one study. Evidence review C Page 75 focus on physical symptoms - line 38 to 39 acknowledges research in people with ME/CFS in BME groups is sparse so considered this an important finding. The solution offered was to refer to existing NICE guidelines on patient experience in adult NHS and adult social care services in the information and support section of the guideline, rather than make a specific mention or any recommendations in this guideline. There was no discussion of the additional information needs of ethnic minority populations or additional needs for education amongst health care workers, either due to their own racial stereotyping, or due to attitudes in ethnic minority populations. Elsewhere the committee made recommendations based on their own experiences even when confidence in review findings was low. It is possible that if the committee had had personal experience of people with ME/CFS from ethnic minorities who had talked openly about the specific difficulties they faced in obtaining a diagnosis and adequate care, the findings on ethnic minorities might not have been disregarded. It is known that ME/CFS is more prevalent in some ethnic groups (67–69). The guideline review neither seeks any evidence for this, nor asks questions why this may be so. The surveys commissioned by, or occurring following discussion with, the NICE guideline development group did not include	understanding and choice of management.' to recommendation 1.1.3. *Recommendations for research* To raise awareness of this gap in the evidence pregnant women and women in the post-natal period, black, Asian and Ethnic minority populations have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations.

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				ethnicity in their questions; this seems a collective failure by the committee and two eminent research institutions. Reviewing a sample of recent population based surveys of care of people with ME/CFS, it appears there was no exploration of ethnicity (70,71), although we understand that referral to secondary care is actually lower amongst ethnic groups than the white population. Hence, the lack of any focus on the deficits in research and the lack of research recommendations by the committee to fill existing gaps in knowledge creates an ongoing dangerous lack of consideration of the additional needs of ethnic minorities with ME/CFS. It is known that occupation was an important factor in the increased rate of infection in people with COVID-19 infection. Given that a significant proportion of people report an infection prior to the development of ME/CFS (72), and that previous SARS infections led to ongoing fatigue illnesses (73–75), it is very likely that a proportion of people with long-COVID symptoms will ultimately be diagnosed with ME/CFS. A recent follow-up of patients post-COVID-19 failed to include ethnicity despite other demographic data (76). Recent research by the BMA showed that doctors from ethnic minority backgrounds were less likely to feel confident in the provision of adequate personal protective equipment against COVID-19, and were bullied and harrassed when pointing this out (77), a clear example of systemic racism within the NHS. The BMJ devoted a March 2020 journal to this issue (78,79) and the Joint House of Commons House of Lords Committee on Human Rights has recently reported on systemic issues in United Kingdom services including in the National Health Service (80). Unless there is increased focus on the needs of ethnic minorities with ME/CFS now, and a research agenda that seeks to	

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				understand and correct the issues leading to under-diagnosis and lack of care, the health care workers recently infected by COVID-19 who have given much to the NHS but who have already been poorly served, will again suffer disproportionately with ME/CFS. We believe the guideline should make concrete suggestions for research, such as mandatory collection of ethnicity data as suggested in the recent report of Parliament (80), and funding of local pilot studies to increase diagnosis and referral rates for people with ME/CFS within specific communities. The guideline itself should stress that ME/CFS occurs in all population groups (81); that it is currently under-diagnosed in some ethnic minority populations (69); and that stereotyping by healthcare workers or specific beliefs in communities may hinder the diagnosis (82,83). (There was evidence for this in Evidence review C, but little account of this was taken in subsequent discussions). In the paediatric guideline, the specific problem of stereotyping of certain ethnic groups as "lazy" should be directly countered. (Crawley 2011 showed the extent of under-diagnosis of ME/CFS in school populations though no ethnicity data was included on the additional children identified through the screening programme (84)). Given that 33% of school-age children are now from ethnic minority populations, the tackling of under-diagnosis and care of people with ME/CFS from ethnic minorities needs to start now. 64. Public Health England. Disparities in the risk and outcomes of COVID-19. 2020;89. 65. Public Health England. Beyond the data: Understanding the impact of COVID-19 on BAME groups. 2020;69.	

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				C-G. Systematic review and meta-analysis of the prevalence of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). J Transl Med. 2020;18(1):1–15. 82. Bayliss K, Riste L, Fisher L, Wearden A, Peters S, Lovell K, et al. Diagnosis and management of chronic fatigue syndrome/myalgic encephalitis in black and minority ethnic people: a qualitative study. Prim Health Care Res Dev. 2014;15(2):143–55. 83. De Silva REE, Bayliss K, Riste L, Chew-Graham CA. Diagnosing chronic fatigue syndrome in south asians: Lessons from a secondary analysis of a uk qualitative study. J Fam Med Prim Care. 2013;2(3):277–82. 84. Crawley EM, Emond AM, Sterne JAC. Unidentified chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a major cause of school absence: surveillance outcomes from school-based clinics. BMJ Open. 2011;1(2):1–6.	
LDN Research Trust	Evidence Review B C	005 6	004 - 008 4-5	**Ethnic minority research** "What information, education and support do health and social care professionals who provide care for people with ME/CFS need?" and "what are the barriers and facilitators to providing information, education and support to people with ME/CFS for health and social care professionals?" These questions should have prompted the additional question in the minds of the committee "what additional barriers and facilitators to providing information, education and support occur when providing care for people from ethnic minorities". This would have led to specific recommendations/research recommendations for these aspects of care for people from ethnic minorities. The questions on barriers and facilitators to the diagnosis of ME/CFS and the care of people with ME/CFS should have prompted the additional questions "what are the additional	Thank you for your comments. When evaluating all the evidence the committee considered all the groups identified in the Equality Impact Assessment, the applicability and generalisability of the evidence was considered by the committee in their discussion of the evidence. Very little specific evidence was identified for any of the groups and the committee agreed that the recommendations should equally apply to all groups, and did not discriminate against any particular group and separate recommendations were not thought necessary for any of these groups. The committee agree these factors need to be considered when delivering care and have added, 'Be sensitive to the person's socioeconomic, cultural and ethnic background, and faith group, and think about how these might influence their symptoms,

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				barriers and specific facilitators these questions pose for groups specified in the Equality Act 2010 and the Human Rights Act 1998?". Failure to ask this question has led to lack of analysis of data from this perspective, and the contrary conclusion that there no separate recommendations for these groups to be made. For example, population studies of differences in prevalence rates and of rates of diagnosis and referral in different ethnic groups (60) could have informed these questions, but were never included in the review. 60. Jason LA, Taylor RR, Kennedy CL, Jordan K, Song S, Johnson DE, et al. Chronic fatigue syndrome Sociodemographic subtypes in a community-based sample. Eval Health Prof. 2000;23(3):243–63.	understanding and choice of management.' to recommendation 1.1.3. *Recommendations for research* To raise awareness of this gap in the evidence pregnant women and women in the post-natal period, black, Asian and ethnic minority populations have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations.
LDN Research Trust	Evidence Review A B C F	General General General General	General General General General	**Wrong exclusion of articles** Bayliss 2014 and De Silva were excluded from Evidence review A, and de Silva was excluded from B while Bayliss was included. Both were included in C. In fact, they were both analyses of data during the study for Hannon 2012, but all contained original data. Not including them reduced the amount of data on the difficulties ethnic minority people with ME/CFS experience in diagnosis and access to care for ME/CFS. Evidence review A Several other papers were excluded due to using a quantitative analysis, when in fact they should have been excluded for other reasons. For example, Moore 2000 used a structured questionnaire and a semi-structured interview of occupational therapists. It should have been excluded from this review but included in evidence review B; it was included in neither. Richards 1998 was similarly a survey of General Practitioners and should have been excluded from A and included in B; it was included in neither. Sunnquist 2017 was not found or included in any review.	Thank you for your comment. Bayliss 2014 & De Silva 2013 were secondary analyses of Hannon 2012-which was included in both reviews A & B. So, the two aforementioned studies were excluded from both reviews because they did not contribute further relevant information than the original primary study included. Bayliss 2016 is a different study included in both reviews A & B. However, they did contribute further relevant information to review C which had a different question. They contributed to themes for 'continuity of care', the 'relationship with the healthcare professional', 'patient beliefs and attitudes towards ME/CFS', these did not come up in the analysis of Hannon 2012, and have been included in this review. In line with the protocols quantitative papers were excluded from qualitative reviews as their analysis method did not match what was pre-specified we would include.

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	G	5	10-16	Snell 2001 Chronic fatigue syndrome, Amligen and quality of life. "Both women were participants in a cost-recovery, clinical trial of …Ampligen…..Semi-structured in-depth interviews were conducted with 2 CFS patients and their spouses, to discover if these families perceived any changes in their patterns of daily living. Patient diaries were also analyzed for the purpose of triangulation. Content analysis of the interview transcripts and diary entries revealed a number of significant quality of life improvements for the women and their families, for which they perceived the drug therapy responsible. … Both women reported a reduction in pain, increased energy levels and improved cognitive functioning. They each cited numerous cases to illustrate their improvement." This paper was excluded from the analysis in Evidence review F, incorrect study design; qualitative case study. It seemed superficially to be exactly the kind of data on experience of therapy that the committee were seeking. Since the PACE trial, most of the evidence for harms caused by Graded Exercise Therapy and lack of benefit from Cognitive Behaviour Therapy came from patient surveys. Yet review G excluded patient surveys and concentrated on individual comments from focus groups or individual interviews. It found sparse evidence from these sources and hence concluded evidence was lacking, and turned to an expert witness for validation of reasons to downgrade the results of clinical trials of non-pharmacological treatments in line with what people with ME/CFS had been saying for some time. This seems a perverse methodology. NICE needs to review its methodology. This method of working is time consuming and produces false results which are perpetuated over time until a new model of understanding	We note that Snell 2001 was a case study.

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				particular aspects of a disease emerge. Finding ways of incorporating patient knowledge into reviews with appropriate safeguards against bias and using this knowledge to inform research priorities would expedite benefit and reduce harm quicker than the current methodology. In addition, the emphasis on medical peer reviewed literature over other forms of literature is giving a false sense of lack of data when there is a rich source of data currently being unexplored. Bolton 2020 produced a paper which was submitted to a peer reviewed journal and is therefore now accessible by medical search engines (7). Similar experiences to those described in that case report could have as easily been accessed from web reports of improvements to people taking low dose naltrexone. Videos of before and after taking low dose naltrexone can show dramatic changes. The LDN Research Trust have created a wealth of personal testimonies on the effects of low dose naltrexone. https://ldnresearchtrust.org/ldn-videos?field_type_of_video_target_id=All 7. Bolton MJ, Chapman BP, Van Marwijk H. Low-dose naltrexone as a treatment for chronic fatigue syndrome. BMJ Case Rep. 2020;13:e232502.	
LDN Research Trust	Evidence Review A F	Appendix C 6 121	062 13-15 General	**Possible errors in the texts** **Incomplete flow charts** e.g. Evidence review A appendix C page 62 and others. Several of the flow charts are incomplete. This is one example. **Wrong statements** Evidence review F page 6 lines 13 – 15 "non-pharmacological evidence". This may be wrong and should read pharmacological evidence.	Thank you for your comment. The flow charts are not incomplete. *Corrections* • *Non* has been deleted. • The Brooks reference has been corrected.

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	A A	126	General	**<u>Inconsistent reference</u>** Evidence review A page 121, Brooks 2012 is listed as excluded, but page 126 gives the correct reference, as Brooks 2013.	
LDN Research Trust	Evidence Review A B C	005 6 7	020 table 1 7 table 1 5 table 1	**<u>Search methodology</u>** The literature search methodology was the same for all questions regardless of the questions asked and the appropriateness of the search methodology. It seemed a combination of over-focused searches for Ovid Medline and Embase (extracting only randomised controlled trials) and too wide a focus for CINAHL, and Epistemonikos (no apparent restrictions apart from the long list of terms for chronic fatigue syndrome). Thus, whatever the review question, every literature search appeared to generate the same 20,484 papers, conference abstracts and clinical trials registry, despite widely differing review protocols and needs. This is an extremely wasteful methodology and makes the selection of the particular papers for each question more problematic as far more hand searching of documents was necessary. This methodology is not common to NICE guidelines so we question why it was adopted. For example, in other NICE guidelines seeking qualitative data and in Cochrane reviews asking qualitative questions, the searches were specifically tailored to qualitative searches. It also appeared that the focus on either quantitative studies or purely qualitative studies (focus groups or interviews) excluded much useful data from questionnaires and surveys. In evidence review A Prins 2000, Ray 1995, Saltzstein 1998, Sunnquist 2017, Theorell 1999, Tuck 2000, were all listed as containing quantitative data but were excluded. In evidence review J, no evidence was identified from over 20,000 papers	Thank you for your comment. The population was based on the one used in Chronic fatigue syndrome /myalgic encephalomyelitis (or encephalopathy): diagnosis and management -CG53. This was updated and expanded by adding more recent terminology. Many questions overlapped and some of them did not have well define terms to retrieve specific relevant results. The methodology is in line with the NICE manual as running one search for a group of questions that overlap is not unusual and is efficient in these circumstances. See Developing NICE guidelines: the manual, chapter 5, 'Review questions that overlap and can be grouped together should be identified for searching purposes. For example, questions with the same population may involve comparing several interventions. This should make it possible to carry out a single search that covers all the interventions, although this approach may retrieve a large number of studies. For an example of a search with a topic approach see NG95 Lyme Disease. Further detail has been added the ME/CFS Methods chapter about this approach. In addition different study type filters were used in Medline and Embase for randomised control trials, systematic reviews, Observational studies, and qualitative studies – these results were placed in separate folders in Endnote software along with the remaining results for sifting and selecting full text. CINAHL and PsycINFO were additional databases searched for the

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	C F G E F E F	66 90 322 General General General 99	21-22 25 41-42 General General General Section 11 of review protocol	selected in the initial literature search, and all the 508 papers from additional evidence submitted after the call for evidence were also excluded. Evidence review E Pages 51 to 70 gives a large number of excluded studies, some from patient support groups. The Forward ME survey (2274 participants) (42) and the ME Action survey (1906 participants) (43) reports included quantitative data from surveys which were not included, though small amounts of qualitative data apparently were. In fact, apart from their references, very little of their evidence was noted in Evidence review H. For example, the Forward ME survey had clear answers to questions about the impact of Cognitive Behaviour Therapy and Graded Exercise Therapy which appear to have been asked in a non-biased form but these answers were not in the evidence review. "We asked people ''what severity is their condition both before and after treatment [with Cognitive Behaviour Therapy]?'. The percentage of people describing their condition as severe before treatment was 10.9% and this increased to 19.1% after treatment" This resulted in a recurring theme of lack of evidence to inform decision making, while at the same time excluding evidence that could have informed those decisions. Evidence review C page 66 Line 21 – 22 and other examples given in the columns to the left show the problems of the approach taken as confidence in the review findings was described as low with "many studies presenting limited data, often single quotes, to support research findings". The committee did acknowledge that some lower confidence findings reflected their own experience and should not be disregarded. However, it was not uncommon for the committee to make recommendations based entirely on their own experience or backed by very little low quality evidence from the evidence review. It is not clear	qualitative review questions. Thus, in the review appendices it was presented as one search. *Excluded papers* All studies that meet the inclusion criteria in the protocols were included and the excluded studies tables in the reviews explain why a study was excluded. Evidence review H. The surveys didn't meet the inclusion criteria for the cost and clinical effectiveness review, particularly with reference to the design. The percentage data you refer did not meet the inclusion criteria for the analysis experience of interventions review which was exploring themes emerging from qualitative data. Evidence review E As noted above all studies that meet the inclusion criteria in the protocols were included and the excluded studies tables in the reviews explain why a study was excluded. As you correctly note the Polo (2019) was excluded from the reviews based on the study design. It was not excluded from the qualitative analyses as it contained quantitative data, it was excluded because it was based on retrospective data from medical reports and did not employ qualitative methods or include any qualitative analysis. The beginning of the discussion section in Evidence review E states ,'the committee discussed this evidence with the findings from the reviews on Information for people with ME/CFS and their families and carers (report A), Information and Support for health and social care professionals (report B), access to care (report C), Diagnosis (D) non pharmacological management (report G) and the report on Children and Young people

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				why the committee felt their own experience was superior to the evidence from excluded questionnaires. Evidence review E management strategies before diagnosis. This review protocol concentrated on randomised controlled trials, with the inclusion of non-randomised comparative studies if no randomised controlled trials were available. This means no qualitative data or surveys were available for review, although they might have provided sources of information, as evidenced in the 508 reports and the excluded references. In Evidence reviews A, B and C, qualitative studies are included, so it appears contrary not to include them in evidence review E. Questions such as whether to rest or not at the start of an illness might have been partially answered by these means. Polo 2019 was excluded from Evidence review F as it was not a quantitative study (not a randomised control trial but a retrospective chart analysis) but excluded from Evidence review E as it was incorrect study design (no qualitative data). If an independent qualitative researcher had interviewed and listed responses from all 218 of his included patients, it could have been included as a qualitative study, although there would have been less information on response rates from this exercise. Because Polo summarised the data from his original records, it is not included. Although it is only right that recommendations for treatment are based on quantitative data, reviewing qualitative data may have given more scope for recommending areas for research. e.g. Evidence review F review protocol for pharmacological management Page 99 section 11 types of studies to be included. In the current restrictive funding environment, it is vital that NICE make specific recommendations for research. It is possible if patient support groups were aware of the limitations on what data would be admitted for analysis in this	(Appendix 1).' Where appropriate qualitative evidence was considered. This guideline followed the NICE Developing NICE guidelines: the manual. The manual sets out the methods for developing review questions to reviewing the evidence. The committee note below that two qualitative research projects on the experience of children and young people with ME/CFS and people with severe and very severe ME/CFS were commissioned for this guideline to support the committee decision making. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee included members with clinical and personal experience of children and young people with ME/CFS. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresentedunderrepresented in the literature. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations.

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				review, that questionnaires would have been designed differently. One possibility is a recommendation for more funding of qualitative research in ME/CFS specifically to produce evidence for reviewing this guideline. The case reports contained in Bolton 2020 were written by three patients, one of whom had recently completed an MRes, and the paper was supervised by her previous supervisor (7). This is an example of how patient experiences can cross from grey literature into main stream medical literature, although case series are obviously inherently biased. 7. Bolton MJ, Chapman BP, Van Marwijk H. Low-dose naltrexone as a treatment for chronic fatigue syndrome. BMJ Case Rep. 2020;13:e232502. 42. Oxford Clinical Allied Technology and Trials Services Unit Oxford Brooks University. Forward-ME Group CBT & GET survey. Oxford; 2019. 43. Leary S, Sylvester J, Shorter E, Moreno E, Knowles R, Spreag D. Your Experience of ME Services. Survey Report by #MEAction UK. 2019.	(See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed).
LDN Research Trust	Evidence Review B	005	007 - 008	**Deficiencies in evidence review** **Faults in compilation of data about ethnic minorities** "what are the barriers and facilitators to providing information, education and support to people with ME/CFS for health and social care professionals?" It would be expected that this question found evidence of barriers based on ethnicity, either of health care worker or patient. Neither were identified, suggesting this evidence was either not sought or ignored. For example, the patient and carer samples in Hannon 2012 and De Carvalho Leite 2011 both contained minority ethnic participants, but no specific comments on this theme were recorded in the analysis despite appearing in the papers or the subsidiary papers of Hannon	Thank you for your comments. An equality impact assessment (EIA) has been completed for this guideline and is available on the guideline webpage. When evaluating all the evidence the committee considered all the groups identified in the EIA, the applicability and generalisability of the evidence was considered by the committee in their discussion of the evidence. Very little specific evidence was identified for any of the groups and the committee agreed that the recommendations should equally apply to all groups and did not discriminate against any particular group and separate recommendations were not thought necessary for any of these groups.

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				2012, (Bayliss 2014 and de Silva). Bayliss 2014 was excluded as there were "no relevant themes." However, the paper repeatedly quotes patients experiences of their General Practitioners and the barriers created by the General Practitioners' assumptions due to ethnicity. De Silva was excluded as a secondary analysis, although it used qualitative data not previously published on the experiences of Asian patients.	The committee agree these factors need to be considered when delivering care and have added, 'Be sensitive to the person's socioeconomic, cultural and ethnic background, and faith group, and think about how these might influence their symptoms, understanding and choice of management.' to recommendation 1.1.3. *Recommendations for research* To raise awareness of this gap in the evidence pregnant women and women in the post-natal period, black, Asian and ethnic minority populations have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations.
LDN Research Trust	Evidence Review D Evidence Review F	058 006	020-21 009 - 011	**Exclusion of fibromyalgia from evidence reviews** Fibromyalgia and hypermobility spectrum disorder were counted as separate conditions to ME/CFS, rather than part of a continuum, or as conditions where the two diagnoses often coexist. No research evidence was sought to justify this position. The committee recognises that "approaches can also be used for co-morbid conditions such as irritable bowel syndrome, migraine-type headaches, postural orthostatic tachycardia or vitamin D deficiency." We believe there is an omission of fibromyalgia from this list. Currently there is conflicting evidence for whether fibromyalgia is a related condition to ME/CFS, part of a continuum of conditions with only ME/CFS at one end and only fibromyalgia at the other and most patients showing evidence of both diseases, or whether the two diseases are not related but happen to co-exist in a large proportion of people. The view that the committee took, without presenting evidence, was by default that the two conditions were completely different. We would dispute the value of this,	Thank you for your comment. The guideline population is people with suspected or diagnosed ME/CFS, it was not in the remit of the guideline to review the difference in diagnosis between ME/CFS and other conditions. *Diagnosis of ME/CFS* Based on the evidence (Evidence review D) and the committee's clinical experience, they agreed the four criteria for the diagnosis of ME/CFS were fatigue, post-exertional malaise, unrefreshing sleep and sleep disturbance (or both), and cognitive difficulties. Key to the diagnosis of ME/CFS is the presence and combination of the four symptoms. Pain may be associated but is not exclusive to with ME/CFS, this was supported by the IOM diagnostic criteria (2015). The committee note that pain is the dominant symptom in fibromyalgia and as such the two populations are differentiated. Joint hypermobility, the key symptom in hypermobility spectrum disorder is not included in the list of symptoms that maybe associated with ME/CFS.

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				as so many people exhibit evidence of both diseases. In addition, this view meant that randomised clinical trials of drug treatments for fibromyalgia were not included in the review. There have been several published therapy trials of low dose naltrexone in people with fibromyalgia. The longest study, a 24 week double-blind placebo-controlled randomised trial in 74 people with fibromyalgia (8) found that 16 of the 37 in the naltrexone group had clinically important improvements in the Fatigue Impact Questionnaire total scores and quality of life component, P <0.001 Mean and standard deviation results for the Fatigue Impact Questionnaire were;- Baseline at 24 weeks Naltrexone 63.7 (SD +/- 13.2) 38.5 (SD +/- 16.1) Placebo 63.0 (SD +/- 13.0) 57.9 (SD +/- 15.6) SD = standard deviation The results also showed significant reductions in pain on a visual analogue scale, p <0.001. The only significantly increased side effects for naltrexone were head-aches and vivid dreams. Other studies in fibromyalgia include a blinded cross-over study of 31 patients (9), and several open label or single blinded studies (10–12) showed improvements in 50% or more of participants receiving low dose naltrexone, with average improvements in symptom scores in responders being around 30%. The blinded cross-over study also confirmed that the only two significantly increased side-effects were head-aches and vivid dreams (9). Although all studies are of small sample size and short duration and all are potentially subject to significant problems with bias, the results they produced are	*Exclusion of RCTs* In evidence review F the protocol states the population is people with diagnosed ME/CFS and accordingly studies with different populations have been excluded. Based on the evidence (Evidence review D) and the committee's clinical experience, they agreed the four criteria for the diagnosis of ME/CFS were fatigue, post-exertional malaise, unrefreshing sleep and sleep disturbance (or both), and cognitive difficulties. Key to the diagnosis of ME/CFS is the presence and combination of the four symptoms. Pain may be associated but is not exclusive to with ME/CFS, this was supported by the IOM diagnostic criteria (2015). The committee note that pain is the dominant symptom in fibromyalgia and as such the two populations are differentiated.

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				consistent enough to suggest that low dose naltrexone is worth subjecting to more rigorous trials for people with fibromyalgia. Unfortunately, as explained elsewhere, it has proved impossible to attract funding for further studies in the United States or elsewhere. 8. Abou-Raya S, Abou-Raya A, Khadrawi T. Efficacy of naltrexone in the treatment of fibromyalgia: randomized controlled trial. Ann Rheum Dis. 2013;72(Suppl. 3):719. 9. Younger J, Noor N, McCue R, MacKey S. Low-dose naltrexone for the treatment of fibromyalgia: findings of a small, randomized, double-blind, placebo-controlled, counterbalanced, crossover trial assessing daily pain levels. Arthritis Rheum. 2013;65(2):529–38. 10. Younger J, Mackey S. Fibromyalgia symptoms are reduced by low-dose naltrexone: a pilot study. Pain Med. 2009;10(4):663–72. 11. Metyas SK, Chen CL, Yeter K, Solyman J, Arkfeld D. Low Dose Naltrexone in the Treatment of Fibromyalgia. Curr Rheumatol Rev. 2018;14(2):177–80. 12. Parkitny L, Younger J. Reduced Pro-Inflammatory Cytokines after Eight Weeks of Low-Dose Naltrexone for Fibromyalgia. Biomedicines. 2017;5(2):16.	
LDN Research Trust	Evidence Review F	General	General	**Difficulties in funding clinical trials of low dose naltrexone** We do not suggest that low dose naltrexone is a cure for ME/CFS. In fact, we are clear that people who respond to low dose naltrexone need to remain on it long term, but lack of research makes it impossible to say whether people can safely stop it after some time. This does indeed have financial implications, and the draft guideline and discussion in evidence review F were right that there is a danger of people	Thank you for your comment and information. When considering the evidence for pharmacological interventions the committee agreed that there was insufficient evidence of benefit to recommend any medicines. Neither did the committee consider recommending clinical trial research for any specific drug. It is true that if safe and even partially effective, low dose naltrexone could be cost effective. But the same could be said for many off- patent drugs.

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				spending large amounts of money on dubious treatments for ME/CFS. However, we contend that a well conducted clinical trial of low dose naltrexone in individuals with ME/CFS would quickly establish whether naltrexone fulfils the NICE cost-effective requirement of less than £20,000 per quality-adjusted life year gained. Clinical experience has taught us that some people take up to 2 months to respond, so this is the minimum length for a parallel trial. By private prescription this would cost approximately £66 per person, but people who responded might then be able to return to work, or at least be less dependent on carers, both of which are financially beneficial outcomes for the person, as well as saving the National Health Service and care services through the reduction in need for supportive services. In summary, the evidence for low dose naltrexone is that there is potential that it may be beneficial in at least a proportion of people with ME/CFS, and there is a very low risk of harm. Thus, the group of United States physicians experienced in prescribing for people with ME/CFS and a drug repurposing company both felt that low dose naltrexone was worth prioritising in research efforts. None of these results are the type of high quality data NICE would accept as evidence, but they do suggest further clinical and laboratory studies and clinical trials are warranted. Sadly, despite these promising results, no researcher in either the United Kingdom or United States of America has been awarded a grant for the large scale studies that are needed. In the United States, Jarred Younger (lead author of several studies on low dose naltrexone in people with fibromyalgia) has had repeated applications to the National Institute of Health refused, despite his initial positive results. The LDN Research Trust was set up in 2003 in the United Kingdom to promote high quality	

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				research into low dose naltrexone. It is a small charity itself so cannot independently fund work. So far, it has not enabled a single clinical trial to take place in the United Kingdom. Specific efforts to enable a clinical trial of low dose naltrexone in people with ME/CFS over the past 10 years have failed to produce results. For example, a clinical trials unit was approached to cost a n-of-1 study of 10 patients in a General Practice based trial. As the cost was over £160,000 for data of only very preliminary value, further work on the study was abandoned. In the United Kingdom, the difficulties surrounding clinical trials of cheap off-patent drugs make it very unlikely that further advances in knowledge will be forthcoming unless NICE specifically advocates for clinical trials of drugs in ME/CFS, of which we believe low dose naltrexone is the top candidate. A report commissioned by the United Kingdom CFS/ME Research Collaborative in 2016 found research funding to be low-level and patchy and that investments needed to be increased, particularly for high-quality studies of biological mechanisms and treatments (40). We are delighted that this has proved possible for biological mechanisms, with the award of £3.2 million funding for Decode ME, the largest ever ME/CFS DNA study. However, awards for clinical studies are few, exploratory and conducted on small samples so results will still be liable to challenge or need replicating. Even though naltrexone itself is cheap, clinical trials are expensive. This is due to the need for involvement of a clinical trials unit and for the extensive independent monitoring necessary which is summarised in the Medicines and Healthcare products Regulatory Authority Good Clinical Practice Guide (41). Such a trial may cost nearly as much as the Decode ME study, which explains the problems of obtaining funding. However, if the trial	

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				was positive, this could bring immediate benefit to at least a proportion of people with ME/CFS. We have discussed elsewhere the benefit of limited but controlled prescribing of low dose naltrexone in specialist clinics in order to build up knowledge of low dose naltrexone in practice and to aid in clinical trial design. We believe this is a potential way forward which would be within the scope of recommendations within this guideline. 40. Radford G, Chowdhury S. ME/CFS Research Funding An overview of activity by major institutional funders included on the Dimensions database. 2016. 41. Medicines and Healthcare products Regulatory Agency, editor. Good clinical practice guide. London: The Stationary Office; 2012. 542 p.	
LDN Research Trust	Evidence Review F	088	007 - 008	**Evidence for low dose naltrexone** There have been no randomised clinical trials of low dose naltrexone in ME/CFS, although there is some published data. Polo 2019 published a retrospective analysis of his university based clinical practice in Finland from 2010 to 2014 (3). The medical records of 218 consecutive patients diagnosed with ME/CFS using the Canadian Consensus Criteria (or in a few cases Fukuda but always with the inclusion of unrefreshing sleep and post exertional malaise) were analysed. The severity of ME/CFS symptoms ranged from mild to very severe. Patients were started on naltrexone 1.5 mg daily increasing to 4.5 mg in stages. Outcome data was available in 92.2% of patients, with an average follow-up of 1.7 years (range 0.1 to 6.8 years, with 63% followed up for more than 1 year). An improvement in any symptom was reported by 73.9% of patients, with the commonest improvements in vigilance/alertness (51.4%), and physical (23.9%) or cognitive	Thank you for your comment and information. As you correctly note the Polo (2019) was excluded from the reviews based on the study design. It was not excluded from the qualitative analyses as it contained quantitative data, it was excluded because it was based on retrospective data from medical reports and did not employ qualitative methods or include any qualitative analysis.

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				(21.1%) performance. About half of patients noted an improvement in two or more symptoms, and 5 patients noted improvements in 5 or more symptoms. 18.3% of patients discontinued low dose naltrexone for lack of effectiveness. 7.5% stopped therapy due to adverse events, just over half of these while still in the introductory phase. About 50% of the group experienced transient side effects, mainly at the start of treatment or on dose increases, and these were mostly mild. The commonest side effects were nausea and insomnia. Some patients returned to gainful employment as a result of improvement in symptoms. This paper was excluded from the quantitative analysis in this review as it was not a randomised controlled trial, and excluded from the qualitative analyses as it contained quantitative data. If an independent researcher had held a focus group of several patients from this practice and produced a paper from this, the resulting paper would have been included in the qualitative analyses. The exclusion of this paper is therefore illogical as it provides more information than the focus group analysis could have done, for example, data on the proportion of people having no response to the drug. We accept the data will be inherently biased, as it is retrospective and unblinded, but still contend its inclusion would have been helpful, at least to inform research recommendations. Holtorf described the results of treating over 500 patients with ME/CFS (4). Where there was evidence of immune dysfunction (case history of allergies or blood tests including immune cell dysfunction), he prescribed low dose naltrexone in doses up to 4.5 mg, and claimed very good results. He subsequently trained other doctors in the same methodology,	

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				and published the results of another 4000 patients. Sadly this paper is no longer in the public domain as the journal it was published ceased to exist, but he more recently commented "LDN (low dose naltrexone) has proven so effective that doctors can prescribe it with a reasonable hope that patients will improve without extensive time and multiple interventions." (5) Low dose naltrexone has been a subject of discussion at many conferences in the United States of America, including the 2020 International Association for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis research conference. MacKay from Vancouver described treating 97 patients with diagnoses including ME/CFS with low dose naltrexone using doses up to 4.5 mg (6). She noticed beneficial effects including increased energy, decreased pain, improved sleep, improved cognition and reduction in crashes. Side effects included insomnia, skin rashes and gastrointestinal upset. She concluded that low dose naltrexone was safe with minimal side effects and offers some benefits to patients. Bolton 2020 reported the response of three people to low dose naltrexone in a paper published in BMJ Case Reports (7). The three contributors all had ME/CFS and compiled their own case reports supervised by a professor of General Practice. This paper was not identified in the literature searches performed for this NICE guideline, being a series of case reports. However, it contained comments by patients, which, if these had occurred in a paper of comments extracted as part of a focus group discussion, would have been included. The comments are included here for information.	

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				Case one commented;- "For me, low-dose naltrexone was truly life changing. From being virtually house bound, always limited by a multitude of symptoms, pain and low energy, I found my life returning. Every treatment or therapy I had tried previously involved effort— pacing myself, training myself, coping with symptoms. With low-dose naltrexone, the improvement just happened—I didn't have to try, I just got better. I went for walks and started cycling again. The first time I ate out when I was no longer limited by food allergies, I could select from the whole menu—the shock of all that choice! My husband commented I was no longer a shadow of a person but a genuine companion again. From being unable to string sentences together coherently for much of my adult life, I returned to university .. when aged 62!" Case two commented;- "After 25 years of living with the devastating effects of myalgic encephalomyelitis, I was struggling to cope with the limited options for symptom and pain management. Having had many bad reactions to medications, I was hesitant to try a medication that would affect my immune system so I started out at an extremely low dose and slowly increased dosage. While the dreaming was at times disturbing, the positive changes gave me a hope for improvement I had not had in many years. The subsequent improvements have led to a much higher quality of life and I would like to see this medication as an approved option for others in my situation." Case three commented "Since I was 14 (when I had my first chronic fatigue episode), whenever I have had any form of illness I have suffered from depressive episodes, including needing to withdraw socially and becoming very insular. This included the period prior to any illness, where I have felt run down or could tell a cold etc was forming. I started taking low-	

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				dose naltrexone when I was 37 and for the first time in 23 years, I have not had a depressive episode linked to colds or any other illness. Low-dose naltrexone has really helped improve my quality of life and also helped in social situations where I am not withdrawing and being insular like I had been previously." These comments fit the general pattern described by Polo and our knowledge gained from contact with people taking low dose naltrexone. Few people improve markedly, but most people gain some benefit, although the symptoms which improve vary between individuals. However, improvements in fatigue, sleep, cognitive dysfunction and mood can all occur. There have been several published studies in the possibly related disease of fibromyalgia. The longest study (8), a 24 week parallel placebo controlled randomised controlled trial in 74 people with fibromyalgia found that 16 of the 37 in the naltrexone group had clinically important improvements in the Fatigue Impact Questionnaire total scores and quality of life component, P <0.001. Mean and standard deviation results for the Fatigue Impact Questionnaire were;- Baseline at 24 weeks Naltrexone 63.7 (SD +/- 13.2) 38.5 (SD +/- 16.1) Placebo 63.0 (SD +/- 13.0) 57.9 (SD +/- 15.6) SD = standard deviation The results also showed significant reductions in pain on a visual analogue scale, p <0.001. The only significantly increased side effects for naltrexone were head aches and vivid dreams. Results from a blinded cross-over study of 31 patients (9), and several open label or single blinded studies (10–12) showed	

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				improvements in 50% or more of participants receiving low dose naltrexone, with average improvements in symptom scores in responders being around 30%. The blinded cross-over study also confirmed that the only two significantly increased side-effects were head aches and vivid dreams (9). There is also a published randomised double-blinded placebo-controlled crossover trial in Gulf War illness (13) which showed that 14 out of 37 people responded to naltrexone (38%) with 6 of the patients reporting much improvement. Using the SF-36 Health Survey and VAS scores as outcome measures, the differences in responses between naltrexone and placebo arms were clinically and statistically significant. Several summaries of clinical research to date have been published (14–16). Small randomized controlled trials have taken place in several immune modulated diseases including Crohn's disease (17–19), showing improvement in symptoms and mucosal healing, and HIV infection (20). These have shown a good safety profile with clinically significant improvements. Numerous case reports have shown low dose naltrexone is effective for treating various conditions with few other treatment options such as the skin disorder Hailey-Hailey disease (21), complex regional pain syndrome (22) and intractable pruritus (23,24). In Norway, an explosion of interest after a TV documentary led to an increase in prescriptions for low dose naltrexone from almost none in 2013 to 0.3% of the population having had at least one prescription by a few months later (25). Using the Norwegian Prescription Database, a centralised record of all drug prescribing in Norway, and comparing drug use for the 2 years before and after starting low dose naltrexone, it has	

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				been shown that persistent users of low dose naltrexone showed reductions in other medication use, including of disease modifying drugs in inflammatory bowel disease (26) and sero-positive arthritis (27). Analysis of the database also revealed there were reductions in use of opioid drugs without concomitant increase in other pain killers (28), and reductions in several psychotropic medicines and antiepileptics (29). Although there was no analysis of the underlying diagnosis requiring the use of opioids and psychotropics, it could be postulated that these groups might have included some people with ME/CFS whose use of other medication declined as their ME/CFS symptoms improved. One problem with naltrexone is the lack of published dosing studies. Pharmaceutical companies have never been interested in researching or promoting naltrexone even when it was under license, and the initial research on its use in opioid addiction and alcohol use disorders was funded by US government grants. Hence, the optimum dose for treatment using lower doses is unknown. In the case series by Bolton (7), case 1, who had an excellent response to low dose naltrexone takes 12 mg daily (6 mg bd) which is higher than the usual recommended dose of up to 4.5 mg daily. Personal correspondence with several leading prescribers of low dose naltrexone for people with ME/CFS including Nancy Klimas (a major ME/CFS researcher in the United States of America, who, among other research contributed to the Institute of Medicine report (30) and the Multisite Clinical Assessment of ME/CFS (31) and Ros Vallings (a member of the group drawing up the International Consensus Criteria (32)) confirms they routinely use doses up to 9 mg daily or higher. One recent short dosing study in 27 women with fibromyalgia, which used 3 mg twice daily as the highest dose tested, seemed to	

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				suggest this was the optimum dose in this study though data was very sparse (33). It is not known whether the use of a suboptimal dose of naltrexone accounts for some of the partial responders in published studies. There is some understanding of underlying mechanisms which may account for the effects of naltrexone. A genomic study by a group at Griffith University Australia showed polymorphisms of transient receptor potential melastatin 3 ion channel genes in people with ME/CFS (34). Lab studies of natural killer cells from people with ME/CFS, compared to control samples, revealed reduced numbers of transient receptor potential melastatin 3 ion channels which also had impaired calcium mobilization (35). Given that these are excitatory signalling channels in the cell membranes of many human cells including immune cells, and transient receptor potential dysfunction is already associated with some disease states, they postulated this may indicate a role in the pathomechanism involving natural killer cell cytotoxicity in ME/CFS. The group demonstrated that this abnormality reverses with the addition of naltrexone, which is a non-selective opioid antagonist (36). Although their work has not been replicated, this is the only in-vitro study of a drug improving cell function in ME/CFS. Other researchers have shown mu-opioid receptors specifically inhibit transient receptor potential melastatin 3 ion channels, playing an immunomodulatory and immunosuppressive role in immune cells (37). In a study of 8 women with fibromyalgia given naltrexone under blind conditions (cross-over design starting with placebo but not informing participants when the switch to naltrexone occurred), improvement in symptoms were associated with statistically significant reductions in a broad range of pro-	

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				inflammatory cytokines including interferon alpha and tumour necrosis factor-alpha (12). This result parallels lab study findings that naltrexone inhibits production of interleukin-6 and tumour necrosis factor-alpha in human immune cell subsets following stimulation with ligands for intra-cellular Toll-like receptors (38). There is more extensive research on naltrexone as a glial cell modulator and with activity at Toll-like receptor 4 and this is summarised by Toljan 2018 (15). These results are all preliminary, but if confirmed by other researchers, would suggest that naltrexone is correcting a cellular abnormality which may be of significance in the underlying mechanisms in at least some people with ME/CFS. Finally, the safety profile of naltrexone is well established, and shows it is safer than many commonly used symptomatic treatments. Naltrexone was discovered in 1963 and has been licensed for opioid addiction after withdrawal and the treatment of alcohol use disorders, at an oral dose of 50 mg daily, since the mid-1980s. Recently it has been licensed at 32 mg daily as part of the combination naltrexone-bupropion for the treatment of obesity in the United States of America and Europe. Thus, there is long term safety data available. A systematic review and meta-analysis of 89 parallel placebo-controlled randomised clinical trials longer than 4 weeks in 11,194 participants using naltrexone at any dose (median dose 50 mg, range 3 to 250 mg), showed that naltrexone did not increase the risk for serious adverse events compared to placebo, risk ratio 0.84, (95% confidence interval 0.66 – 1.06) (39). Long term safety data, such as from the "Yellow card system" supports this, the only caveat being in those taking opioids where the opioids should be withdrawn first. The same systematic review found only six marginally significant adverse	

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				events which were all of mild severity, decreased appetite, dizzyness, nausea, sleepiness, sweating and vomiting. Sensitivity analyses revealed these to be only of a mild nature and common among all patients (39). 3. Polo O, Pesonen P, Tuominen E. Low-dose naltrexone in the treatment of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Fatigue Biomed Heal Behav. 2019;7(4):207–17. 4. Holtorf K. Diagnosis and Treatment of Hypothalamic-Pituitary-Adrenal (HPA) Axis Dysfunction in Patients with Chronic Fatigue Syndrome (CFS) and Fibromyalgia (FM). J Chronic Fatigue Syndr. 2008;14(3):59–88. 5. Holtorf K. Chronic fatigue syndrome and fibromyalgia. In: Elsegood L, editor. The LDN Book. White River Junction, Vermont, USA: Chelsea Green Publishing; 2016. p. 79–80. 6. Stephens C. The 2020 IACFS-ME conference report. Gawcott, Bucks: The ME Association; 2020. 7. Bolton MJ, Chapman BP, Van Marwijk H. Low-dose naltrexone as a treatment for chronic fatigue syndrome. BMJ Case Rep. 2020;13:e232502. 8. Abou-Raya S, Abou-Raya A, Khadrawi T. Efficacy of naltrexone in the treatment of fibromyalgia: randomized controlled trial. Ann Rheum Dis. 2013;72(Suppl. 3):719. 9. Younger J, Noor N, McCue R, MacKey S. Low-dose naltrexone for the treatment of fibromyalgia: findings of a small, randomized, double-blind, placebo-controlled, counterbalanced, crossover trial assessing daily pain levels. Arthritis Rheum. 2013;65(2):529–38. 10. Younger J, Mackey S. Fibromyalgia symptoms are	

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				6 and TNFα Production in Human Immune Cell Subsets following Stimulation with Ligands for Intracellular Toll-Like Receptors. Front Immunol. 2017 Jul 11;8:809. 39. Bolton M, Hodkinson A, Boda S, Mould A, Panagioti M, Rhodes S, et al. Serious adverse events reported in placebo randomised controlled trials of oral naltrexone: A systematic review and meta-analysis. BMC Med. 2019;17(1):1–13.	
LDN Research Trust	Evidence Review F F F F F F F	091 091 091 092 092 093 088	012 - 013 041 - 042 051 023 043 022 - 023 007 - 008	**Specific example – Low dose naltrexone not explored as outside the committee's experience** The evidence reviews contain frequent comments that committee members used their experience to make recommendations (particularly noted examples, in the adaptation of the Institute of Medicine criteria for diagnosing ME/CFS, in noting intolerance to drug therapy in people with ME/CFS, and "the evidence for non-pharmacological and pharmacological interventions for ME/CFS is heterogeneous and inconclusive…… and this supported the committee's experience" The committee appear to have little experience of low dose naltrexone. This may be because their experience is mainly based within the United Kingdom National Health Service and therefore constrained by the previous NICE guideline. We note the contrast between this statement and that by the ME/CFS Clinician Coalition (a group of leading researchers and physicians treating people with ME/CFS in the United States of America), issued in March 2019.	Thank you for your comment. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will take into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence

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				"The field of ME/CFS needs evidence-based treatments. The combined clinical experience of ME/CFS clinicians supports efficacy of several treatments that have potential and warrant testing. Appropriate funding mechanisms are warranted. In addition, funding should support a clinical trials consortium. The ME/CFS Clinician Coalition agrees that our first priority is a trial of LDN (low dose naltrexone)." (1) In 2011, Solve ME/CFS Initiative, a US charity financing and promoting research into treatments for ME/CFS, engaged a drug repurposing company called Biovista to search for potential drug therapies for ME/CFS. Biovista highlighted low dose naltrexone as a potentially useful drug, but despite efforts by Biovista and Solve ME/CFS to look for partners to finance drug trials, they have failed (2). 1. Linford A. What's next for the ME/CFS Clinicial Coalition? [Internet]. Bateman Horne Centre News. 2019 [cited 2020 Dec 5]. Available from: https://batemanhornecenter.org/whats-next-cfs-clinician-coalition/ 2. Johnson C. Low Dose Naltrexone Drug Combination Proposed for Chronic Fatigue Syndrome (ME/CFS) by Biovista [Internet]. healthrising.org. 2016 [cited 2020 Dec 21]. Available from: https://www.healthrising.org/blog/2016/02/04/low-dose-naltrexone-combo-chronic-fatigue/	sections in the review chapters. As you note in comment 72 no evidence was identified that met the review protocols for low dose naltrexone and without this the committee were unable to evaluate the impact of naltrexone for people with ME/CFS.
LDN Research Trust	Evidence Review F	094	024 - 033	**Symptomatic treatment** Most people with ME/CFS use some medication to help symptoms, and we believe the recommendations should have acknowledge patient experience here. The current wording discourages any symptomatic treatment, which is unhelpful.	Thank you for your comment. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for

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				Symptomatic treatments of sleeping difficulties and pain would rely on cheap out-of-patent drugs, and in the current system of funding clinical trials and current expense of running clinical trials, it is unlikely that such trials will ever be funded. NICE, the National Institute for Health Research and the Medical Research Council need to urgently rethink other ways of establishing whether drugs are effective. These might, for example, be based on prescription databases and therefore examine trends in populations over extended periods of time. The Norwegian Prescription Database has been used recently in this way to track the use of low dose naltrexone in the Norwegian population (25). By this means it has been shown that persistent users of low dose naltrexone showed reductions in other medication use, including of disease modifying drugs in inflammatory bowel disease (26) and sero-positive arthritis (27). Analysis of the database also revealed there were reductions in use of opioid drugs without concomitant increase in other pain killers (28), and reductions in several psychotropic medicines and antiepileptics (29). Although there was no analysis of the underlying diagnosis requiring the use of opioids and psychotropics, it could be postulated that these groups might have included some people with ME/CFS whose use of other medication declined as their ME/CFS symptoms improved. In a world where funding is in better supply, such as in cancer research, large amounts of charitable donations enable innovative new drugs to be researched and findings such as outlined above, might rapidly be followed by double blind randomised clinical trials. In contrast, for diseases such as ME/CFS which, in comparison, attract tiny amounts of charitable funding, and where governmental sources of funds are very competitive, clinical trials are extremely difficult to	unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will take into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. When considering the evidence for pharmacological interventions the committee agreed that there was insufficient evidence of benefit to recommend any medicines but recognised that people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis. As you note in comment 72 no evidence was identified that met the review protocols for low dose naltrexone and without this the committee were unable to evaluate the impact of naltrexone for people with ME/CFS. Non-randomised study designs or data from databases, such as the one you mention, are considered to have too high a risk of bias for decision making purposes, particularly with regards to assessing the efficacy of interventions. For this reason, this

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				fund. This is particularly so for off-license cheap drugs in which pharmaceutical companies have no interest. 25. Raknes G, Småbrekke L. A sudden and unprecedented increase in low dose naltrexone (LDN) prescribing in Norway. Patient and prescriber characteristics, and dispense patterns. A drug utilization cohort study. Pharmacoepidemiol Drug Saf. 2017;26:136–42. 26. Raknes G, Simonsen P, Småbrekke L. The effect of Low Dose Naltrexone on medication in inflammatory bowel disease: a quasi experimental before-and-after Prescription Database study. J Crohn's Colitis. 2018 Jan 27;jjy008. 27. Raknes G, Småbrekke L. Low dose naltrexone: Effects on medication in rheumatoid and seropositive arthritis. A nationwide register-based controlled quasi-experimental before-after study. PLoS One. 2019;14(2):1–13. 28. Raknes G, Småbrekke L. Low-dose naltrexone and opioid consumption: a drug utilization cohort study based on data from the Norwegian prescription database. Pharmacoepidemiol Drug Saf. 2017;26(6):685–93. 29. Raknes G, Småbrekke L. Changes in the consumption of antiepileptics and psychotropic medicines after starting low dose naltrexone: A nation-wide register-based controlled before-after study. Sci Rep. 2019;9(1):1–8.	review was limited to RCT evidence. See chapter 4, Developing review questions and planning the evidence review in Developing NICE guidelines: the manual about approaches to considering the design of studies to be included in a systematic review.
LDN Research Trust	Evidence Review G	005	018 - 019	**Non-pharmacological treatments, search strategies** The committee states it reviewed patient experiences of non-pharmacological interventions. It reviewed a very limited sample of patient experiences, probably selected through a search of medical literature for qualitative studies. However, as the actual literature search is non-specific, it is not possible to	Thank you for your comment. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that

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				assess the methods used. In addition, patient experience is more adequately contained in grey literature, which it appears were excluded from searches (though this is unclear) although the NICE manual states it can be included.	were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation.
LDN Research Trust	Evidence Review G	198	002 - 006	**Economic evaluations** Developing NICE guidelines: the manual states in chapter 7 that where no economic evaluation has been performed, this should be done by the committee. The evidence review states that the existing health economic evaluation is based on the costs of cognitive behaviour therapy. We believe an evaluation of the cost-effectiveness of treatments, by means of a graph of cost of hypothetical drug per patient against quality-adjusted life year improvement is a worthwhile exercise, as it would reveal whether any potential drugs, including off-license drugs, could be included in NICE guidelines at what level of improvement in quality-adjusted life year. We believe that most off-patent drugs currently being used in patient care would be cost-effective within the parameters roughly set by NICE of an incremental cost-effectiveness ratio of £20,000 per quality-adjusted life year gained. The cost of 28 tablets of naltrexone 50 mg already available in the National Health Service formulary can be as low as £23, the drug tariff price is £68.74. There is currently no listed formulation of naltrexone tablets at 1.5 mg, 3 mg or 4.5 mg in the British National Formulary, but private prescriptions typically cost less than £390 per year (current cost £31.50 for 28 tablets at any of these low doses). Hence, the improvement necessary for the drug to be cost-effective using NICE's criteria would be small (we estimate only 2%, though obviously treatments would only be recommended if they resulted in clinically important improvements).	Thank you for your comment. There are many low-cost interventions that if even partially effective could be highly cost effective. However, this can only be the case where there is trial evidence indicating a treatment effect. The evidence reviews in this guideline indicate that may trials have been carried out for people with ME/CFS but sadly few if any have shown a trend towards treatment benefit. It would be misleading to conduct a cost or threshold analysis for any particular drug or non-drug intervention, unless there was good evidence of a benefit, since those interventions might represent a harm rather than a benefit, albeit a small harm.

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				Patients similarly weigh up cost-effectiveness in their decision making, and many patients continue to pay for low dose naltrexone privately even when only gaining a partial response. The consequences of having no baseline economic evaluation is that the current costs of the status quo are vastly under-rated in the review of evidence, and that measures producing small increases in benefits are ignored. Many patients however, show the benefits gained by only small reductions in fatigue by continuing on National Health Service prescribed drugs for sleeping, pain etc, and their willingness to pay for private prescriptions of drugs such as low dose naltrexone, and complementary measures	
LDN Research Trust	Guideline	General	General	**Summary** This guideline, if put into practice, will be transformative for the lives of people with ME/CFS in England and Wales. We commend the committee on their bold statement on page 4 section 1.1.2, of the harm that misbelief in the illness has caused and hope the guideline will add understanding for health care practitioners unfamiliar or previously doubtful about this condition. We also commend statements on severe or very severe ME/CFS (including the need for home visits), and the need for early suspicion of ME/CFS, all of which should lessen stigma and improve care of people with ME/CFS. Although we think this guideline has in general been well thought out for the clinical and care needs of people with ME/CFS, we think too little thought has been given to the research implications of the guideline and the research needs of this community. This was obviously not the primary focus of the guideline which is a clinical guideline, but recommendations within it have far-reaching consequences. We believe the guideline should have been more explicit about the problems involved in clinical research of ME/CFS and therefore included more research recommendations. For example, we commend the guideline	Thank you for your comment. *Research recommendations* *Design of trials* As you note the committee have made a research recommendation for the development of a core outcome set to improve the implementation of research in ME/CFS. The committee have included the importance of long term follow-up in the research recommendations on interventions. All NICE research recommendations are reviewed by the NIHR to consider for their funding streams. Other research funders also consider NICE research recommendations. It is beyond the remit of the guideline to provide more detailed information on how research in these areas should be conducted. *Medicines* The committee recognised the lack of research in medicines but did not identify any one medicine to prioritise for research and as such did not make any research recommendations on this topic.

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				for the recommendation of a core outcome set. But this alone will not solve the problem of poor design in clinical trials of people with ME/CFS. Further research is needed on objective outcome measures and optimum length of trials, and a recommendation on what research diagnostic criteria to use is needed. We also believe the committee has not taken account of the lack of funding opportunities for research into ME/CFS in not prioritising the need for drug research. The lack of funding arises due to a combination of lack of interest by pharmaceutical companies in the disease, low profile in charitable giving, and reduced budgets for research in the United Kingdom with a refocus on COVID-19 research. It is compounded by the lack of route to research for off-patent drugs such as low dose naltrexone and many symptomatic drug therapies, leading to continuing paucity of high quality evidence into efficacy.	
LDN Research Trust	Guideline	General	General	**<u>Problems with NICE methodology</u>** We believe that NICE needs to urgently review its methodology and the impact it is having on the research agenda in the United Kingdom The NICE methodology was originally developed to increase the quality of data on which economic based decisions were taken in a cost-limited health system. It works well in diseases where there is an active research agenda, new treatments and technologies are emerging fast and investments by pharmaceutical companies or large charitable institutions are high. In these situations, NICE can systematically examine evidence of high quality to make recommendations. For diseases which are neglected in public and business consciousness and which are therefore dependent for research by competing for scarce public funding (in the United Kingdom and also world-wide), there will inevitably be a dearth of high quality data. The NICE search criteria excludes all data apart from high quality randomised	Thank you for your comment and information. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee included members with clinical and personal experience of children and young people with ME/CFS. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two

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	Guideline	24	4-5	controlled trials, so any case reports or retrospective case note analyses are ignored. Thus, when neither industry nor academic researchers are producing robust evidence, NICE is left with insufficient evidence to make recommendations. Instead of looking at patient experiences, its recommendations are conservative and unhelpful. It is simply untrue that there are no pharmaceutical treatments which can help symptoms in at least some people with ME/CFS. As NICE makes no mention of these possibilities, medical practitioners and patients remain ignorant of their value, a body of clinical experience is not built up, and even if clinical trials are suggested, much basic knowledge about the drug remains unknown (including, for example, the optimum dose, which may vary in different diseases and for different uses), hindering optimum clinical trial design. NICE should examine why the current situation exists, and think carefully what the impact of the current restrictive emphasis on high quality data is having on prescribing in the National Health Service. The paradoxical effect is, instead of driving down costs, that very few cheap off-patent drugs are trialled, and most NICE recommendations are for expensive new drugs rather than repurposing of existing cheap drugs whose safety profile is already well known. In the current draft guideline, by not recommending research into drug treatment options, physicians, even in research centres, continue to lack knowledge of potential drug candidates. Even if such therapies are trialled, this is likely to lead to suboptimal clinical trial design due to lack of experience with the drug. Consider the difference between the guideline statement on drugs (guideline page 24 line 4-5) and the statement by the ME/CFS Clinician Coalition (a group of leading researchers	commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The committee use their experience to develop the protocols for the reviews and consider the most appropriate design for the question. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. When considering the evidence for pharmacological interventions the committee agreed that there was insufficient evidence of benefit to recommend any medicines but recognised that people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis. As you note in comment 72 no evidence was identified that met the review protocols for low dose naltrexone and without this the committee were unable to evaluate the impact of naltrexone for people with ME/CFS.

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				and physicians treating people with ME/CFS in the United States of America), issued in March 2019. “The field of ME/CFS needs evidence-based treatments. The combined clinical experience of ME/CFS clinicians supports efficacy of several treatments that have potential and warrant testing. Appropriate funding mechanisms are warranted. In addition, funding should support a clinical trials consortium. The ME/CFS Clinician Coalition agrees that our first priority is a trial of LDN (low dose naltrexone).”(1) In 2011, Solve ME/CFS Initiative, a United States of America charity financing and promoting research into treatments for ME/CFS, engaged a drug repurposing company called Biovista to search for potential drug therapies for ME/CFS. Biovista highlighted low dose naltrexone as a potentially useful drug, but despite efforts by Biovista and Solve ME/CFS to look for partners to finance drug trials, they have failed (2). In view of the shortage of funding opportunities, particularly for any therapy other than new pharmaceutical agents, other ways of monitoring people and assessing improvements in health are urgently needed which are sufficiently reproducible to warrant confidence in these initial results. We believe that NICE should consider whether it could facilitate data collection using novel methodologies, or by updating methodologies other than double blinded randomised trials. For example, the Clinical Practice Research Datalink collects all prescriptions from a proportion of the population, currently 16 million patients. It would be possible to set up prospective studies of resource use including prescription use, following patients from before they were prescribed low dose naltrexone for a period of time afterwards to track progress. Patients could complete,	

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				outcome measures, preferably a standard Core Outcome Set which includes an objective measure of outcome. Other non-comparative studies need developing if the National Health Service is to benefit from repurposing of off patent drugs. Population based studies with outcomes such as total medicine use, return to work or school, reduction in benefits and even death rates, may be worth exploring, and NICE should consider adding such studies to its methodologies if the results of such studies are borne out by patient experience. We are not suggesting that these measures supplant rigorous large double blind randomised controlled trials of adequate length. But such trials are more likely to be funded, and adequately funded, if preliminary evidence is available to hone clinical trial design. This is more likely to happen when guideline recommendations include potential drug candidates and novel monitoring methodologies to improve initial data collection. Even when clinical trials are conducted, there may be problems with generalisability of trial results to clinical practice, and the use of novel methods initially may reveal where more work will be necessary in this area for particular treatments. 1. Linford A. What's next for the ME/CFS Clinicial Coalition? [Internet]. Bateman Horne Centre News. 2019 [cited 2020 Dec 5]. Available from: https://batemanhornecenter.org/whats-next-cfs-clinician-coalition/ 2. Johnson C. Low Dose Naltrexone Drug Combination Proposed for Chronic Fatigue Syndrome (ME/CFS) by Biovista [Internet]. healthrising.org. 2016 [cited 2020 Dec 21]. Available from: https://www.healthrising.org/blog/2016/02/04/low-dose-naltrexone-combo-chronic-fatigue/	

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LDN Research Trust	Guideline	General	General	**Problems outside control of NICE** The lack of clinical trial data for low dose naltrexone despite the slow increase in its use is disappointing. It is not uncommon to read patient views expressing disappointment that trials have not taken place and wondering why this is. We place some relevant facts before the committee. Some diseases are able to benefit from large charitable bodies which have sufficient funding for independent research, as well as the organizational ability to apply for government agency funding of clinical trials. For example, using the Charities Aid Foundation website's search engine (61), and searching using the term "cancer research", there are over 8000 charities listed on the Charities Aid Foundation website. Only the first 500 charities are displayed following such a search, but of these, 14 have incomes of over £10 million per year, and 31 have incomes between £1.6 million and £9.9 million per year. The total incomes of the first 500 charities amounted to £355 million. By contrast, searching on the terms myalgic, ME or CFS revealed 24 charities in total (research and support), their total yearly income being £3.4 million per year, with less than half of this devoted to research and the majority used for patient support. The total grants funded by ME Research UK (the largest United Kingdom charity supporting ME/CFS research) in 2019 amounted to £215,000 which was broken into several small grants (62). This is insufficient income to fund even a stage 1 clinical trial. Even combining the income from all ME/CFS charities together could not fund a phase III trial. By contrast, cancer research charities routinely fund large trials, and even whole departments in cancer treatment centres. Even supposing that low dose naltrexone was subjected to clinical trials which proved positive, there are further barriers	Thank you for your comment and this information.

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				before it could be accepted by NICE. The licensing system in the United Kingdom is set up primarily as a route for new drug licensing, with no easy pathway for off-patent drugs. Two Private Members' bills aimed at providing an easier route for licensing of off-patent drugs which have proved beneficial in clinical trials were rejected by the Government, despite overwhelming cross-party support and the support of nearly all medical charities and professional associations. Following this rejection, the Government agreed to work collaboratively to identify and mitigate barriers to ensure patients could receive the care they needed. The Association of Medical Research Charities was commissioned and produced a report in 2017, "Facilitating adoption of off-patent, repurposed medicines into National Health Service clinical practice" (63). One particular section of recommendations, on financial incentives, suggested several mechanisms to increase research into off-patent drugs. None of the recommendations, including a ring-fenced fund for research of out-of-patent drugs, and tax incentives for generic drug manufacturers researching new indications, were taken further. Even if such incentives were to come into place, many of them were aimed at existing formulations of off-patent drugs. Low dose naltrexone suffers from a further disadvantage as the dosage is so much lower than the current licensed formulation for opioid and alcohol addiction (50 mg), that further work is needed on product stability and dosage range including a formal dosing study, and this further complicates licensing requirements. In fact, the small manufacturers and importers of naltrexone tablets of 3 mg and 4.5 mg strength have spent considerable time and money ensuring their products are compatible for and with the necessary documentation to be used in clinical trials. Thus, this product could be listed in the	

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				British National Formulary under unlicensed medications. Due to lack of awareness, it is currently not stocked by standard pharmacists but by a few known specialist providers, and this leads to further confusion when writing and dispensing prescriptions. 61. Charities Aid Foundation. CAF online charity search [Internet]. 2020 [cited 2020 Dec 21]. Available from: https://www.cafonline.org/my-personal-giving/start-giving/donate-now 62. ME Research UK. ME Research UK Annual Report and Accounts 2018 - 2019. Perth, Scotland; 2019. 63. Association of Medical Research Charities. Facilitating adoption of off-patent, repurposed medicines into NHS clinical practice. 2017.	
LDN Research Trust	Guideline Guideline Guideline Evidence Review I Evidence Review J Supporting documentation 3 Evidence Review I Evidence Review I	022 - 026 058 011 General General 020 - 021 019 025	General 019 - 029 013 onwards General General General Table 5 017 - 025	**Multidisciplinary care and review of care** The examples in the columns to the left show there was little or no evidence in the evidence reviews on which to base the recommendations for multidisciplinary care and review of care. These whole sections of the draft guideline and Evidence reviews I and J are based on the experience of committee members (for example see evidence review I page 23 lines 24 – 26, evidence review J page 9 lines 39 - 43 and evidence review J page 12 line 12 -13) and supporting documentation 3 expert testimony 3 pages 20 - 21, the expert statement by Dr Mujtaba Husain, additionally informed by comments from people with ME. While we welcome the recommendation and do not dispute that it will be very beneficial for people with ME/CFS, it will be hugely time and therefore cost expensive. It will only ensure that people with ME/CFS do not deteriorate due to wrong advice, rather than offer treatments that can improve their condition. It is interesting that the committee ignored the only cost-benefit analysis of multi-disciplinary team	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what

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				care when making their recommendation (evidence review I page 19 table 5 and discussion on page 25 lines 17 to 25). Yet again, it shows that what has been included in the guideline was what the committee had experience of where there were gaps in the evidence, and very occasionally in spite of the evidence. It would have been possible to invite expert testimonies from practitioners with wide experience of prescribing drugs for ME/CFS and enquire which of those were worth further exploration. This would have enabled clinics to build up knowledge of drugs which could have informed clinical trial design. In general, only doctors working outside the National Health Service are currently able to gain experience of low dose naltrexone, and hence, although it is cheap, safe, and, we believe, beneficial in at least a proportion of people with ME/CFS, no recommendation for research was made. This contrasts sharply with the decision for multidisciplinary care, which is very cost-heavy. The NICE manual states;- When no relevant published studies are found, and a new economic analysis is not prioritised, the committee should make a qualitative judgement about cost effectiveness by considering potential differences in resource use and cost between the options alongside the results of the review of evidence of effectiveness. This may include considering information about unit costs, which should be presented in the guideline. The committee's considerations when assessing cost effectiveness in the absence of evidence should be explained in the guideline. We quote, Kent Holtorf (5), a United States of America specialist in treating ME/CFS. (We have left the words as original, including the abbreviation LDN for low dose	recommendations can be made and the appropriate strength of the recommendation. The committee will take into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). With regard to Advice for people with suspected ME/CFS. The beginning of the discussion section in Evidence review E states ,'the committee discussed this evidence with the findings from the reviews on Information for people with ME/CFS and their families and carers (report A), Information and Support for health and social care professionals (report B), access to care (report C), Diagnosis (D) non pharmacological management (report G) and the report on Children and Young people (Appendix 1). The committee took this evidence into account as well as their own experience and expertise. This has been clarified in the discussion section. *low dose naltrexone* As you note in comment 72 no evidence was identified that met the review protocols for low dose naltrexone and without this the committee were unable to evaluate the impact of naltrexone for people with ME/CFS.

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				naltrexone) "Having treated patients with CFS and fibromyalgia for the past 15 years, I have come to the conclusion that I cannot do so effectively if I am forced to see them for fifteen minutes or less each visit. A visit …. usually requires an hour to adequately assess the progress of the patient, rather than the standard ten- to twenty- minute visit that is reimbursed by insurance companies and paid for by a patient co-op. Doctors are forced to chose between high patient volume with superficial ineffective care in order to pay the bills, and comprehensive care with a dramatically lower patient volume that isn't economically feasible….. Why do I emphasise the current predicament in a book about LDN? Because LDN has proven so effective that doctors can prescribe it with reasonable hope that patients will improve without extensive time and multiple interventions. While nothing works for everyone, LDN has some benefit in most patients and has a dramatic effect in a good percentage. The key is that there are no significant side effects. Only a small percentage of patients report minor side effects, and I have never seen a major side effect, unless given concurrently with a contraindicated opioid drug. This allows doctors who care about their patients to stay within "the system" until another alternative proves feasible."(5) We believe that evidence such as this should be taken seriously. We propose the guideline could recommend that selected secondary care centres use low dose naltrexone in a quasi- research situation, which we believe would prove to be cost-effective. The off-license implications of prescribing low dose naltrexone would need to be fully explored and accepted by both prescribing doctor and patient volunteer, and there should be stringent monitoring of results (for example, recording outcome measures before and during therapy,	

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				providing activity monitors with facilities to extract data for analysis, performing some objective tests before and after starting low dose naltrexone). This data collection could also be used to further research on outcome measures for both clinical and research monitoring of people with ME/CFS. The potential savings to the National Health Service of such an approach may be very large. Should low dose naltrexone prove effective in even a proportion of those attending the specialist clinic, the time taken to manage their condition would rapidly lessen, leaving more time to engage in management along the lines of the draft guideline in those who do not respond. In addition, those clinics would gain experience in prescribing low dose naltrexone and provide preliminary data on which to base the design of a clinical trial, which any subsequent clinical trial would benefit from. Obviously, such a quasi-research setting is no substitute for clinical trials. Like all drugs, patients taking low dose naltrexone may have a placebo response. The placebo response in a large systematic review and meta-analysis was 19.6% (95% confidence interval 15.4 to 23.7) using pooled data from 29 trials of therapy in people with ME/CFS, 28 of which were randomised controlled trials and one controlled clinical trial (44). However, the placebo response in the phase III rituximab was 35.1% compared with 26.0% in the rituximab group (45). Kosek found an association between a longer illness duration and lower placebo response to drug therapy in a clinical trial of milnacipran for fibromyalgia (46), and this might be so also for ME/CFS. The circular situation therefore occurs, that what is outside NICE guidance, even when used in other countries, for example, drugs for treating ME/CFS, are not recommended. There will be no suggestions from physicians within National	

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				Health Service clinics of potential new treatments, so NICE will not recommend any (remember, the advice for people with suspected ME/CFS was drawn up using the knowledge and experience of committee members, not from evidence). Unless NICE allows specific drug treatments in secondary centres with appropriate monitoring, there will be no recommendations for clinical trials of advances in treatments. 5. Holtorf K. Chronic fatigue syndrome and fibromyalgia. In: Elsegood L, editor. The LDN Book. White River Junction, Vermont, USA: Chelsea Green Publishing; 2016. p. 79–80. 45. Fluge Ø, Rekeland IG, Lien K, Thürmer H, Borchgrevink PC, Schäfer C, et al. B-lymphocyte depletion in patients with myalgic encephalomyelitis/chronic fatigue syndrome: A randomized, double-blind, placebo-controlled trial. Ann Intern Med. 2019;170(9):585–93. 46. Kosek E, Rosen A, Carville S, Choy E, Gracely RH, Marcus H, et al. Lower Placebo Responses After Long-Term Exposure to Fibromyalgia Pain. J Pain. 2017 Jul 1;18(7):835–43.	
LDN Research Trust	Guideline Guideline Guideline Guideline Guideline	004 006 013 019 017 - 018	016 - 021 007 onwards 011 onwards 008 onwards	**Recommendations we highly commend** The statement on the effect of experiencing prejudice and disbelief is bold, timely and we hope will effect a change in culture amongst health and social care workers towards people with ME/CFS. The discussion of severe or very severe ME/CFS is accurate and very timely. We commend the committee for this clear description of the needs of those with severe ME/CFS. This, along with offering home visits, for assessment and management, and comments on hospital care, we hope will fill	Thank you for your comment.

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			020 onwards	the vacuum of current management for people with very severe ME/CFS. The section on access to care is well worded and should improve care access if implemented well.	
LDN Research Trust	Guideline	004	005 - 006	**Additional wording needed** The statement on page 4, lines 5-6 of the Guideline is not as convincing as the Institute of Medicine 2015 statement "ME/CFS is a serious, chronic, complex, and systemic disease that frequently and dramatically limits the activities of affected patients" (30). We believe it should be strengthened. For example, add after medical (not psychological) /or add after pathophysiology is unclear, although research is uncovering metabolic, immunological and other abnormalities or some other wording directly aimed at addressing some health and social care providers' continuing disbelief in the physical (as opposed to the psychological or imagined nature) of the disease. 30. Institute of Medicine of the National Academies. Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness. Washington, D.C.: The National Academies Press; 2015. p. 9	Thank you for your comment. The committee disagree, this wording acknowledges the reality and seriousness of ME/CFS as a medical condition. Throughout the guideline the committee have made recommendations reinforcing that health and social care professionals should acknowledge the seriousness and reality of living with ME/CFS and take into account the impact of not being believed has had. This bullet point has been edited to,' and its pathophysiology remains under investigation' to clarify that there is not enough evidence to make any conclusions about the pathophysiology of ME/CFS and this is an active area of research. The context of the guideline also expands on this.
LDN Research Trust	Guideline Guideline Guideline Guideline	005 009 011 051	010 - 011 017 - 020 005 - 006 022 onwards	**Diagnostic criteria – reduction in time to diagnosis** There is a difference between the need for rapid provisional diagnosis, correct advice to avoid harm and for referral, and the need for definitive diagnosis. The committee appear to have confused the two. We support early provisional diagnosis. We do not support reduction of the time from 6 months to 3 months without an evidence base. We commend	Thank you for your comment. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are:

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				the committee for the recommendation "do not delay making a provisional diagnosis of ME/CFS". However, the diagnosis needs time to establish the longer term nature of the condition. People also need time to accept the reality of the diagnosis, so the 6 month wait with a provisional diagnosis in the mean time, would not affect management and would give more credibility. We discuss this more under diagnostic criteria – changes from Institute of Medicine criteria.	- 'Provisional' diagnosis has been deleted. The committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. - Further investigation/differential diagnoses. The committee have recommended that investigations should be done to exclude other diagnoses and this should continue where ME/CFS is suspected. If in any doubt specialist advice should be sought. The committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'. *Reduction in timeline* After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. People with ME/CFS do experience delays in diagnosis and the committee recognised that referral to a specialist team for confirmation of diagnosis can take months, taking this into account it is important that this process is started at 3 months and people are given appropriate advice until they are seen by a ME/CFS specialist team.
LDN Research Trust	Guideline Guideline Guideline Guideline Evidence Review D	008 46 49 51 048	017 box 1 5 10-26 21-26 018-20	**Diagnostic criteria – changes from Institute of Medicine criteria** The wording in various parts of the guideline and evidence reviews is contradictory. In some places, it appears to suggest that the draft guideline is not suggesting new diagnostic criteria even though the discussion on page 51 lines 22 to 26 and in the Evidence review D suggests otherwise. We think that the final guideline should make it very clear that these criteria are for use to suggest early suspicion of disease, not for use as	Thank you for your comment. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your point and added some clarity for readers. In summary the edits to the point you make are: - 'Provisional' diagnosis has been deleted. As you note the symptoms should be investigated for other causes and the

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	Evidence Review D Guideline	058 052	043 - 045 005 - 015	final diagnostic criteria. If it is a new set of criteria, we would be opposed to this in principle at this time, even though we believe the need for early suspicion of this illness is important for correct management in the early stages of the disease. Evidence review D page 48 lines 18 to 20. The committee itself agreed that "in the absence of a reference standard it cannot be assumed previous criteria are superior and it is not possible to assess if the level of agreement between new and previous criteria represents a positive or negative outcome." Hence, why did the committee decide to make new diagnostic criteria? The Institute of Medicine of the National Academies in the United States of America undertook a major review of diagnostic criteria for ME/CFS and in 2015 published their work which included proposals for new clinical criteria (30). They recommended a multidisciplinary group should re-examine their diagnostic criteria, and for such a group to consider, in no more than 5 years, whether modification of the criteria was necessary. They felt this move should be based on firm evidence supporting modification. There have been no breakthroughs in diagnosing ME/CFS since then, and the diagnostic criteria in this draft guideline is based on a less solid basis than the original Institute of Medicine criteria, having been adapted following committee members' experience. Without specific funding for research to validate or otherwise this and the Institute of Medicine definitions, this criteria will simply add confusion, and put the United Kingdom at variance with the rest of the world. Rather than doing this, the committee should have emphasised the need for additional research and set a date for review of the Institute of Medicine criteria in order to adapt it – as the Institute of Medicine had itself wished.	committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. • It is clear in the diagnosis section that diagnosis is dependent on the criteria persisting for 3 months and other conditions have been excluded. As you note the rationale section of the guideline linked to this recommendation is clear that the criteria recommended are a modification of the IOM criteria. Evidence review D describes in detail the reasons why. To summarise: o Cognitive difficulties and orthostatic intolerance .In summary the committee maintain that cognitive difficulties are a key symptom in suspecting ME/CFS and are commonly reported in people with ME/CFS. They note that cognitive difficulties (such as brain fog) are described in most of the criteria (7 of the 9) criteria) reviewed in Evidence review D in contrast with orthostatic intolerance (4 of the 9 criteria) supporting further their experience and expertise. o Time to diagnosis .After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. The committee acknowledge that this further reduced from the 6 months in the IOM criteria The committee agreed that although a 6-month delay to diagnosis is built into the IOM criteria, the criteria could be safely amended by the reduction of this delay period to 3 months. It was agreed that the function of a delay is partly to reduce

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				Evidence review D states "specificity not sensitivity of diagnostic criteria is more important in ensuring validity of research studies". The committee have recognised that research and clinical definitions may not be identical. There is a need for clarity on what diagnostic criteria should be used for research in the United Kingdom. This should be a separate recommendation or recommendation for research. Without this, the United Kingdom is likely to remain at variance with the rest of the ME/CFS research community, as happened previously with the Oxford and NICE 2007 case definitions. The discussion in draft guideline page 52 lines 5 to 15 touches on the need for research criteria without confronting it fully. 30. Institute of Medicine of the National Academies. Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness. Washington, D.C.: The National Academies Press; 2015. p. 9	the number of misdiagnoses through allowing short-lived fatigue to be excluded. In addition to not being disadvantageous, removal of the delay was seen as beneficial, as this might facilitate earlier management and potentially allow improvement in longer term outcomes. o People with ME/CFS do experience delays in diagnosis and the committee recognised that referral to a specialist team for confirmation of diagnosis can take months, taking this into account it is important that this process is started at 3 months and people are given appropriate advice until they are seen by a ME/CFS specialist team. *Research recommendation* The committee agree there is a need for validated diagnostic criteria but recognised the importance of clear and informative guidance to assist clinicians, who may not be experts in ME/CFS, in identifying people with ME/CFS Recognising the absence of a validated diagnostic criteria they made a research recommendation to develop validated criteria (see the. committee discussion in evidence review D).
LDN Research Trust	Guideline	030	003 onwards	**Orthostatic intolerance.** We do not have strong views on the removal of orthostatic intolerance when adapting the Institute of Medicine definition of ME/CFS as we are not clinicians. However, orthostatic intolerance is a very disabling part of ME/CFS amongst those we know with ME/CFS, and its removal may downgrade the likelihood of a person with ME/CFS obtaining advice on this symptom, for which symptomatic advice, mechanical and drug aids are available. We believe there should be a specialist in	Thank you for your comment. The committee agree that orthostatic intolerance is one of the symptoms that people with ME/CFS commonly experience and have included this in the recommendation raising awareness about such symptoms. In addition, the committee have included recommendations on the general management of orthostatic intolerance. These include that medicine for orthostatic intolerance in people with ME/CFS should only be prescribed or

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				diagnosing orthostatic intolerance and in prescribing drugs where symptoms are sufficiently severe in every secondary centre, with referral to a tertiary centre for more intractable cases. From our perspective as an organisation keen on research, by excluding orthostatic intolerance from the definition of ME/CFS, the possibility of research into this disabling aspect of ME/CFS would be lessened. This in turn reduces the possibility of drug related research into ME/CFS, whereas this is an area where symptomatic relief may be possible, but needs specifically validating in the ME/CFS population.	overseen by a healthcare professional with expertise in orthostatic intolerance.
LDN Research Trust	Guideline	031	010 - 014	**Drug intolerance** Some decisions are based solely on the experience of the committee. For example the statement "take into account when prescribing that people with ME/CFS may be more intolerant of drug treatment and have more severe adverse effects." There is no research evidence on which this statement is based but it is none-the-less included in the draft guideline. We would not refute the statement (which accords with the experience we know of people with ME/CFS) – but it has less of an evidence base than our assertion that low dose naltrexone is beneficial to at least a proportion of people with ME/CFS (for which there are large amounts of anecdotal reports and some published work, though none of it included in this review (3,7). In addition, low dose naltrexone is a possible exception, in that experience by a group in Norway familiar with naltrexone is finding that starting at a dose of 3 mg twice daily produces fewer side-effects than when starting at 1.5 mg daily. Although data was sparse, the dosing study in fibromyalgia also found this to be so (33). The Norwegian group believe this may be due to naltrexone having several	Thank you for your comments. After considering the stakeholder comments the committee agreed to delete 'and have more severe adverse effects' but have retained the information that people with ME/CFS maybe less tolerant of drug treatment. The committee agreed that in their clinical experience and consensus view intolerance of drug treatment was not uncommon in people with ME/CFS and prescribers should take this into account when starting drug treatments. Based on the evidence (Evidence review D) and the committee's clinical experience, they agreed the four criteria for the diagnosis of ME/CFS were fatigue, post-exertional malaise, unrefreshing sleep and sleep disturbance (or both), and cognitive difficulties. Key to the diagnosis of ME/CFS is the presence and combination of the four symptoms. Pain may be associated but is not exclusive to with ME/CFS, this was supported by the IOM diagnostic criteria (2015). The committee note that pain is the dominant symptom in fibromyalgia and as such the two populations are differentiated.

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				different modes of action predominating at different low doses, though this is very hypothetical. 3. Polo O, Pesonen P, Tuominen E. Low-dose naltrexone in the treatment of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Fatigue Biomed Heal Behav. 2019;7(4):207–17. 7. Bolton MJ, Chapman BP, Van Marwijk H. Low-dose naltrexone as a treatment for chronic fatigue syndrome. BMJ Case Rep. 2020;13:e232502. 33. Bruun-Plesner K, Blichfeldt-Eckhardt MR, Vaegter HB, Lauridsen JT, Amris K, Toft P. Low-Dose Naltrexone for the Treatment of Fibromyalgia: Investigation of Dose-Response Relationships. Pain Med. 2020;21(10):2253–61.	
LDN Research Trust	Guideline Guideline Guideline Guideline D F F J Supporting documentation 3 F	045 52 46 60 64 87 87 9 Expert testimony 1 87	024 - 026 16-24 1-3 9-17 19-22 14-17 27-28 9-17 General 27-28 General	**<u>Clinical trial research needs - Diagnostic tests, core outcome set</u>** This recommendation for research is restricted to clinical needs, but could easily have been extended to cover diagnostic tests to use when identifying the correct cohort of people with ME/CFS for research, with very little cost implication. The research on validity and reliability of tests is usually carried out in a research setting first, so it is illogical to ask one question without the other. There were several discussions in the evidence reviews on which outcomes were important, and although lists were drawn up none were recommended as provisional outcome measures in clinical or research settings. A core outcome set is essential for standardising outcomes in clinical trials of people with ME/CFS and we welcome the priority given to this recommendation for research. However, this is not the only methodological problem in clinical trials of people with ME/CFS, as the expert testimony of Jonathan Edwards	Thank you for your comment. The committee have made recommendations to address the difficulties and limitations in diagnosing ME/CFS (see Evidence review D for the committee discussion on this). The committee identified these as high priority for research. This committee hope this will enable future research to accurately identify people with ME/CFS and determine the impact of interventions on them. They thought this was particularly important before recommending any research trials on physical activity or exercise interventions. The committee recognised the lack of research in medicines but did not identify any one medicine to prioritise for research and as such did not make any research recommendations on this topic.

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	Supporting documentation 3 B D Guideline Guideline	Expert testimony 1 52 64 43 45	11-18 19-22 9-19 1-7	extensively showed (supporting documentation 3 expert testimony 1). There is also a need for more research into;- • a single best case definition • a simple diagnostic marker or set of diagnostic tests • objective outcome measures which are not harmful to patients (47) • specific methods of measuring and monitoring symptoms including post exertional symptom exacerbation (48) • a specific scale of function for use both clinically and in research (49) • validation of existing standard outcome measures in ME/CFS populations. The committee itself commented that there was little consensus on the value of different symptom scales for recovery but did not explore the validity of outcome measures in the ME/CFS population as part of the assessment of outcomes in clinical trials of people with ME/CFS, apart from accepting Professor Edward's expert testimony on subjective outcome measures being subject to bias. Evidence review D page 64 line 19 to 22 states that only validated outcome measurement scales were included in the evidence review, but there was no substantiation of this claim. An evidence review of outcome scales validated in ME/CFS populations would have been a useful exercise as a prelude to the review of quantitative evidence on treatments (evidence reviews F, G and H). We believe more work is needed on what constitutes minimum clinically important differences for different outcome scales as has occurred in other diseases (50), as we are aware of research showing lack of consensus on defining recovery in CFS (51) and of differences in responses across medical conditions for even well established measures such as	*Design of trials* The committee agree that the design and measurement in trials is important and have included that the trials should be RCTs and the long term follow up of trials as a minimum 2 and 5 years. The committee hope that the development of a core outcome set will address some of the difficulties in measuring outcomes in people with ME/CFS in trials. With the accurate identification of people with ME/CFS and a core outcome set it will then lead to the development of other areas of research, such as minimally important differences for the outcomes. All NICE research recommendations are reviewed by the NIHR to consider for their funding streams. Other research funders also consider NICE research recommendations. It is beyond the remit of the guideline to provide more detailed information on how research in these areas should be conducted. *Subgroups* To raise awareness of this gap in the evidence pregnant women and women in the post-natal period, black, Asian and ethnic minority populations have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations.

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				the SF-36 (52,53). In ME/CFS there has been initial research on Patient reported outcome measures (54,55) and the SF-36 in paediatric ME/CFS (56) but more is needed. There are also gaps in some outcomes such as function specifically for ME/CFS. The definitions of severity given on draft guideline pages 43, lines 9 to 19 and page 45 lines 1 to 7 are useful clinical guides of severity. For research, further subdivisions would be useful. Without this, a person may improve substantially, but as their activity level increases their experience of fatigue can stay largely unchanged. This may be captured in generic scales such as the SF-36, which has the advantage of universality, but a specific ME/CFS measure would also be useful and may be more sensitive to small but still clinically important changes. In addition, an optimum minimum length of trial may be important; researchers gave one possible explanation for the failure of the stage III rituximab trial despite previous positive stage II and open label trials as being due to the longer length of trial more effectively controlling for the fluctuating nature of ME/CFS between groups (45). Hence, any short trials are likely to give false positive results. However, the optimum length of trial is still unknown, but lengthier trials inevitably lead to increased costs. Unless NICE, through the guideline prioritises research into all aspects of clinical trial design, and also makes a broad recommendation for research into treatments (symptomatic or otherwise and both pharmaceutical and non-pharmaceutical) for ME/CFS, there will continue to be insufficient funding opportunities for clinical trial research in the United Kingdom. This will continue to lead to clinical trials with too small sample	

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				sizes, too short in duration and continuing biased or inconclusive results of potentially promising treatments. Our particular concern is that by not prioritising clinical trial research per se, there will be a lack of research centres in the United Kingdom with expertise in this difficult area. Clinical trial design has improved with the involvement of clinical trial centres, but we believe it is still too easy to design trials with obvious flaws leading to bias, including insufficient blinding of both participants and assessors or the use of only subjective outcome measures (57). The particular fatiguability of people with ME/CFS also introduces problems for clinical trial methodology and conduct which needs experienced researchers to tackle. In order for a clinical trial to be granted funding, a Principal Investigator with the necessary skill-set needs to head the application team and oversee the trial. For a trial in ME/CFS patients, such a person would ideally already have wide experience of involvement in, and preferably already been a Principal Investigator in large scale clinical trials of drugs, and also have experience of managing patients with ME/CFS. Such a combination is extremely unlikely in the United Kingdom. There are currently very few specialist medical clinics for people with ME/CFS where such a person would be likely to work, and where such a trial could be based. This situation needs to change as a matter of urgency, to cope with emerging research revelations about ME/CFS which could affect treatment. Only specialist centres can work out the methodologies for randomised controlled trials and evaluate alternative methods of capturing data for effectiveness in clinical practice.	

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				Finally, far too few clinical trials have involved people from ethnic minorities generally, and specifically in ME/CFS. It has been shown that some outcome measures do not translate perfectly across different ethnic groups. As an example, the structural validity of the Multidimensional Fatigue Symptom Inventory-short form was not supported in a community based sample of African Americans (58). We believe the guideline should have specifically recommended the inclusion of ethnic minority groups in ME/CFS research, the piloting of methods to reach such groups and incorporate them in research, with more understanding of the potential differences in treatment responses between different ethnic groups. There were already defects in the evidence presented to the committee, in that neither of the commissioned surveys for this evidence review included a question on ethnic minorities. This is a major failure by the groups involved – the NICE Guideline Development Group, the University of Manchester group undertaking the severe ME/CFS survey, and the Oxford Brooks University Clinical Trials service and Forward ME for their CBT and GET survey. Unless this gap in the research recommendations specifying the inclusion of ethnic minorities is closed, there could be avoidable limitations in the Decode ME study (59). Including sufficient ethnic minority samples in that analysis might show up interesting genetic variations which in themselves could be revealing. 47. Twisk FN. Accurate diagnosis of myalgic encephalomyelitis and chronic fatigue syndrome based upon objective test methods for characteristic symptoms. World J Methodol. 2015;5(2):68–87. 48. Jason LA, Holtzman CS, Sunnquist M, Cotler J. The development of an instrument to assess post-	

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				exertional malaise in patients with myalgic encephalomyelitis and chronic fatigue syndrome. J Health Psychol. 2018;October 24. 49. Rowe PC, Underhill RA, Friedman KJ, Gurwitt A, Medow MS, Schwartz MS, et al. Myalgic encephalomyelitis/chronic fatigue syndrome diagnosis and management in young people: A primer. Front Pediatr. 2017;5(June):121. 50. Myles PS, Myles DB, Galagher W, Chew C, MacDonald N, Dennis A. Minimal Clinically Important Difference for Three Quality of Recovery Scales. Anesthesiology. 2016;125(1):39–45. 51. Adamowicz JL, Caikauskaite I, Friedberg F. Defining recovery in chronic fatigue syndrome: a critical review. Qual Life Res. 2014 Nov;23(9):2407–16. 52. Frendl DM, Ware JE. Patient reported functional health and wellbeing outcomes with drug therapy: a systematic review of randomised trials using the SF-36 health survey. Med Care. 2014;52(5):439–45. 53. Wyrwich KW, Tierney WM, Babu AN, Wolinsky FD. A comparison of clinically important differences in health-related quality of life for patients with chronic lung disease , asthma, or heart disease. Health Serv Res. 2005;40(2):577–91. 54. Parslow R, Patel A, Beasant L, Haywood K, Johnson D, Crawley E. What matters to children with CFS / ME? A conceptual model as the first stage in developing a PROM. Arch Dis Child. 2015;100:1141–7. 55. Haywood KL, Staniszewska S, Chapman S. Quality and acceptability of patient-reported outcome measures used in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME): a systematic review.	

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				Qual life Res. 2012 Apr;21(1):35–52. 56. Brigden A, Parslow RM, Gaunt D, Collin SM, Jones A, Crawley E. Defining the minimally clinically important difference of the SF-36 physical function subscale for paediatric CFS / ME: triangulation using three different methods. Health Qual Life Outcomes. 2018;16:202. 57. Collatz A, Johnston SC, Staines DR, Marshall-Gradisnik SM. A Systematic Review of Drug Therapies for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis. Clin Ther. 2016 Jun;38(6):1263–1271.e9. 58. Asvat Y, Malcarne VL, Sadler GR, Jacobsen PB. Validity of the multidimensional fatigue symptom inventory-short form in an African-American community-based sample. Ethn Heal. 2014;19(6):631–44. 59. Decode ME. Get Involved - DecodeME [Internet]. web page. 2020 [cited 2020 Dec 11]. Available from: https://www.decodeme.org.uk/	
LDN Research Trust	Guideline G G Guideline Guideline Guideline Guideline	046 323 336 47 63-64 47 66-67	008 18-21 36-42 1 28 onwards 4	**Other research recommendations** The research recommendation on self-monitoring strategies could usefully have been extended to a question on self-monitoring techniques for research. Indeed, it needs addressing first as a research question examining what methods of self-monitoring are useful in clinical trial research, for assessing degree of activity and changes in activity levels in people with ME/CFS. Only after this has been established, can self-monitoring clinically be addressed. If the approach starts with clinical monitoring, those likely to research it may have little experience of the complexities of activity monitoring, reliability and reproducibility of equipment results etc. We agree that self-monitoring techniques should not increase the	Thank you for your comment. Management strategies Based on the evidence the committee recognised that people with ME/CFS often want information and support on how to manage their ME/CFS symptoms and decided to make research recommendations in the areas where there was an absence of evidence. Diagnosis The committee have made recommendations to address the difficulties and limitations in diagnosing ME/CFS (see Evidence review D for the committee discussion on this). The committee identified this as high priority for research. This committee hope this will enable future research to accurately identify people with

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	Guideline Supporting documentation 3 Guideline Guideline	65 Expert testimony 1 Page 6 43 45	24 onwards 8-14 General 9-19 1-10	burden on a person, but this is needed as part of good clinical trial design in people with ME/CFS in any case. Sleep management strategies Dietary strategies Managing pain These subjects cannot be addressed until there is clarity on diagnostic criteria for research, diagnostic tests, optimum clinical trial length, reproducible outcome measures which have been validated in ME/CFS populations, (preferably as a Core Outcome Set), and at least one objective outcome measure which is valid and which does not harm participants in the trial. Jonathan Edwards stated in his expert testimony stated;- "The central difficulty for trial design in ME/CFS is the high risk of systematic expectation bias in a fluctuating condition with subjective core features. Crucially, that means that trials must either be effectively blinded or outcome measures must be underpinned by objective evidence. (Supporting documentation 3 expert testimonies page 6 7th paragraph lines 1 - 4) The Hawthorn effect is also of relevance here – the very fact of monitoring a person changes the aspect of the behaviour being monitored. All the areas outlined for research are subjective experiences and therefore modifiable under influence, making trial design and monitoring more	ME/CFS and determine the impact of interventions on them. They thought this was particularly important before recommending any research trials on physical activity or exercise interventions. Design of trials The committee agree that the design and measurement in trials is important and have included that the trials should be RCTs and the long term follow up of trials as a minimum 2 and 5 years. The committee hope that the development of a core outcome set will address some of the difficulties in measuring outcomes in people with ME/CFS in trials. With the accurate identification of people with ME/CFS and a core outcome set it will then lead to the development of other areas of research, such as minimally important differences for the outcomes. All NICE research recommendations are reviewed by the NIHR to consider for their funding streams. Other research funders also consider NICE research recommendations. It is beyond the remit of the guideline to provide more detailed information on how research in these areas should be conducted.

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				problematic. The committee itself acknowledged the lack of existing objective outcome measures of effectiveness and the limitations of subjective measures so it is unclear why this particular aspect was not emphasised more as a research need. Without any of these additional measures, any trial will produce inconclusive, biased or disputed results, as has happened previously. Professor Edwards expert testimony concentrated on the problems of subjective outcome measures, but there was no quality assessment of outcome measures in the evidence reviews, and no detailed discussion apart from lists of what outcomes were important. There does not appear to be an adequate body of research validating outcome measures in the ME/CFS population and within clinical trials. This is important. There are also gaps in some outcomes such as function specifically for ME/CFS. The definitions of severity given in the draft guideline pages 43, lines 9 to 19 and page 45 lines 1 to 10 are useful clinical guides of severity. For research, further subdivisions would be useful. Without this, a person may improve substantially, but as their activity level increases their experience of fatigue can stay largely unchanged. This may be captured in generic scales such as the SF-36, which has the advantage of universality, but a specific ME/CFS measure would also be useful and may be more sensitive to small but still clinically important changes.	
LDN Research Trust	Guideline Evidence Review F F	060 060 091 091	002 - 004 002 - 004 012 - 013 041 - 042	**Efficacy of drugs** We note the statement that "the evidence for non-pharmacological and pharmacological interventions for ME/CFS is heterogeneous and inconclusive," (with which we agree) "and this supported the committee's experience". It appears that the committee have little experience of low dose	Thank you for your comment and information. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as

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	F F F F F Guideline Guideline Guideline	091 092 092 093 024 029 031	051 023 043 022 - 023 004 - 005 017 onwards 001 - 006	naltrexone and we hypothesise this is because their experience is based on recommendations from the previous NICE guideline and because their practice is based within the National Health Service. Due to the constraints imposed on National Health Service prescribers by NICE and local commissioning group guidelines, it is problematic for doctors not working privately to gain experience in prescribing off-license drugs, despite both General Medical Council and Medicines and Healthcare products Regulatory Authority advice saying this may be possible. Therefore, committee members are unlikely to prescribe, or have a wide experience of people taking low dose naltrexone, and this affected what was discussed and what the committee stated as their experience. As noted elsewhere, some recommendations in the guideline were made solely on the experience of committee members. Had committee members experienced the use of low dose naltrexone, as specialists in the United States have, they might have made a recommendation for research. This has produced a bias against drugs such as low dose naltrexone which is regrettable. The circular situation therefore occurs, that what is outside the current NICE guideline, for example, drugs for treating ME/CFS, are not recommended even when used in other countries. There can be no suggestions from physicians within National Health Service clinics of potential new or symptomatic treatments, so NICE will not recommend any in any new guideline. Unless NICE allows specific out-of-patent drug treatments in secondary centres with appropriate stringent monitoring, there will be no recommendations for their use even when people with ME/CFS find them beneficial. Thus, little likelihood of clinical trials of drugs for ME/CFS will occur.	practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee included members with clinical and personal experience of children and young people with ME/CFS. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The committee use their experience to develop the protocols for the reviews and consider the most appropriate design for the question. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. When considering the evidence for pharmacological interventions the committee agreed that there was insufficient

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	Evidence Review F Guideline Evidence Review F	088 031 094	007 - 008 006 030 - 033	We also welcome the statement that there is no current cure for ME/CFS but strongly argue there are current treatments which the methodology used in this review made unavailable to the committee. We believe the evidence used in the review was too specific, as it was based solely on quantitative evidence based on randomised clinical trials (which were rightly used as the only source of data for the quantitative syntheses leading to firm recommendations on therapy in the guideline), and qualitative evidence based on transcript data collected from focus groups or semi-structured interviews and surveys (but only extracting the qualitative data from surveys). It excluded several papers and surveys which contained only quantitative data but were not randomised controlled trials and the results of retrospective case analyses, such as Polo (3). It also excluded the quantitative data from surveys such as Forward ME and ME Action (42,43). The protocol for quantitative searches states that "non RCTs will not be considered as they will yield data that is at too high a risk of bias for decision making". We contend that surveys and quantitative data from large retrospective case analyses give less biased results than qualitative data extracted from individual interviews or a limited number of participants in focus groups. Although such data could not be used for decision making, it could have informed recommendations for research, if findings were consistent across several different methods of collecting data. By excluding any reference to drug therapy for sleep and for nausea, the impression is given that no drugs are worth prescribing for people with ME/CFS, which is untrue. Symptomatic treatment with drugs particularly on days when sleep has been very disrupted or nausea is worse can be helpful. The links in the draft guideline on page 31 line 9 to	evidence of benefit to recommend any medicines but recognised that people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis.

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				NICE guidelines on medicine adherence and medicines optimisation specifically mention the principles of evidence-based medicine when discussing the available treatment options with a person. However, as most drugs used in symptomatic treatment are out of patent, there is very little chance of efficacy trials being conducted. NICE (and this guideline) needs to encourage more innovative ways of collecting data on drug use and symptom control in people with ME/CFS to start to develop an evidence base on what drugs are beneficial and in what circumstances. Research in this area is badly needed and would be more likely to occur if the committee was consistent in saying when evidence bases are lacking and then suggesting research rather than trying to fill that gap with committee members' experiences. "Do not offer any medicines or supplements to treat or cure ME/CFS" This statement strongly discourages prescribers from symptomatic treatment of specific symptoms. By implication it also discourages research into drug therapy for ME/CFS and this is a retrograde step. Evidence review F page 94 lines 30 to 33 acknowledges that people with ME/CFS have found some drugs helpful in managing symptoms. Why did the Committee confine themselves to the expert witnesses they chose? They could, for example, have interviewed one of several United States physicians familiar with prescribing drugs for patients with ME/CFS, to understand how familiarity with these drugs in clinical practice changes the understanding of their place in the management of ME/CFS. We quote again the statement from the ME/CFS Clinician Coalition (a group of leading researchers and physicians treating people with ME/CFS in the United States of America), issued in March 2019. "The field of ME/CFS needs evidence-	

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				based treatments. The combined clinical experience of ME/CFS clinicians supports efficacy of several treatments that have potential and warrant testing. Appropriate funding mechanisms are warranted. In addition, funding should support a clinical trials consortium. The ME/CFS Clinician Coalition agrees that our first priority is a trial of LDN (low dose naltrexone)."(1) Once underlying mechanisms for ME/CFS are established there will be a need for clinical trials of potential drug treatments. Unless experience of clinical drug trials in people with ME/CFS occurs in the United Kingdom, there will be no centres with the expertise to carry out clinical trials when definitive treatments become possible. At that point, either the United Kingdom will carry out substandard trials (as appeared to happen in the execution of the PACE trial) or rely on data from other countries. 1. Linford A. What's next for the ME/CFS Clinicial Coalition? [Internet]. Bateman Horne Centre News. 2019 [cited 2020 Dec 5]. Available from: https://batemanhornecenter.org/whats-next-cfs-clinician-coalition/ 3. Polo O, Pesonen P, Tuominen E. Low-dose naltrexone in the treatment of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Fatigue Biomed Heal Behav. 2019;7(4):207–17. 42. Oxford Clinical Allied Technology and Trials Services Unit Oxford Brooks University. Forward-ME Group CBT & GET survey. Oxford; 2019. 43. Leary S, Sylvester J, Shorter E, Moreno E, Knowles R, Spreag D. Your Experience of ME Services. Survey Report by #MEAction UK. 2019.	

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Leeds and York Partnership Foundation Trust	Appendix 3	020	1	Expert Testimonies - Mujtaba Husain It is unclear why this expert testimony has been included as it is not representative of CFS/ME services across the UK. The subject of this testimonial is intended to be the different models of multidisciplinary care and yet only one model is presented. This testimony describes a service run in a Liaison Psychiatry setting where patients are seen as part of a persistent physical symptom pathway. Our service is operated by a Liaison Psychiatry service and we have a Consultant Liaison Psychiatrist as part of our multidisciplinary team and Mental Health Nurse. The Multidisciplinary Approach is therefore able to benefit from a wide perspective of Holistic health and draw upon a range of other specialties. We also refer to CBT. However, the specialist CFS/ME service is run independently of the Medically Unexplained Symptoms Pathway – and the approach they take is different to the CFS/ME and they work with persistent medical symptoms. There are several differences between our CFS/ME service and our this other trust's service: • Referral processing- we require a specific minimum set of blood tests to be included with every referral and we contact GPs if there are concerns regarding abnormal or missing results. We regularly contact GPs to advise on further investigations that may be warranted from the information provided in the referral e.g. advising referral for sleep studies, screening or orthostatic intolerance, addressing mental health issues, chronic pain management, medication concerns etc. • Diagnostic assessment- Our initial contact with a patient is a detailed diagnostic assessment and we	Thank you for your comment and information on your service. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Stakeholders during the scoping process and the committee in early meetings identified areas of the scope where there was a lack of evidence. Where this is the case additional evidence can be sought to support the committee in their decision making. There are several approaches that can be taken to provide the committee with additional evidence and these include calls for

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				regularly discharge patients after initial assessment as a result of identifying that their symptoms do not fit with a diagnosis of CFS/ME or because other causes of their fatigue have been identified or because we feel further investigations are warranted which is beyond the scope of our service to organise. • Treatment for many conditions with persistent symptoms requires learning self management strategies. In our unique service this can be alongside dietary and medical interventions for symptom management combining both a rehabilitative approach and holistic understanding of mental and physical health. • Therapists are expert at harnessing the motivation to make changes to maximise function and individualise around the persons needs because they have both a rehabilitative and consider psychological factors can impact upon managing fatigue and other symptoms. • Our therapy programme starts with a detailed explanation of the neurobiological aspects of ME/CFS which is an essential part of the process of engaging a patient in the subsequent therapy programme. It encourages and motivates patients to make changes to their routines, behaviour and all inputs to the body systems in the hope of effecting neuroendocrine, biological changes in how the body regulates and achieves homeostasis. The aim is to harness the body's recovery processes and target particular mechanisms that drive systems. It is an active process to build resilience, self efficacy and self	evidence, expert testimonies, and in exceptional situations commissioned reports. See Developing NICE guidelines: the manual for further information on the process for including additional evidence (section 3.5 for expert witnesses). This guideline included 3 expert testimonies. Dr Husain was invited to discuss his experience of the different models of multidisciplinary care, including team composition, for people with ME/CFS. The summary of his presentation and the following committee discussion is in Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee members have their own clinical and personal experience of specialist services and the summary of their discussion acknowledges and details the different structures and MDT approaches across the NHS. A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.

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				awareness to address those most troublesome factors of concern to the patient. • We start with a formulation and shared understanding of the areas of most concern and agree the focus for treatment. In any rehabilitation programme a person needs to believe they can make improvements in function, coping, understanding and although the extent of recovery is never guaranteed, it must always be hoped. • The Service Therapy Team works from a formulation driven approach to helping patients appreciate the different contributions to symptoms. This includes explaining the Mind-Body Link and help patients manage those components of anxiety and mood issues that are commonly seen as part of the overall presentation in people seen in the CFS/ME Service. It is really important that psychological and emotional work is undertaken for those who need it and our base within Liaison Psychiatry allows us to liaise with other specialists when required and provide helpful assessment and diagnosis of complex presentations • All therapists take a holistic view of wellbeing and it is important to acknowledge Mental Health distress and issues as these issues may prevent effective management of symptoms. Our therapy programme is designed to address the specific needs of people with ME/CFS which includes energy and rest management, dietary issues, employment related issues, emotional issues, regulation of routines and lifestyle factors which impact on wellbeing and how the body regulates.	

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				We are aware that the majority of NHS specialist CFS/ME services are not operated through mental health trusts and this expert testimony does not correlate with our service model which is run by a mental health trust. We therefore feel that this testimony has no relevance to the wider delivery of specialist CFS/ME care in the NHS and we would ask the committee to consider how inclusion of this testimonial may have influenced other aspects of the guideline that has been produced.	
Leeds and York Partnership Foundation Trust	Guideline	General	General	Our service is concerned about the overall negative tone of the guideline which portrays a very pessimistic outlook regarding prognosis and availability of effective management strategies with a view to improving symptoms and level of function. This is in contradiction to our clinical experience where our team are able to provide information and education to patients along with engaging them in a therapy programme that commonly results in patients reporting improvement in their understanding of the condition along with many reporting improved emotional and physical wellbeing, and some, seeing significant improvement in levels of function. Some patients report recovery and most define this as achieving sustainable levels of activity maintained by helpful strategies and greater awareness of triggers and managing setbacks. Our 2016-2017 service outcome data demonstrated that over 59% of patients reported some degree of improvement (based on 327 returned questionnaires). In 2017-2018 our Clinician Rated Overall Outcome measures (CROM) demonstrated 71.7% had some improvement at the end of the service contact with 46.1% reporting moderate to major improvement (based on 259 discharges)	Thank you for your comment and information. *Tone of the guideline* When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.) In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of

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				Question 3 examples of good practice: This is a selection of feedback comments from our patients regarding what they found most useful about the service: ➢ Felt listened to by someone who understands. ➢ Therapists are informative and knowledgeable. ➢ Staff understand and are encouraging. ➢ Staff are sensitive and respectful. ➢ Tailored treatment plan to meet specific needs. ➢ Learning how to rest properly. ➢ Helped with pacing greatly. ➢ Support in returning to work. ➢ Useful information/resources provided, including phone apps. ➢ Great information booklets for advice. ➢ "Generally I have learnt to pace myself, and give myself permission to rest. ➢ I was very privileged to have the attention of a specialist clinic, I really don't know what my life would be like now if you hadn't taught me how to cope" ➢ Personalised one to one sessions. ➢ Valuable group sessions. ➢ Being able to meet others who have this condition. ➢ Attending the service has had a positive impact on my life and condition. ➢ Improved my confidence to deal with my symptoms more effectively. We give all patients the opportunity to provide a narrative reflection of their journey with the condition and request their comments upon the approaches offered and the outcomes they experienced. We have many such testimonials and use these in patient and supporter events, to encourage and inspire others that progress is possible.	people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. However the committee agree there currently isn't a cure for ME/CFS and it is important that people with ME/CFS are aware of this.

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				I may not be fully recovered, but I feel that I have improved significantly with the help of the friendly and supportive staff at Leeds. My symptoms have subsided and I am feeling positive about the future …….“The treatment has taught me about pacing and allowed me to gradually increase my activity and eventually get back to work (I was off sick for 9 months). The things I learned during my sessions have allowed me to come to terms with my ME symptoms, realising my limitations and controlling my symptoms. The treatment from the service has enabled me to be in control of my symptoms and not them being in control of me. Without the CFS/ME Service I am not sure I'd still be working.” “Before I came to the service I felt very isolated and didn't know how to cope with my condition during bad episodes. The CFS Service has been so helpful in providing me with structure, coping mechanisms and scientific reasoning behind this illness. The individual treatment plan has focussed on my needs but has also shown me I am not alone in fighting CFS. I now have a greater understanding of my illness and always try to find the positives in what I am able to do” “….after a number of inactive years I sought to fight things and have been fighting to lead a normal life ever since. The clinic has taken my condition seriously, helped me to reassess things as well as helping with medication (at least dealing with the extreme pain I experienced) pushing for tests for Vitamin D, helping explain what my body is going and my eating habits have all helped.	

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				The reassessment of my life has meant that I can see that I do not become my condition but manage it. I want to work for as long as possible and with pacing myself this is very possible. I am learning to be kinder to myself and therefore achieving more" I have lived with what I consider a relatively mild form of CFS/ME for about nine years. Attending group sessions at LYPMHT helped me to learn about the condition and think about strategies to manage my energy levels. Prior to CFS, I was a very energetic person, at work, in sport and in voluntary work. Since CFS, I have found that managing my expectations concerning what I can achieve with the energy I have and coming to terms with that, is really important. This helps me to set reasonable goals for what I could achieve, although I sometimes fail. However, failing from time to time does not make me a failure. CFS/ME affects people in different ways, so offering a variety of solutions/therapies is helpful and should continue.	
Leeds and York Partnership Foundation Trust	Guideline	General	General	There is over emphasis on the 'lack of cure or effective treatment'. This will have wide reaching negative effects including: • a very negative emotional impact on a person newly diagnosed with ME/CFS • creating barriers to someone engaging in a therapy process – in order to expect someone to make behavioural changes there has to be an expectation of positive outcome – provision of hope is an essential component of any healthcare interaction • creating a sense of pessimism in healthcare professionals who encounter people with ME/CFS which will perpetuate the unhelpful attitudes –	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. However the committee agree there currently isn't a cure for ME/CFS and it is important that people with ME/CFS are aware of this. *Tone of the guideline*

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				empathy comes from feeling you have something to offer a person who is experiencing distress. - discouraging GPs from considering referral to specialist services - disincentivising commissioners to fund the provision of specialist services at a time when more investment is desperately needed - discouraging therapists and medics from wanting to work in this field - demoralising staff currently working in ME/CFS services who feel that the highly skilled and effective care that they deliver has been massively undervalued The tone of the NICE Tinnitus guideline could be used as a model for how to approach the ME/CFS guideline with use of the phrase '*there are a variety of management strategies that help many people live well with tinnitus'*	When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.) In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS.
Leeds and York Partnership Foundation Trust	Guideline	004	5	*it's pathophysiology is unclear'* – this initial statement does not acknowledge how much is known about the physiological abnormalities that occur in ME/CFS and has the potential to contribute to the harm caused to patients. - The statement that 'the pathophysiology is unclear' is in direct contradiction to the huge amount of published research which has identified evidence of changes in multiple different systems in the body. It is recognised that the symptoms of ME/CFS come	Thank you for your comment and information. The committee agree there is published research in this area and also that there is much controversy, which is reflected in the stakeholder comments. This bullet point has been edited to,' and its pathophysiology remains under investigation' to clarify that there is not enough evidence to make any conclusions about the pathophysiology of ME/CFS and this is an active area of research.

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				about as a result of dysregulation in dynamic systems such as the immune system, the autonomic system, metabolic processes and neuroendocrine systems. It is recognised that the process of dysregulation means there is not a single identifiable common factor between all people who have the symptoms of ME/CFS, however that is not the same as stating that we do not know or understand a lot of the physiological abnormalities that occur. • In the Supporting Documentation – Children and Young people Appendix 1 page 8 line 5 states: 'Myalgic encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS) are serious and chronic, debilitating conditions characterised by immune, neurological and cognitive impairment, sleep abnormalities, and autonomic dysfunction, resulting in significant functional impairment accompanied by a pathological level of fatigue.' Why has this description not been used in the guideline? • Our service provides information and education to patients based on the research studies that have demonstrated altered physiological responses in the body. Not having this knowledge and expertise acknowledged on the guideline undermines our work and also fails to provide education to other healthcare professionals and the wider community. Question 3 re existing resources and examples of good practice: Our GPwSI has co-authored a document detailing the extensive evidence base behind the understanding of complex and inter-relational dysregulated physiological systems that is the model that our service uses to understand the illness.	*Appendix 1_Children and Young People.* This text is the background to the report written by the Oxford Clinical Allied Technology and Trial services Unit commissioned to undertake this project. Question 3 We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme

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Leeds and York Partnership Foundation Trust	Guideline	004	10	In addition to the statement acknowledging that it can affect each person differently, it would be helpful for the guideline to acknowledge the heterogenicity of the condition and the potential for there to be multiple different subsets under the umbrella term of ME/CFS. This is important to acknowledge as it is possible that different therapy approaches will be needed for different people. It could also mean different therapy approaches are more or less effective for different subgroups of patients. Outcomes could also be influenced by the different patterns and severity of symptoms experienced. It is also important for the commissioning of services as there can be complex decisions to make regarding which secondary care services should provide therapy programmes and have ongoing responsibility for people with co-existing conditions such as chronic pain, fibromyalgia, dysautonomia and mood disorders.	Thank you for your comment. The variation in the impact of ME/CFS and the importance of personalised care is highlighted throughout the guideline and for this reason this hasn't been added to the recommendation.
Leeds and York Partnership Foundation Trust	Guideline	006	7	The Leeds and West Yorkshire CFS/ME service sees patients with severe ME/CFS and has some capacity to provide home visits for this group of patients. We therefore welcome the recognition of the impact of severe ME/CFS, however we feel that placing it in the guideline before the diagnostic section could lead to confusion as the symptoms listed also occur in people with mild and moderate ME/CFS. Therapy for this group of patients can be complex and requires a very individualised approach different to that provided for people with mild-moderate ME/CFS so we would recommend creating a separate section later on in the guideline to provide guidance on care provision for this group.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and as you comment is reflected in the Access to care section of the guideline. To note after considering the stakeholder comments the committee agreed to bring the recommendations on people with severe and very severe ME/CFS together in one section after the main set of recommendations to ensure their particular needs were not hidden within the guideline. We hope this will provide clarity.

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				Question 1 re challenging to implement and Question 2 re cost: The recommendations regarding more extensive provision for Home Treatment for the Severely Affected patient has potentially a great impact on practice with cost implications and enormous challenges. Making the case for exceptional funding from funders needs to focus upon the intended likely outcomes for the patient and deliver both treatment and cost effectiveness. Those specialist services who offer input do so using a range of remote modalities and in collaboration with Primary Care and community provision. These new ways of working should be considered as part of the provision for supporting patients and their families. It is important to offer a goal focused, time limited rehabilitation model of input with expectation of improvement in order to engage all stakeholders in this approach. Remote delivery offers challenges, and it is unclear whether the guideline is suggesting greater involvement by Specialist Services to advocate for the provision. In our experience in Leeds an inpatient rehabilitation approach has been important for some patients for medical management, diagnosis and to stabilise the patient before building up function. ***These interventions are costly at a time when all commissioners are managing very tight budgets- take out***. Prevention of severe disability through effective timely rehabilitation is always preferable and therefore offering tiered provision and stages of therapy is required, ***The current long Covid investment makes this point – take out***. Question 3 existing resources: Our ***previous consultant liaison psychiatrist w***as involved in developing the BACME Severe CFS/ME shared clinical practice document available from the BACME website: Severe CFS/ME: BACME shared clinical practice	The following section on suspecting ME/CFS includes the symptoms that all people with ME/CFS experience and those symptoms that are commonly associated with ME/CFS and now precedes this section. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as home visits, to implement some recommendations in the guideline. guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned. The committee do anticipate that much of the support given to people will be provided remotely but they have emphasised the importance of a face-to-face initial assessment. We will pass this BACME document to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme

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Leeds and York Partnership Foundation Trust	Guideline	006	22	The gastrointestinal and dietary issues that can arise in people with severe ME/CFS can be very serious and at times life threatening. It can be difficult to access appropriate help for this aspect of the condition so it would be helpful if there could be more emphasis on the seriousness of these symptoms and acknowledgement that in some cases it can lead to someone not being able to maintain adequate oral nutritional and may need specialist nutritional support including hospital admission and/or enteral feeding. Question 3 example of good practice: Our service has a dietician as part of the team so we are aware of the importance of nutritional risk assessments for people with all severities of ME/CFS. We would recommend NICE promotes the role of specialist dietitians as part of a specialist ME/CFS team and push for increased funding to facilitate this.	Thank you for your comment and information. The dietary management and strategies sections of the guideline (including that for people with severe and very severe ME/CFS) has further recommendations and indicates when people should be referred to a dietician with a special interest in ME/CFS.
Leeds and York Partnership Foundation Trust	Guideline	008	1	We found the whole of the diagnostic section confusing to follow and do not understand or agree with the rationale for changing the timescale for diagnosis or for providing multiple different timescales through the diagnostic section. The initial section regarding the early identification, investigation and management of fatigue takes place in primary care so it may be helpful to identify this as a separate section. We would advise not using the diagnostic label of ME/CFS at such an early stage before appropriate investigations have been performed as other causes for the fatigue symptoms could come to light.	Thank you for your comment. *Suspecting ME/CFS* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion sections of evidence review D. The committee note in the rationale for suspecting ME/CFS that it is also the combination and interaction of the symptoms that is critical in distinguishing ME/CFS from other conditions and illness. The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. They noted

					that the advice recommended at this stage would not be detrimental to people who are then not diagnosed with ME/CFS. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted. As you note this combination of symptoms cannot be considered normal and should be investigated but the committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. • Further investigation/differential diagnoses. The committee have similar experience of people being referred and having another diagnosis and throughout the section on suspecting ME/CFS the committee have recommended that investigations should be done to exclude other diagnoses and this should continue where ME/CFS is suspected. If in any doubt specialist advice should be sought. The committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'. *Reduction in timeline* After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. Based on the evidence and their clinical experience the committee found no reason why the time to diagnosis should be different in adults compared to children and young people noting that 5 of the 7

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					diagnostic criteria reviewed in Evidence review D do not have separate time referrals. As you note people with ME/CFS do experience delays in diagnosis and the committee recognised that referral to a specialist team for confirmation of diagnosis can take months, taking this into account it is important that this process is started at 3 months and people are given appropriate advice until they are seen by a ME/CFS specialist team.
Leeds and York Partnership Foundation Trust	Guideline	008	11	This guideline is recommending that ME/CFS should be considered as a diagnosis when symptoms have been present for 6 weeks in adults and 4 weeks in children. The committee have acknowledged that this decision is not based on any published evidence. We are concerned there could be a number of negative consequences from making this recommendation: • Confusion regarding when to diagnose and refer- could result in an increase in referrals to specialist services for people who do not have ME/CFS • Missing alternative diagnoses: There are many conditions that present initially with fatigue and other symptoms that are seen in ME/CFS and it may only become apparent over the course of many weeks or months when more identifying symptoms occur or investigative abnormalities show up. Although our service has 2 doctors on the team we do not have access to investigations and there is therefore a risk that patients could be referred to our service early in the development of their illness and experience significant delays in being diagnosed with a condition that requires specific treatment such as coeliac disease, autoimmune conditions, diabetic autoneuropathy, endocrine disorders, nutritional deficiencies etc.	Thank you for your comment. The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. The committee discussion in Evidence review D and E set out the rationale for the committee's decision making on when to suspect ME/CFS and what advice to give people. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. In reference to your comment they agree there is a lack of evidence on the advice to give people with suspected ME/CFS, but they agreed the advice they have recommended in section 1.3 would not be harmful in the short term. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and it would not cause harm to anyone. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted for the following reasons:

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				- Overdiagnosis. There are many acute illnesses that cause fatigue that take longer than 4-6 weeks to improve, but full recovery will still occur. Post-viral fatigue commonly takes more than 4-6weeks to resolve. It is routine for people to need 2-3months off work following major surgery. We would welcome better guidance to GPs on fatigue management advice that can be given to people experiencing significant fatigue symptoms. We do not feel it is appropriate to label someone as having ME/CFS at a stage when many people will recover with time. - Fails to acknowledge that an emotional event can be a trigger for the onset of the condition e.g. a bereavement. We believe its unhelpful It is unhelpful and inappropriate to imply someone should have recovered from the impact of a significant bereavement in a matter of weeks. Negative psychological impact of being given a serious diagnosis only a few weeks into an illness. Given that this guideline describes ME/CFS as a lifelong condition for which there is no cure or effective treatments this diagnosis could have a potentially devastating effect on someone at a time when there is still potential for them to recover spontaneously. - Failure to recognise treatable causes of fatigue: In our clinical experience a diagnosis of ME/CFS can signal the point that doctors stop looking for treatable causes of fatigue. Making a diagnosis of a condition which is thought to have no treatments can mean both patients and Doctors stop looking for positive changes that may improve fatigue symptoms such as management of nutritional deficiencies, management	○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis - Further investigation/differential diagnoses. The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have added examples of investigations to be done when suspecting ME/CFS and have added that ME/CFS should be suspected if the 'symptoms are not explained by another condition.' The committee discussed the inclusion of triggering events but decided not to include reference to this as it is not clear what causes ME/CFS and the inclusion of any examples of triggers may be taken as an absolute list.

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				of emotional stressors, reducing work or care demands etc. We feel that accuracy of diagnosis should not be compromised in the desire for patients to be diagnosed earlier.	
Leeds and York Partnership Foundation Trust	Guideline	008	16	The statement 'symptoms are new and had a specific onset' doesn't include patients who develop symptoms gradually over months or years.	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the symptoms have developed and have not always been present covering that the symptoms are not lifelong. This now includes the cohort of people who develop symptoms gradually sometimes over months or even years.
Leeds and York Partnership Foundation Trust	Guideline	008	17	We are concerned at the removal of the key symptom of Post-Exertional Malaise (PEM) from the diagnostic criteria. Our service has been using diagnostic criteria that includes Post-Exertional Malaise for many years and we have been providing education to other healthcare professionals regarding the importance of taking fatigue histories from patients in order to be able to identify PEM as a key symptom that could indicate they have ME/CFS. We are unclear as to the rationale behind this change and how this would serve any advantage clinically to healthcare professionals or patients. We feel that the term PEM indicates that the tiredness and fatigue that people with ME/CFS experience is different to the 'normal' tiredness that healthy people experience. By removing this symptom term and replacing it with clumsy sentences that are hard to remember has the potential to have a negative and devalidating impact on patients. It will also be a much harder	Thank you for your comment. After taking into consideration the range of comments made by stakeholders about the potential for misunderstanding the committee agreed to change *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.

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				concept to explain in educational presentations meaning the important message risks getting lost. We are also at a loss to understand why PEM has not been included in the diagnostic section given that the committee considered it a compulsory symptom in diagnostic criteria for research inclusion for this guideline, as detailed in the guideline evidence review sections.	
Leeds and York Partnership Foundation Trust	Guideline	008	17	The listing of sleep symptoms is confusing and demonstrates a lack of understanding of how to take an accurate sleep history. Primary sleep disorders are a common missed diagnosis in people referred to our service and it is therefore a specific aspect of our diagnostic assessment to take a detailed sleep history. It is recognised that changes in sleep occur in people with ME/CFS and it can be difficult to identify when sleep symptoms are due to ME/CFS or could indicate a primary sleep condition so it would be helpful if the diagnostic section on sleep symptoms was clearer. Unrefreshing sleep is a symptom in its own right and can occur in someone who has a normal amount of sleep without any additional sleep symptoms. In this guideline it has been confused with numerous other sleep symptoms which should be listed separately and not necessarily considered key symptoms.	Thank you for your comment. *Unrefreshing sleep* After considering the stakeholder comments on the description of sleep symptoms the committee edited the bullet points to, 'unrefreshing sleep and /or sleep disturbance, which may include: • feeling exhausted, feeling flu-like and stiff on waking • broken or shallow sleep, altered sleep pattern or hypersomnia. The committee hope this has added some clarity for readers.
Leeds and York Partnership Foundation Trust	Guideline	009	4	The committee have based the diagnostic criteria on the Institute of Medicines Criteria which lists Orthostatic Intolerance as one of the key symptoms. It is not clear why the committee have felt it appropriate to downgrade this symptom. The rationale provided on page 64 line 21 is that the symptoms of orthostatic intolerance can be hard to differentiate from other ME/CFS symptoms.	Thank you for your comment. The decision not to include orthostatic intolerance as a key criteria was not based on the rationale is that the symptoms of orthostatic intolerance can be hard to differentiate from other ME/CFS symptoms and this has been edited to make this clearer. The decision was based on the evidence of the criteria reviewed in evidence review D . They note that orthostatic intolerance is only described in 4 of the 9 criteria compared to

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				Our team have been aware of the evolving research into the role of dysautonomia in ME/CFS and therefore we regularly screen for symptoms of dysautonomia including orthostatic intolerance. We have not found any difficulty doing this and we are therefore not sure why the committee have made this statement. It is only through clinicians exploring this aspect of symptoms that they develop skills in identifying the different patterns and this adds to their understanding of the underlying physiological mechanisms. By giving doctors and therapists guidance that implies they should cease looking for this symptom because it is deemed 'too hard' massively underestimates the skills that ME/CFS clinicians already have and it will also hinder progress in the field as it will discourage others from developing these history taking skills We also find it an extremely useful part of our therapy program as we can provide understandable explanations for the physiology that underlies the symptoms of orthostatic intolerance, we can acknowledge the ongoing and evolving research in this field and we can validate patient's experiences which can have a beneficial and therapeutic effect. Unfortunately the set-up of our service means we are not able to perform physical examinations or request investigations which often leaves us frustrated that this aspect of care for people with ME/CFS could be developed further if more clinicians were aware of it.	cognitive difficulties that is described in 7 out of the 9 criteria reviewed. The four symptoms (debilitating fatigue, PEM, unrefreshing sleep and sleep disturbance (or both), and cognitive difficulties) were agreed by the committee as the best basis for identifying people with ME/CFS and as essential to a diagnosis of ME/CFS. The committee emphasised it is the combination and interaction of the symptoms that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail).
Leeds and York Partnership Foundation Trust	Guideline	009	21	This guideline has not provided any guidance on investigations and the current statements could potentially be interpreted as saying no investigations are required. Despite having medical input, our service does not have access to investigations and we therefore require that all appropriate investigations are completed in primary or secondary care prior to referral to our service.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations

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				We have a standard minimum requirement for blood tests which was based on the list provided on the previous NICE guideline and it will be harder for us to specify to GPs which tests must have been completed without this being included in the guideline.	is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
Leeds and York Partnership Foundation Trust	Guideline	009	21	This guideline has chosen to use an adapted version of the Institute of Medicines diagnostic criteria but we are concerned that the committee has not addressed one of the major concerns regarding this criteria in that it does not have any exclusion criteria. We are concerned this will lead to lower accuracy of diagnosis including the potential to miss conditions which require further investigation or treatment such as • Primary sleep disorders including obstructive sleep apnoea • Untreated infections including Lyme disease • Autoimmune and inflammatory joint conditions • Symptomatic hypermobility • Substance abuse and high dose opiate use Primary mood disorders	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses and to tailor management appropriately. Taking into consideration the stakeholder comments the committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. In addition the committee have added that ME/CFS should be suspected if the, 'symptoms are not explained by another condition.'
Leeds and York Partnership Foundation Trust	Guideline	009	21	The diagnostic criteria used for this guideline does not provide any acknowledgement or guidance regarding overlapping conditions which can present with a similar pattern of symptoms to ME/CFS but the underlying mechanisms are potentially different and therefore different treatment strategies may be required and prognosis may also be different. Clarification is required regarding whether these conditions should constitute an exclusion to a diagnosis of ME/CFS and whether care should be provided in a specialist ME/CFS service.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses and to tailor management appropriately. Taking into consideration the stakeholder comments the committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. In addition the committee have added that ME/CFS should be

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				Question 1 re challenging to implement: This could have significant implications regarding the volume and complexity of patients being referred to ME/CFS services and the skills and resources required by services. Examples of common presentations in our fatigue service that we would welcome clarification on regarding use of a diagnostic label of ME/CFS and which services should be responsible for providing specialist care: • A patient with an established diagnosis of Ehlers Danlos Syndrome or Hypermobility Spectrum Disorder who has symptomatic joint hypermobility including recurrent joint subluxations as well as symptoms that would meet this guidelines criterion for diagnosis of ME/CFS • A patient with Psoriatic arthritis who is on a Biological agent for treatment of their rheumatological condition who has symptoms that would meet this guidelines criterion for diagnosis of ME/CFS with the onset of their fatigue coinciding with the onset of their Psoriatic arthritis symptoms • A patient with a diagnosis of Autism who experiences sensory sensitivity and has restrictive eating patterns who gradually develops fatigue symptoms that would meet this guidelines criteria for diagnosis of ME/CFS • A patient with PTSD with ongoing significant anxiety symptoms, disturbed sleep and flashbacks who presents with significant fatigue symptoms that would meet this guidelines criterion for diagnosis of ME/CFS • A patient with an established diagnosis of Fibromyalgia who has ongoing significant pain issues and is on long-term opiate medication who has been	suspected if the, 'symptoms are not explained by another condition.' Therefore, the examples that you give would not fall within the scope of this guideline. With that clarification, we think the guideline should be less challenging to implement.

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				discharged from rheumatology and the pain management service. • A patient with post-exertional fatigue (but not malaise), unrefreshing sleep and cognitive symptoms who has a pulse rate rise on a stand test consistent with a diagnosis of POTS. Question 1 re challenging to implement: As our service has doctors as part of the team we regularly provide complex patients such as those listed above with diagnostic formulations which would acknowledge their primary condition as being a relevant factor in the development of their fatigue symptoms. The diagnostic criteria we use currently would indicate that if an alternative cause for fatigue is identified then a label of ME/CFS would not be given. The new criteria created for this guideline would mean that we would be diagnosing many more people with ME/CFS than we do currently. Often these patients have much more complex needs and it is not suitable for them to access our group therapy programme which means there are potentially significant resource implications if specialist ME/CFS services are expected to take responsibility for this broad spectrum of fatigue presentations. We are often aware that our service cannot provide wider aspects of care with important issues relevant to fatigue management such as dealing with recurrent joint subluxations in someone with hypermobility, providing treatment for PTSD, prescribing medications for dysautonomia, managing medications in people with chronic pain on long-term opiates. We would welcome clarification from the committee or at the very least some acknowledgement of the complexity of presentations seen within specialist CFS/ME services.	

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Leeds and York Partnership Foundation Trust	Guideline	010	1	It is unclear from this statement whether the diagnosis of ME/CFS is expected to be made in primary care or in a secondary care specialist service. We have audited the diagnostic rate for patients assessed by the GP with a Specialist Interest in our service and 40% of patients referred, who were felt to need a medical assessment, were found to have alternative causes for their fatigue and were not given a diagnosis of ME/CFS. Despite not having access to investigations we consider our service to provide specialist diagnostic assessments in a way that could not be performed in primary care. We typically have 1.5hour long consultations and spend significant time before and after the assessment gathering additional information regarding their other health problems and the investigations they have had done and specialist opinions. We also have access to weekly MDT meetings where all the complex presentations are discussed. Many patients have co-morbidities which also need to be taken into account when formulating an understanding of the causes of their symptoms and looking at appropriate ways to approach managing them. Our service covers a wide geographic area and therefore we commonly encounter CCG's who make different funding decisions for their patients. We have also had experience of a CCG advising GPs that they must refer patients to a local IAPT service first before considering referring a patient to a specialist CFS/ME service. Question 2 re cost to primary care and commissioning decisions: We feel that all patients with ME/CFS should have access to a specialist diagnostic assessment and feel that the guideline should make it clearer that this is provided by specialist CFS/ME services with an expectation on commissioners to provide this service for their patients.	Thank you for your comment. The qualitative evidence and the committee experience reflect your comments about the lack of confidence in GPs in diagnosing ME/CFS, the high rates of different diagnoses and the complex assessments carried out by ME/CFS specialist centres. The committee agreed it was not clear in the recommendations about when a diagnosis is made and after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • Provisional' diagnosis has been deleted. The committee agreed the term 'provisional diagnosis' was confusing while waiting for a diagnosis for both the clinician 'provisionally diagnosing' and the person with the symptoms. • It has been clarified that if symptoms continue for 3 months then a person should be referred to a ME/CFS specialist team for confirmation of the diagnosis (this is adults is most likely from primary care and in children and young people they referral is from a paediatrician). It is at this point a detailed assessment is then recommended. *Implementation costs* The committee agree there are areas that may need support and investment, such as training costs and access to ME/CFS specialist assessment, to implement some recommendations in the guideline. Your comments will also be considered by NICE where relevant support activity is being planned.

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Leeds and York Partnership Foundation Trust	Guideline	010	17	This section should be more clearly labelled as advice that can be given in primary care while investigations are being conducted or while waiting for a specialist diagnostic assessment. It is not helpful to include the word 'perceive' in the statement about energy as it implies the fatigue is not real. The 'energy envelope' term is not something our service uses, and it is not a concept that we have ever included in our educational material or training for GP's although some patients find it helpful.. People who have significant fatigue issues will have a feeling of fatigue to some degree all the time so there is not an 'envelope' in which they don't have symptoms. The concept that would be much more useful to educate GP's about would be the one of pacing. The 2 key principles being: the recognition that all types of activity constitute a demand on energy reserves so physical activity, cognitive activity, emotional activity and social activity all need to be considered when giving advice regarding how much activity someone should be trying to maintain. The fact that rest needs to be taken pre-emptively before the point of complete exhaustion Many people in the early stages of experiencing fatigue have not recognised the delayed exacerbation pattern and do not realise that their worse days are a consequence of doing too much on their better days. It would therefore be helpful to introduce the concept of delayed exacerbation of fatigue commonly referred to as the 'boom and bust' pattern.	Thank you for your comment. The previous section 'suspecting ME/CFS' is clear that investigations should continue to exclude or identify any other conditions and in this section on advice the committee advise that people are told that a diagnosis of ME/CFS can only be confirmed after 3 months. The committee disagree that the word 'perceive' implies that the fatigue is not real, perceive is clarified in the next part of the recommendation advising people to stay within this limit acknowledging the fatigue is real and individual to the person. *Energy envelope* After considering the stakeholder comments the committee agreed that this concept of an energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits. The principles around energy management are set out in section 1.11 Managing ME/CFS.

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Leeds and York Partnership Foundation Trust	Guideline	010	20	The statement 'rest as they need to' is far too vague to be of use for GPs to understand how to support someone experiencing fatigue. Many people are used to ignoring tiredness so when they develop fatigue, they commonly continue to push through in a way that can aggravate their fatigue symptoms. It is therefore important that GP's feel confident to give people 'permission' to rest which may also include taking time off school, work or carer duties. However, as fatigue is generally present all the time, giving advice to rest when fatigued would be effectively advising someone to become completely inactive which would have secondary negative consequences on physical and emotional wellbeing. It would therefore be more useful to use the model of pacing where activities are broken down into short sections and rest is taken as a planned, structured 'activity'. It would also be helpful to qualify what effective rest looks like in terms of resting the mind as well as the body.	Thank you for your comment. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment the committee note there is a lack of trial evidence to support more specific advice on rest, but they agreed the advice would not be harmful in the short term. The committee agreed it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and this advice should not result in harm to anyone. As you note the committee recommend a personalised approach and this would include discussing with the person with suspected ME/CFS about how much rest is appropriate. The principles around energy management are set out in section 1.11 Managing ME/CFS.
Leeds and York Partnership Foundation Trust	Guideline	013	12	The guideline makes no mention of the provision of specialist in-patient care for the management of severe ME/CFS. It would be helpful if it could be acknowledged in this guideline that some people with severe ME/CFS may benefit from specialist in-patient care to help with the management of their ME/CFS. This would also help provide validity to requests for funding for this level of care. Question 3 existing resources: The National Inpatient Centre for Psychological Medicine is a specialist inpatient unit based at Leeds General Infirmary run by the Leeds and York	Thank you for your comment. The committee agree that access to services for people with ME/CFS is very important and have reinforced this throughout the guideline. They agree there is variation in the delivery of some of the recommended services across the NHS including the provision of inpatient care for people with ME/CFS. The guideline addresses access to hospital care in the access to care section and also includes recommendations for people with severe or very severe ME/CFS. There was no evidence identified in any of the reviews on the provision of specialist inpatient care

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				Partnership Foundation Trust. They are able to provide specialist in-patient care for people with severe CFS/ME which can also include involvement from other specialities within the acute hospital setting if required.	and the committee were not confident in making service delivery recommendations in this area. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme
Leeds and York Partnership Foundation Trust	Guideline	014	28	It would be helpful to include surgery on the list of potential triggers for a relapse as this needs to be factored into surgical treatment decisions.	Thank you for your comment. There were several stakeholder comments about the examples of triggers that worsen ME/CFS. Some of the examples were considered potentially misleading information and not always a trigger and as you have commented there are other examples that could be added. After considering the stakeholder comments the committee agreed to delete the examples and not provide any examples in the recommendation recognising the variation in triggers in people with ME/CFS.
Leeds and York Partnership Foundation Trust	Guideline	020	2	*"If a person needs support at home, conduct a social care assessment, record and provide information and support on…."* In the Leeds CFS/ME service we would recognise the skills of an Occupational Therapist to undertake such assessments and refer to or liaise with the most suitable community service to undertake this in the patient's locality. Furthermore, we have developed a specific Risk Assessment for ME/CFS considering domains such as function, nutritional status, sensitivities, transfers etc. This is undertaken by the practitioner working with the individual and their family.	Thank you for your comment and information.

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				An Occupational Therapist would work with the family and carers to optimise independence but also empower the carer to promote this and be supported themselves.	
Leeds and York Partnership Foundation Trust	Guideline	020	20	"*Provide aids and adaptations identified*" Specialist services do not retain equipment for loan or have provision for this and needs to be handed over to specialist therapists to make their assessment. Occupational Therapists are the key professional to consider the full range of needs and function. However, It is not cost effective or good practice for ME/CFS therapists to remain knowledgeable about a range of equipment that is constantly evolving and would place a burden upon services to do so. It is much more effective for the person to be assessed by a specialist community team beyond the general recommendations for example, bathing equipment or rails in order that equipment is ordered and fitted correctly. The funding and means testing for minor and major adaptations also varies and requires a localised response that an Occupational Therapist will be able to recommend or advise after referral from an ME/CFS Service.	Thank you for your comment. These recommendations refer to the social care needs assessment and the aids and adaptions identified as part of that assessment. This has been made clearer in the recommendations
Leeds and York Partnership Foundation Trust	Guideline	021	11	"*offer to liaise on the person's behalf (with their informed consent) with employers, education providers and support services. Give them information about ME/CFS and discuss the person's agreed management plan and any adjustments needed."* Vocational Rehabilitation support is more effective when supporting the person concerned to develop the literacy in describing their own needs and negotiating with their line manager or tutor, or whomever is the key person for considering reasonable adjustments. It is preferable that the intervention equips the employee or student rather than offering to do this on their behalf. Furthermore, the employee	Thank you for your comment and information. After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support. Additional text on work has been added to the committee discussion in evidence review A and includes that adaptions and adjustments should be discussed with the person and gives examples including flexible working and reference to the Access to work scheme. A personalised collaborative approach is reinforced throughout the guideline and applies to this section too. The committee

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				or student may have existing relationships with student support or Occupational Health who already have an advocacy role within the organisation. Education about ME/CFS and helpful suggestions can be provided generally but it is much more effective to support the person concerned to reflect upon the job role, expectations, environment and relationships in work and what works for them. They can then decide about future roles and have strengthened self-awareness and self-efficacy which promotes better self-management and engagement in their roles and choices. Employers may purchase employee assistance or insurance cover for employees which should be utilised, and their expertise can be purchased, as not all CFS/ME specialists have the vocational training and knowledge to negotiate or mediate with the organisation. Empowering the individual to navigate these issues is therefore used with greater effect in our NHS Service. We offer to provide training and resources to employers but not at the expense of the support for the patient. Potential resources implication – Question 1 re challenging to implement: limitations of clinician and admin time to do letters for every patient. It is important to understand the needs of the patient but not reasonable to always offer letters because vocational assessment visits, understanding workplace contexts may be better undertaken by vocational specialists who match the functional capability to the work setting and make suggestions for compensation for disability or limitation.	agree that any discussion on work, school or training should be led by the person with ME/CFS with the support of health and social care professionals that have training and understand ME/CFS. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as admin time to do letters, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas.
Leeds and York Partnership Foundation Trust	Guideline	022	14	"Provide care" Occupational Therapists and other healthcare workers are trained to promote wellbeing, independence and optimise function. Many of the strategies listed in lines 17-21 are	Thank you for your comment and information. The committee agree that a collaborative approach is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this

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				inherent in the skill set of Occupational Therapists and constitute treatment, not care as this supposes something that is done to a person rather than working alongside collaboratively. The expertise and effectiveness is also about working with the person's values motivations and by seeking meaningful engagement in their life roles and relationships.	underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and collaborative person centered care is directly reinforced in the guideline sections approach to delivering care, assessment and care planning and in the management of symptoms.
Leeds and York Partnership Foundation Trust	Guideline	023	4	*"Care for people whose ME/CFS is managed in primary care should be supported by advice and direct clinical consultation from a specialist team*. There is an element where a specialist team may act as a resource for other professionals for general advice and education. However, clinical responsibility and knowledge for a patient follows assessment and collaborative care planning with the individual concerned or their proxy. Specialists may only offer specific input and support the GP with recommendations by having delivered an episode of treatment or completed an assessment only. Specialist care when indicated may need funding and will be focused upon a particular outcome or problem, before discharging back to primary care. There is no such retainer arrangement and governance determines that pathways and protocols are followed from referral to discharge even if the patient returns for several episodes of care.	Thank you for your comment. Throughout the guideline there is reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support plan and supervision for the management of some symptoms. The committee agree that clinical responsibility and knowledge for a patient follows assessment and collaborative care planning with the individual concerned or their proxy and this is underpinned in this section. The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no one single model of care. Some of the committee members described experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to specialist care, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas.

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Leeds and York Partnership Foundation Trust	Guideline	024	4	*Be aware there is no current treatment or cure (non-pharmacological or pharmacological) for ME/CFS.* We find this statement unhelpful and will potentially undermine engagement in a therapy programme. Most people would consider advice and support from a trained healthcare professional to constitute 'treatment'. As we collect outcomes at the start and end of therapy, we have evidence that people make changes in function, coping, self-efficacy and in the scales of fatigue, pain, anxiety and mood. Changes in employment outcomes may need interpretation as retaining employment may be a good outcome but changing or ending employment may also be helpful to the person if their workplace was not a healthy environment for them. So, to talk of cure with a complex condition that can relapse and be retriggered is unhelpful. To not include the outcomes reported by specialist services that patients and practitioners have fought for with additional NHS money, is unhelpful.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. However committee agree there currently isn't a cure for ME/CFS and it is important that people with ME/CFS are aware of this. For this reason, the committee have not further edited the recommendation.
Leeds and York Partnership Foundation Trust	Guideline	024	7	*Energy management.* Occupation Therapists are trained in the approaches of energy conservation, activity analysis and activity management. Therapists working in Specialist services such as ours use tools and techniques to support the patient to establish their baselines and build awareness of setting limits by utilising a tailored and flexible approach. The principles of pacing and grading are well established and there are numerous examples of outcomes following structured stages of therapy of stabilisation, increasing tolerance, maintenance and is established around the individual's goals.	Thank you for your comment. The role of occupational therapists in supporting people with ME/CFS are acknowledged in the guideline and particular with reference to supporting people with ME/CFS who have difficulties caused by reduced physical activity or mobility or feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or exercise programme into managing their ME/CFS.

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Leeds and York Partnership Foundation Trust	Guideline	025	18	*Reduce activity as the first step* This statement is too prescriptive for a secondary care service to follow. This section reads as if it is part of a comprehensive therapy assessment, but this advice would be more appropriate in a section aimed at initial advice which is more commonly delivered in primary care. A therapist in a specialist service would assess where a person is at with regard to symptom stability and understanding of pacing strategies. It is possible that some people have already established these strategies effectively and therefore do not need to be told to reduce their activity. There needs to better acknowledgement of the fact this illness changes over time and therefore different approaches are needed at different stages of the illness and therefore need to be individualised and done in collaboration with the patient.	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to, agree a sustainable level of activity as the first step, which may mean reducing activity.'
Leeds and York Partnership Foundation Trust	Guideline	026	1	When to refer to physiotherapy or occupational therapy This is an extremely limited understanding of the skill set and approach of a therapist trained to work people with all forms of disability, volition, and self-awareness. Fundamentally people may be referred to assist with adjustment and adaptation, and then devise programmes of lifestyle management, activity according to the goals and readiness of the individual.	Thank you for your comment. This section refers to referral for physical activity, earlier in the guideline in section 1.5 there are recommendations on a holistic assessment and developing a care and support plan. This includes the points you make.
Leeds and York Partnership Foundation Trust	Guideline	029	3	*The use of the term Relapse:* we will use this term in more persistent situations where there is a significant increase in symptoms usually with a clear trigger but generally, we have tried to move to the term managing setbacks. This term feels emotionally more temporary and something that is to be expected and managed.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.

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Leeds and York Partnership Foundation Trust	Guideline	029	8	*Providing access to support after a flare.* The purpose of agreeing a 'managing setbacks' plan early in treatment, in advance, is that the person themselves has strategies to implement. This may include asking for additional support from their support network to restabilise. This is more empowering and sustainable over time and helps manage the expectation that specialist service personnel are not always available akin to a crisis service. In Leeds we do offer a duty system during office hours when it may be possible to speak to a clinician who will try to offer help and support by discussing the plan and actions to take in these circumstances.	Thank you for your comment. The committee agree that planning for flare ups and relapses is an important part of the care and support plan (including energy management and physical activity and exercise if appropriate).
Leeds and York Partnership Foundation Trust	Guideline	029	17	*Rest and Sleep* This section needs to be expanded to reflect the complexity and importance of advice given around managing rest and sleep.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Leeds and York Partnership Foundation Trust	Guideline	031	6	'Do not offer any medicines or supplements to treat of cure ME/CFS'. Our service has 2 doctors as part of the multidisciplinary team and we do not currently prescribe any medication for managing ME/CFS and do not have capacity to provide medical monitoring of prescribing. However, many patients do benefit from prescribing overseen in primary care that can help with symptom management. We therefore feel that this statement is unhelpful, does not reflect current care and could	Thank you for your comment. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.' The committee note the following subsection in the guideline is, 'medicines for symptom management' and provides advice for prescribers and includes that people with ME/CFS should be offered a medication review in line with the NICE guidelines on medicines adherence and medicines optimisation. The

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				have a detrimental effect on a patient's emotional wellbeing to read that there are no treatments available. We also feel there could be a role for more specialist involvement in managing medication use in people with ME/CFS as they can often experience medication intolerances so require careful prescribing with access to regular review. Equally some patients can end up on many different medications that can become problematic and contribute to their symptom burden and it would be beneficial if ME/CFS specialists could be involved in supporting patients and GPs with recommendations regarding medication, when appropriate. We believe more guidance around the role of supplements and prescribing, and promoting research in this area is needed. This should be supported by the NICE guidance. We are also aware of the potential for trials involving medications to take place and we would find it hard to take part given that we do not have structures in place to offer prescribing and medication reviews. Therefore, statements that deny the role of the use of any medications will hinder research progression in this field.	discussion section of Evidence review F: Pharmacological management recognises some people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and this should be discussed on an individual basis. *Supplements* The committee agree and recommendation 1.12.24 includes advising people with ME/CFS about the lack of evidence to support routinely taking vitamins and supplements as either a cure or to manage symptoms and the potential side effects of taking higher doses.
Leeds and York Partnership Foundation Trust	Guideline	031	6	The section on medication fails to acknowledge areas of clinical practice where there could be a role for prescribing to help manage key symptoms of ME/CFS. We are slowly starting to see patients who have seen cardiologists who are able to identify dysautonomia conditions such as POTS and we have seen patients who have found symptom benefit from medications used to manage dysautonomia including cognitive symptoms improving with	Thank you for your comment. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.' The committee note the following subsection in the guideline is 'medicines for symptom management' and provides advice for prescribers. The discussion section of Evidence review F: Pharmacological management recognises some people with

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				medications used to lower heart rate. However, we are more used to seeing patients in whom we feel medication could be of benefit but they are unable to access any specialists in their locality who have any expertise in the field. We had hoped that the NICE guideline would acknowledge this developing area of treatment and promote expansion in the provision of this aspect of care. We are also aware of the developing knowledge and research regarding Mast Cell Activation Syndrome and suspect that we are seeing patients with this condition in our ME/CFS service. There is minimal access to specialists with clinical expertise in this field but we are hopeful that this will improve in the coming years. We are aware that simple agents such as antihistamines and H2 blockers can be used as mast cell stabilisers and this is another area of clinical practice and prescribing that we would like to see patients with ME/CFS able to access when appropriate.	ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and this should be discussed on an individual basis.
Leeds and York Partnership Foundation Trust	Guideline	032	8	*Refer people with ME/CFS for a dietetic assessment by a dietitian who specialises in ME/CFS if they are losing weight and at risk of malnutrition, or they have a restrictive diet*. Question 3 re example of good practice: Our service has a dietician as part of our specialist CFS/ME multidisciplinary team. They are a valuable asset to our team both with direct patient contacts and also to improve the level of confidence within the team regarding assessing for nutritional risk factors. The dietary needs of many people with CFS/ME is complex and referring to the NHS eat well guide is far too simplistic. We would advocate for there being an increase in the provision of dieticians with specialist training in ME/CFS and for them to be a standard part of ME/CFS multidisciplinary teams.	Thank you for your comment. The committee agree that people with ME/CFS need access to dieticians with a special interest in ME/CFS. This guideline focused on clinical recommendations and the committee did not comment on the delivery of services, which can be determined locally. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS.

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Leeds and York Partnership Foundation Trust	Guideline	037	2	*Flares* In our specialist service we do not use the term flare and are more likely to say exacerbation of symptoms as with PEM, or a dip in energies. We might talk about a set back	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
Leeds and York Partnership Foundation Trust	Guideline	040	11	ME/CFS should be included in the undergraduate medical curriculum, and postgraduate Physician, Paediatric and General Practice curriculums. Question 3 examples of good practice: Members of our team have been involved in many different training events including lectures delivered to GPs, GP registrars, Psychiatrists, other teams within our own trust, as well as presentations and workshops at CFS/ME conferences and hosting webinars for BACME. Wherever possible we involve patients in these training events and during the Covid lockdown recorded an interview with a past patient which served as an excellent teaching resource for 2 training events we have delivered.	Thank you for your comment and information. It is beyond the remit of NICE to recommend what should be included in undergraduate medical curriculum, and postgraduate Physician, Paediatric and General Practice curriculums. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme
Leeds and York Partnership Foundation Trust	Guideline	042	4	*Energy Envelope* This term is not used in our service as energy fluctuates daily dependent upon many factors related to expenditure, rest, dietary intake, blood sugar regulation, environment etc. Energy may be depleted or even increased depending upon how the person interacts with their environment and demands. We find that it is preferable to work with establishing baselines of different activities by experimenting over time and establish the persons capacity to meet demands and not exceed these baselines even on good days.	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.

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Leeds and York Partnership Foundation Trust	Guideline	046	1	The statement about outcome measures only references their use in a trial setting but outcome measures are an essential part of clinical practice as well. It is important that consideration is given to the development of standardised measures that NHS services can use that are meaningful to patients and useful for therapists to aid with their reflective learning. Question 3 re existing resources and example of good practice: Our team has been working on developing an ME/CFS specific Therapy Outcome Measure tool, we have used this within our own service and shared it with other services and other therapists working in the field at a BACME conference workshop. We would be happy to be involved in any further development of clinically relevant outcome measures for ME/CFS.	Thank you for your comment. As you comment this refers to the development of core outcomes sets for research, to date one for ME/CFS has not been developed. See https://www.comet-initiative.org/. The committee agree that outcome measures are important in clinical practice however research recommendations can only be made where the evidence has been searched for within the guideline. The use of outcome measures in practice was not included in the scope of this guideline as a topic to consider, and therefore the committee are unable to make research recommendations on this topic. Therapy Outcome Measure tool We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme
Leeds and York Partnership Foundation Trust	Guideline	071	10	Question 1 re challenging to implement for NHS admin staff and Question 2 re cost: Our service is currently called a CFS/ME service and this term is used on all of our printed literature including an extensive stock of printed information leaflets on many different aspects of this illness. It is also on our GP referral forms and our trust website. Changing the name of the service to ME/CFS will incur a big demand on admin staff to change all of our current documentation both printed and online. Clinical staff time will also be required to change clinical documents, group programme presentations etc. There will also be a cost implication if we are expected to dispose of all current printed literature that refers to the condition as CFS/ME.	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental.*

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					For consistency, the abbreviation ME/CFS is used in this guideline.' There is no requirement to immediately update signage and stationery. However, we expect that new services will use the guideline's nomenclature and that existing services will adopt it when it is time for them to reprint their materials.
Local ME	Guideline			LocalME as stakeholders, represent a national forum and network of "local" group leaders, advocates, their medical/academic and research advisors. LocalME are uniquely placed to report back on the reality of 'Policy into Practice' and life as we know it at the coalface. It is the widely held view amongst Group leaders, that whatever the new Guide Guideline might say on the label, it's what's in the tin that counts and may prove to be a mixed bag; the reality being that it is *guidance,* it is not mandated and comes with no real clear outcome measures. Therefore we feel, whilst the change in steer and effective U turn by NICE is welcome, there appears little hope in the current crisis and circumstances of any new consistent national delivery for the foreseeable future. This situation unquestionably puts patients at risk from neglect, especially the severely affected. Self management advice (often over the phone/internet/zoom), by Health and Care practitioners, will not suffice. The situation for children & young people is dire and a national disgrace. Accusations of FII amount to a breach of Human Rights in our view. Difficulties surrounding Safeguarding *must* be dealt with. Without a system of accredited training of ME and CFS required for practising Paediatricians and Social Care assessors, it is unlikely difficulties will resolve for the foreseeable future. A	Thank you for your comment. The consultation period was the standard length for consultations on NICE guidelines as set out in Developing NICE guidelines: the manual. An e-mail was sent to all stakeholder groups in August 2020 to confirm the consultation dates when they were amended. We are grateful to your organisation for engaging with the consultation and for the comments you have submitted.

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				Serious case review may be required which uses new NICE guidelines to effect. While there are many aspects of the guideline that we warmly welcome, we can see some obvious flaws in the detail which will limit it's potential to improve patient care unless rectified. We would ask the GDC, it's expert witnesses and it's lay members who have given of their time so generously to accept our thanks for their work, and to consider this submission as providing some constructive criticism, which we feel obliged to lodge given that the guideline is likely to have a substantial effect on professional practice and capacity for any delivery for decades to come. Please note too that we have not been able to appraise all parts thoroughly, due to regrettable time constraints imposed by NICE who are non compliant once again with Government Recommendations on Consultations (Appendix A). As stated recently to NICE on the phone to Senior Guideline Commissioning Officer at *NICE* a formal complaint to NICE in 2017 regarding the time allocated was accepted and allowed. As stated recently to NICE on the phone to Senior Guideline Commissioning Officer at *NICE* a formal complaint to NICE in 2017 regarding the time allocated was accepted and allowed. A 2 week informal extension from 22nd DECEMBER - 5th January 2021 which we feel is reasonable and proportionate in these extenuating circumstances was not allowed. Equally **NICE are not operating under Disability Discrimination Act by making suitable arrangements for People with ill health/disability to respond. Would suggest that the NICE Manual governing such matters as consultation is revisited and reviewed as a matter of some urgency**. We in LocalME are aware that review of the manual itself recently took place a while back, but obviously this issue and	

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				lack of compliance as to best practice on consultation appears to have been overlooked or not drawn to your attention during that process. It is our view that NICE are in breach of Government Guidelines on Consultation "The Compact". (Appendix A)	
Local ME	Guideline	General	General	Draft guideline document https://www.nice.org.uk/guidance/gid-ng10091/documents/draft-guideline • Evidence review A - Information for people with ME/CFS • Evidence review B - Information for health and social care professionals • Evidence review C - Access to care • Evidence review D - Diagnosis • Evidence review E - Strategies pre-diagnosis • Evidence review F - Pharmacological management • Evidence review G - Non pharmacological management • Evidence review H – Non pharma management appendices • Evidence review I – Multidisciplinary care • Evidence review J - Review of care • Supporting documentation - Children and Young people • Supporting documentation - People with severe ME/CFS • Supporting documentation - Expert testimonies The template provided by NICE for us to use for our submission asks in addition for our answers to the following 3 questions in addition to your comments on our guideline document.	Thank you for your comment.

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				1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why? • IN ORDER FROM LIST ABOVE- SA,C&YP, E,F, B. See general comments.	
Local ME	Guideline	General	General	the following 3 questions in addition to your comments on our guideline document. 1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why? • IN ORDER FROM LIST ABOVE- SA,C&YP, E,F, B. See general comments. 2. Would implementation of any of the draft recommendations have significant cost implications? • Yes for CCGs see general comments. CCGs have not prioritised ME and CFS in NHS 5 year Forward Plans, have consigned services to divested (secondary) community private services. CCGs decision making on this is not public and behind closed Clinic Executive Committee doors. 3. What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.) See references to Suffolk co production in general reality comments. All evidence available much found on following blog. www.nandsme.blogspot.co.uk http://nandsme.blogspot.com/p/homepage.html	Thank you for your comment and information. There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned. Your comments will be considered by NICE where relevant support activity is being planned'. We will pass this information to our resource endorsement team. More information on endorsement can be found here (https://www.nice.org.uk/process/pmg29/chapter/overview-of-nice)
Local ME	Guideline	General	General	**Which areas will have the biggest impact on practice and be challenging to implement?**	Thank you for your comment. The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as training development , to implement some recommendations in the guideline. However, this guideline

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				Lack of will & lack of political expediency, including lack of Governmental Non Government Bodies and Department of Health commitment, is a barrier and are major challenges as are the securing of new resources. Local processes are being explored which one would hope will lead to a substantive change of culture, but this improvement will be hard fought and measure if brought in likely to take in years to become embedded. Nationally recognised accredited training and education of Health, Social Care & education staff as well as GPs and primary care specialist urgently need addressing. Unless key partner Non Government Bodies, NHS England, NHS Improvements, NHS Public Health sign up and commit to support and fund change, CCGS, who hold 75% of the funding for service delivery, will procrastinate and delay for years, just has been the case since the 2004 roll out of national services under the Long Term Conditions Programme.	highlights areas where resources should be focussed to provide appropriate care for people with ME/CFS.. Your comments will also be considered by NICE where relevant support activity is being planned.
Local ME	Guideline	General	General	Few CCGS/GP Federations or Transformation & Strategic Alliances (unlike Suffolk who have led by example): have enshrined ME and CFS services in their 5 /(10) year NHS Forward Plans and have them discussed in the public domain. Service providers, as Social Enterprise (private divested Community Services) preclude any open meetings with patients and meet behind closed doors in private; meetings notes or minutes are not released for public scrutiny. The public's only recourse is to take matters to elected members and Strategic Health Overview and Scrutiny foreword agendas and work programmes. These providers are also outside FOI legislation they claim, even when suppling NHS Standard contracts for services. Poor/inadequate and limited though the Norfolk & Waveney Community Based tertiary service therapy provider- East Coast Community Health (ECCH) is, they also	Thank you for your comment and information.

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				have the ICC Criteria referenced and referred to on their Service website. So we can say Suffolk (and ECCH) have gone through some due process, found NICE wanting in 2008 and have adapted NICE Guideline to demonstrated local needs, backed up by a robust co production methodology from 2006-2012, (and Suffolk have continued until present day) through; • Enshrining ME on their PCT/CCGS forward 5/(10) year Forward Plan (Suffolk only) • An NHS Public Health assessment (first in UK 2009) (Norfolk and Suffolk) • Patient Surveys and patient satisfaction audit 2009- 2015 • Joint HOSC examination and Forward Programme (2008-2020) 2015-2016 • Independent Service Evaluation commissioned by lead CCG (2016)-Service Development Feasibility Study (LSHTM) 2016 • Joint Strategic Commissioning - Transformation and Improvements within Alliance 2020 So Suffolk in particular have listened, learnt and have acted accordingly, in effect anticipating a new approach and the new guidance from NICE 2012. They have been testing the water and are ready, willing and able to go forward to a new service specification within their Alliance, modelled on the successful 3 year trial Consultant based Specialist Service for Suffolk patients commissioned by the Suffolk GP Federation/CCG Commissioning and Contracts Team and opened in 2018. They already showing due diligence and planning for the future- doing what all CCGs should have done with their local GP Federations that is going through a due process in anticipation of new improved NICE Guidance.	

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Local ME	Guideline	General	General	**What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice)?** • A NICE Review of current services and scrutiny of the Annual Change Audit supplied to contracting CCGs and Commissioners. How can NICE 'change'/challenge a situation which has not been audited by them or commissioned by them nationally? • NICE should challenge misinformation held within the Royal Colleges literature, website material re training and approaches to patient care • . Also previously referenced BACME and the NOD Data base (ceased effectively in 2015 according to Dr Simon Collin who was involved in it.) is problematic and unreflective. This is therefore outdated material and unreliable. • A dedicated palliative care provision should be coordinated nationally for those most severely affected and at most risk. • **NICE must quantify the problem - Learn from Norfolk & Suffolk ME & CFS Service:** • **Learn from feedback such as Parents as Teachers Forum Summary prepared by the ME & CFS Patient / Carer Group** **-Introduction** In the autumn of 2016 ECCH set up a 'Patients as Teachers' Forum. ECCH stated in the invitations: *'We will be holding a forum to get feedback on your experiences, your ideas to improve the service…..We will then explore ways to improve our service to you. After we have done this, we will write to each patient*	Thank you for your comment and information. *Audit* The committee agree that audit is an important part of measuring performance in services but this guideline focused on clinical recommendations, the development of audit systems was not included as an area in the scope and the committee are unable to make recommendations in this area. Your comments will also be considered by NICE where relevant support activity is being planned. NICE – quality standard? *Training* The committee agree that training materials for health and social care professionals should reflect current knowledge and be evidence based and address this in the Training for health and social care professionals section on the guideline (see the committee discussion section in evidence review B) *Palliative care* This guideline focused on clinical care and service delivery was not included as part of the scope of the guideline and the committee are unable to make recommendations on the provision of palliative care. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme

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				carer and/or relative who attended to tell you the outcome of your suggestions.' There were no attendees for 2 of the 5 events (Norwich & Halesworth). One of our group members attended the forum in Stowmarket in October 2016 and took notes of the points raised. There were 7 patients / carers present. In April 2017 ECCH circulated, an 'Action Plan' in response to the points raised at the forum to be discussed at further forum meetings in July. The Patient / Carer Group representative was unable to attend the July meeting so wrote to ECCH on 2 August. A response was received from ECCH on 5 September. **The following table summarises the concerns raised by the Patient / Carer Group to the 'Action Plan' and the response received from ECCH. (Report available here; https://drive.google.com/file/d/1_szwhq_83iThvhRCkNyUxPRsqFp8smup/view?ts=5fe10dae)** Learn form Suffolk Commissioning & Contracts Team; who have led by example, have enshrined ME and CFS services in their 5 /(10) year NHS Forward Plans and discussed them in the public domain. Suffolk have embraced 'Co production' and partnership working of ME service development for 14 years. Their approach was to reject the problematic areas of 2007 NICE by following a review process of local needs and a rigorous public health assessment and needs assessment.This led to Suffolk adopting the Canadian Diagnostic Criteria in 2014 in preference to NICE to drive their service commissioning, contractual arrangements and review processes.	

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				In 2009, Norfolk Director of commissioning also adopted a 'best practice approach'; fulfilled their obligations to local need with the first comprehensive need assessment for regional ME and CFS[1]; drove a new patient endorsed service agenda and Service Specification which was signed off in 2012. However the political changes and changes to the Health Service under the 2012 Act resulted in the initiative stalling and failing in Norfolk and Waveney CCGS Alliance area. Suffolk have remained true to their word with an exceptional Commissioning and Contract's Team however and have continued to strive to meet local needs which included them commissioning a 2016 Public Health Service development Feasibility Study done by LSHTM[2]. NICE should scrutinise the work done by the charity Hope for ME & Fibromyalgia Northern Ireland, who have demonstrated a comprehensive and proactive approach towards service set up and delivery, including medically endorsed training material and information. Stakeholder and rep for LocalME a national Group leaders organisation. Norfolk & Suffolk ME and CFS Service Development. **http://nandsme.blogspot.com/**	
Local ME	Guideline	General	General	**What does the new guideline do?**	Thank you for your comment and information.

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[1] Needs Assessment for Myalgic Encephalomyelitis and Chronic Fatigue Syndrome Services in Norfolk and Suffolk https://docs.google.com/file/d/0B1KcCpwxF0UHNkpLejk4NlZSTDg/edit

[2] Feasibility assessment of the Implementation of a ME & CFS Consultant-led Service for Norfolk and Suffolk Report to 6 CCGs in Suffolk and Norfolk November 2016 Luis Nacul, Eliana Lacerda, Caroline Kingdon https://drive.google.com/file/d/0B2eUb8PoOndFZHI6UERmc2szNEE/view

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				It *should* provide a clear direction of travel. It is a pathway document not a delivery mechanism. However it is in our view unlikely to translate into good practice or appropriate services in the foreseeable future for a range of reasons. We feel primarily it is about the removal any roadblocks or particular excuses for not changing the 'status quo' of harmful and problematic service delivery as a result of the flawed and harmful 2007 NICE Guidance over the last 13 years. It should empower patients to challenge inappropriate advice and poor services. It should help hold providers to account. We note the setting up of the NICE initiate Improving Patient Safety to address the potential for NICE harms. **'How NICE is improving patient safety**.'..... Not before time. **Annual patient safety update covers the period from September 2019 to September 2020***25 November 2020* *Professor Kevin Harris, NICE's senior responsible officer for patient safety* *The role of the senior responsible officer for patient safety was established to bring together strands of patient safety across NICE, providing a source of advice and oversight accessible throughout the organisation. Last week, the NICE public board meeting considered the my first annual patient safety update. The board paper proposed NICE develops a unified approach to patient safety, integrating the excellent work already occurring in different parts of the organisation. It will build on existing structures and draw on the expertise of the Science, Evidence and Analytics Directorate to consider how new technology such as artificial intelligence could help detect patient safety signals more quickly in the future. The work will also explore how patient safety at NICE can evolve and integrate with NICE Connect, our multiyear project which will*	

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				transform the way we produce and present our guidance and the lives of people receiving care. *In view of NICE's key role in supporting quality health and social care, a clear and accessible patient safety structure across the organisation will help improve not only our own patient safety activity, but also support learning and action in the wider health system. Patient safety is a shared value that reflects a central tenet of care: first do no harm….."* **Other roadblocks do exist** and will need to be addressed through more advocacy. But if the guidelines had remained as they were, t**he brick wall would be extremely solid.**	
Local ME	Guideline	General	General	**Guidelines** NICE guidelines have always been less black and white. Organisations commissioning and delivering services are expected to take the recommendations contained within NICE clinical guidelines into account when planning and delivering services. There is no fixed timescale for implementation because of the different ways services are delivered in very in different organisations. A recent court judgement does however mean that if organisations refuse to put NICE clinical guidelines in place because they disagree with them, this could leave them open to challenge. But by who? Sick patients? *A no-win situation* Apart from dealing with specific symptoms, the guidance offers little in the way of treatment. This is except for 'physical therapy' and 'CBT' which cause our alarm bells to start to ring. It could be used as business as usual with all and attendant problems all over again; i.e. the woeful history of ME services repeating itself. So, NICE has left patients in a no-win situation. Firstly, they don't have any choices over potential treatment. Secondly, the	Thank you for your comment and information.

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				guidance places the emphasis of the management of their health onto them. As it states: *'...the person with ME/CFS is in charge of the aims of their management plan....'*	
Local ME	Guideline	General	General	Suggested changes; - We suggest *'management plan'* is changed throughout the draft document to 'Care Plan' to make it consistent with descriptions under the legislation and understood by all. - For Children and young people Education and Health Care Plan- which affords legally binding protection up until the age of 25 for those who have missed years of vital education-NOT a 'management plan' please. Precision is needed here. The guidance also says doctors should refer patients to ME specialist teams. While these do exist in England, they are all varied. One leader stated. *'Some are led by psychologists like Surrey and Hull; others like the Yorkshire Fatigue Clinic involve immunologists. Moreover, others like in Suffolk have been stopped. So, the idea that people can see specialists is a postcode lottery.* *Other PACE trial authors were less happy with NICE's draft of the guidelines. But the fact that two of the trial's main people are reacting positively should be cause for concern. Because it confirms that, while on paper NICE may have removed GET, it has still left wriggle room for doctors to use exercise therapy."* *But ultimately, ME, GET, CBT, and the NICE guidance are not just health issues. They are political ones: a perfect storm of money-saving from government, the system needing as many*	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) In the section on *supporting people with ME/CFS in work, education and training* there is a recommendation to give parents and carers information about education, health and care plans (EHCPs) and how to request one from their local authority. Based on the evidence (Evidence reviews A.B,C,D and I) and the committee's experience referral to ME/CFS specialist care was recommended for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. ME/CFS specialist teams where seen as the most appropriate place for people with ME/CFS to access support with GPs providing ongoing support and review. Evidence review I includes the committee discussion on ME/CFS specialist services. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services, to implement some recommendations in the guideline. guideline highlights areas

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				people to work as possible and psychiatrists making a healthy living off the back of all of this. But there is now an emerging group of patients also facing the threat of the same treatment as people with ME. And they're people living with long Covid. Particular attention will be needed to make sure the needs of ME patients do not become conflated with many suggested approaches to Long Covid service provision, with some providers already seeing this as a future revenue stream for 'recovery' 'rehabilitation' services, 'MUS'/ 'IAPT', 'CBT/ Rehab' agendas and steer. Many CCGs have already developed a mindset to deal with their obligations to ME and CFS patients in this way. It is hoped that the new NICE Guidance will counter this pressure. *'The draft NICE guidance will do little in a practical sense of delivery of care for ME patients. In fact, it may manifest that not a lot has actually changed.* *It's not good to see that patient groups have largely welcomed the guidelines without proper analysis or understanding of what's really going on here. Sadly, too many people fail to recognise ME as a political issue, not just a health one.'* *But moreover, due to coronavirus, there are now countless more people at risk of falling foul to treatment that is grounded in wealth, not health. Any support of the NICE guidance may only add to the suffering of many, many people. It is now up to patients to demand that NICE changes its course (with Non Governmental Body partners and their processes)."*	where resources should be focussed and those interventions that should not be recommended, saving resource in other areas.
Local ME	Guideline	General	General	**In researching for the SCOPE stage, Local ME as Stakeholders noted NICE guidelines purport to:**	Thank you for your comment and information.

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				make evidence-based recommendations on a wide range of topics in health, public health and social care. Our guidelines recommend the most effective ways to: • prevent and manage specific conditions • improve health and manage medicines in different settings. • provide social care to adults and children • plan services and interventions to improve the health of communities • provide integrated health and social care services that meet the needs of patients and people who use services. Our guidance and other products are for the NHS, local authorities, social care organisations, charities and anyone with a responsibility for commissioning or providing healthcare, public health or social care services. Following our recommendations can help these organisations to reduce variations in practice across the country. Patients, people using services, carers and the public can also use NICE guidance and other products as a guide to the high-quality care they should expect to receive. LocalME widely held belief is that the 2007 NICE guidance has failed ME and CFS patients and others for 13 years. A performance management exercise appraisal by a court or review body would suggest a '*Requires Improvement"* assessment over the whole NICE process. The following were highlighted during Engagement/Scoping meetings. These remain areas of the draft and process which appear lacking in clarity or left substantially unaddressed in draft. • securing of improved access to NHS and Social care services, via **NHS England Commissioning,** especially for the most "vulnerable groups"; **the acute, severely affected and children.** ***(answer as to why, 11 years on from the issue of NICE (CG53) there is a demonstrated erosion and drastic reduction in NHS and Social care service availability nationally- leading to patient harm and in some instances, death).*** • Promote **equality of service provision compared with comparable other long term conditions and** deliver on the 2004 Long Term Conditions Framework core requirements.	

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				• Improve **accuracy of diagnosis which research indicates to be a significant problem with up to 40% misdiagnosed.** • Demonstrate **effective monitoring of the application of it's guidance** to ensure and p**rovide evidence of harm free delivery of service management.** • Address **Post Exertional Malaise, PEM andfluctuating nature of condition.** • 11Promote **prescribing rights** for ME/CFS within services where there has been demonstrated need. • Ensure **effective _ongoing_ supervision and care**, and suitable services, especially for the "at risk" groups, severely affected and children. • **Provide effective guidance on dealing with co morbidity in patients.** **Other bullet points which were drawn to NICE attention are problem areas which also appear to be unresolved by this draft;** • BMJ Guidance on ME/CFS • NHS "non funded" clinics- paediatrics especially. • BACME and NOD Database Bristol University • Robust diagnostic criteria:International Consensus Criteria • **Discuss involvement and influence of the Faculty of Occupational Medicine (FOM)**	

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Local ME	Guideline	General	**General**	**In Janu**ary 2018 LocalME stated during Scope meetings,'Because the current guideline and emphasis directs patient care down a vague fatigue and mental health	Thank you for your comment and information. ıe committee have recommended the investigations to identify and exclude nittee have now included examples of e carried out and that investigations /CFS is suspected. The committee or suspecting ME/CFS and where ed by another condition'.

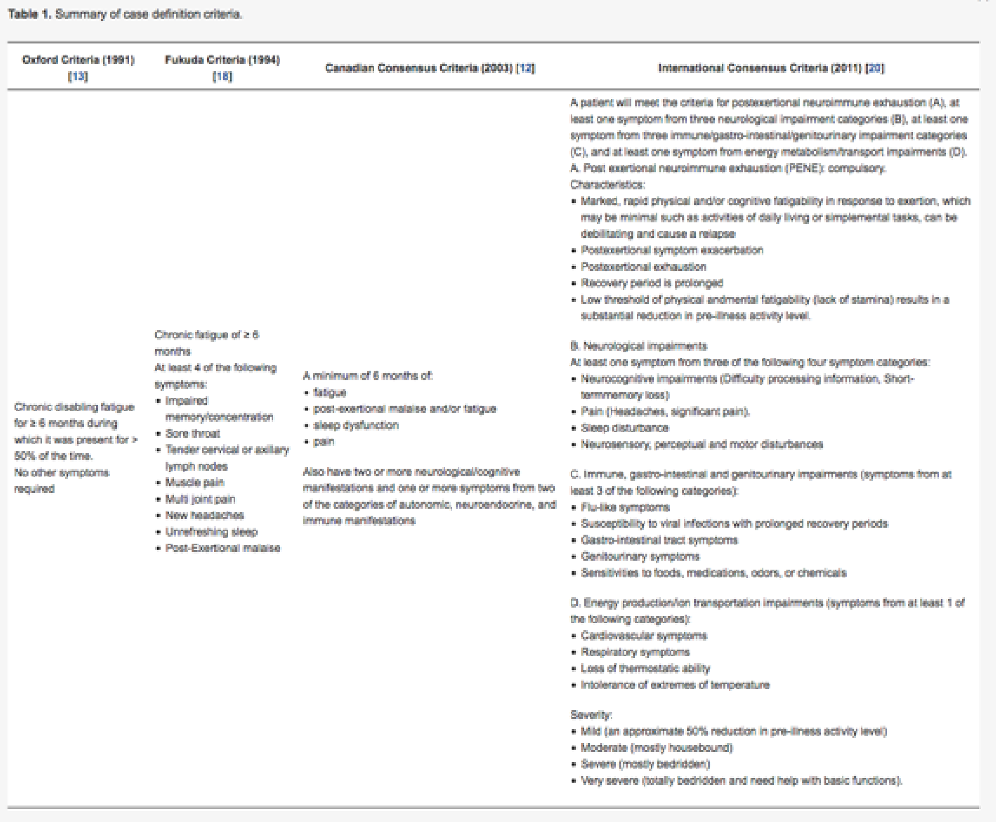

Table 1. Summary of case definition criteria.

Oxford Criteria (1991) [13]	Fukuda Criteria (1994) [18]	Canadian Consensus Criteria (2003) [12]	International Consensus Criteria (2011) [20]
Chronic disabling fatigue for ≥ 6 months during which it was present for > 50% of the time. No other symptoms required	Chronic fatigue of ≥ 6 months At least 4 of the following symptoms: • Impaired memory/concentration • Sore throat • Tender cervical or axillary lymph nodes • Muscle pain • Multi joint pain • New headaches • Unrefreshing sleep • Post-Exertional malaise	A minimum of 6 months of: • fatigue • post-exertional malaise and/or fatigue • sleep dysfunction • pain Also have two or more neurological/cognitive manifestations and one or more symptoms from two of the categories of autonomic, neuroendocrine, and immune manifestations	A patient will meet the criteria for postexertional neuroimmune exhaustion (A), at least one symptom from three neurological impairment categories (B), at least one symptom from three immune/gastro-intestinal/genitourinary impairment categories (C), and at least one symptom from energy metabolism/transport impairments (D). A. Post exertional neuroimmune exhaustion (PENE): compulsory. Characteristics: • Marked, rapid physical and/or cognitive fatigability in response to exertion, which may be minimal such as activities of daily living or simplemental tasks, can be debilitating and cause a relapse • Postexertional symptom exacerbation • Postexertional exhaustion • Recovery period is prolonged • Low threshold of physical andmental fatigability (lack of stamina) results in a substantial reduction in pre-illness activity level. B. Neurological impairments At least one symptom from three of the following four symptom categories: • Neurocognitive impairments (Difficulty processing information, Short-termmemory loss) • Pain (Headaches, significant pain). • Sleep disturbance • Neurosensory, perceptual and motor disturbances C. Immune, gastro-intestinal and genitourinary impairments (symptoms from at least 3 of the following categories): • Flu-like symptoms • Susceptibility to viral infections with prolonged recovery periods • Gastro-intestinal tract symptoms • Genitourinary symptoms • Sensitivities to foods, medications, odors, or chemicals D. Energy production/ion transportation impairments (symptoms from at least 1 of the following categories): • Cardiovascular symptoms • Respiratory symptoms • Loss of thermostatic ability • Intolerance of extremes of temperature Severity: • Mild (an approximate 50% reduction in pre-illness activity level) • Moderate (mostly housebound) • Severe (mostly bedridden) • Very severe (totally bedridden and need help with basic functions).

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				approach, the result is that it effectively *obstructs* patients' access to appropriate biological testing, treatment and support. Misdiagnosis is rife with peered reviewed research indicating it running at some 40% misdiagnosis. This results in patient harm, death and NHS "NEVER" events reported to Healthwatch locally. To avoid this ethical violation, we request that the guideline be revised to present a truthful, helpful guidance reflective of the current debate, emerging exciting new international research findings, and state of play about the nature and optimal management of ME/CFS.	
Local ME	Guideline	General	General	**Other bullet points which were drawn to NICE attention are problem areas which also appear to be unresolved by this draft;** to suggest NICE/NHS England and NHS Public Health embark on an **Equalities Impact Assessment?** NICE to reference and embrace and advise on the **Law of Candour** within new guide scoping exercise? Achieve consistency by challenging "overlapping" guidance like; NICE -Intermediate Care-re ablement" guidance; and addressing inconsistent guidance such as NHS Health & Work: Occupational Health Guidance (2006)[3]	Thank you for your comment and information. *People with severe ME/CFS or very severe ME/CFS* People with severe ME/CFS or very severe ME/CFS are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to people with severe ME/CFS or very severe ME/CFS and if different or additional recommendations were appropriate. Where this was the case separate recommendations were made. This resulted in many additional recommendations, after considering the stakeholder comments the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe

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				to address the shocking denial of any appropriate care to the Severely Affected with ME to address the misguided approaches and actions of statutory services, like education; address issues raised regarding "safeguarding" and Fabricated and Induced Illness (FII) ttp://www.meassociation.org.uk/2014/07/forward-me-meeting-and-the-nice-guideline-on-mecfs-statement-by-the-me-association-10- july-2014/ http://www.meresearch.org.uk/information/publications/misdiagnosis-on-a-grand-scale/ **12 NICE Enquiry (our ref EH82669) 11/07/17 13Intermediate care including reablement** **14 "The presently pervasive ambit of the guideline carries freight in the shape of distortion of the concept of patient choice and "no decision about me without me"- the UN Convention on the Rights of People with Disabilities [UNCPRD].** **Article 19 of the UNCRPD makes clear that Independent Living is not necessarily about disabled people doing things for themselves but rather about having choice and control over the support they need to achieve their goals. The focus for all to benefit from a particular approach, CBT and GET in the draft Guideline is both unrealistic and in our view indicative of a highly restrictive understanding**	ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. *Safeguarding* The committee agreed the topic of safeguarding was very important and agreed to include a separate section in the guideline addressing this. *Choice* The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

NHS Health & Work: Occupational Health Guidance http://www.nhshealthatwork.co.uk/chronic-fatigue.asp Chronic fatigue syndrome/myalgic encephalomyelitis- Information for healthcare professionals, employers and employees providing the current evidence on managing and supporting employees with chronic fatigue syndrome.

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				people with ME's needs and safety.This can be be addressed by dealing with the need to clearly delineate and circumscribe the relevance of the guideline. In doing so the guideline committee and development group may wish to bear in mind that 'autonomy' is the core principle for personal choice." 31/07/17 5 nice_v2.2.doc	
Local ME	Guideline	General	General	**Please note below areas from scoping notes/minutes which are less than clear in the draft.** **Key areas that will be covered** ☐ Identification and assessment before diagnosis ☐ Diagnosis of ME/CFS ☐ Management of ME/CFS ☐ Monitoring and review ☐ Information, education and support for people with suspected ME/CFS, their families and carers **Areas that will not be covered** ☐ The management of comorbid conditions ☐ The specific management of symptoms where NICE guidance already exists **COMBINED RESP** Stakeholders were covered. There wer stakeholders: ☐ **Service delivery** **models of delivery** services, training fo standardised asses developed. ☐ **Medications - s** **treatments for syn** different to POTs in ☐ Medication intole Some stakeholders **management of co** such as manageme symptomatic care s he aforementioned Another issue that needs to be considered with regards to the new guidelines is that the way services are funded has changed considerably since the 2007 NICE guidelines, which assumed that specialist services would be created for severe	Thank you for your comment and information. Thank you for your comment. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as flexible access to care, to implement some recommendations in the guideline. guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned.

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				patients (which obviously never happened). Since the implementation of local commissioning, CCGs have considerable freedom in how they allocate funding for services 'based on local priorities and needs'. This has effectively created a 'postcode lottery' for patients, which is another reason that the new guidelines must recognise that there will be considerable variability in what specialist ME/CFS services individual patients will have access to. The situation is characterised by erosion and closure of existing services, even those which had patient endorsement and appreciation. One member stated, '*For example, in my area all that is on offer is 4 sessions of support and then the patient is discharged back to their GP. I think for this reason, it really is vital that the new guidelines place appropriate responsibility on GPs to monitor and support their ME patients.* *Again, if specialist ME/CFS services are expected to do home visits for patients then the cost of this will be much higher in CCG areas that cover a more rural population. I anticipate some of the CCGs stakeholders highlighting their concerns about costs because of this recommendation."* *'Even the current specialist services that have a consultant doctor are still not fit for purpose. A friend who is under the Royal London College for Integrated Medicine CFS service has told me he has recently been pressurised by the new doctor there to pay for private homeopathy! Previously he saw D* who gave him his formal ME diagnosis, but*	

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				apparently this consultant has since left the service. The new doctor refused my friend the opportunity to see the service's physiotherapist, citing his existing clinical depression (which predated his ME and never caused him the ME symptoms or PEM) as a reason for exclusion, despite the fact that Dr only gave my friend his ME diagnosis after a full consultation and exclusion testing (a much more rigorous work-up than I was ever given).* [*https://www.uclh.nhs.uk/OurServices/ServiceA-Z/INTMED/IMCFS/Pages/Home.aspx*](https://www.uclh.nhs.uk/OurServices/ServiceA-Z/INTMED/IMCFS/Pages/Home.aspx) *I do think we need to be very cautious in what we are hoping to get from any 'specialist ME/CFS team' after the finalised guideline. If you look at the information provided by the above clinic, it seems to be a 'near perfect' model as it includes doctors in the team. Yet the reality of what is on offer is far from what PWME need. So much seems to depend on the individual doctors (and presumably other team members). '*	
Local ME	Guideline	General	General	**NICE State;** • We will address the c**linical and cost effectiveness of treatments**	Thank you for your comments and information.

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				• we also plan to review the published evidence on **patient experience and conduct a call for evidence so that harms are identified and taken into account by the committee.** **But how and when?** https://www.s4me.info/threads/nice-guideline-draft-section-1-11-managing-me-cfs-part-1-energy-mgmt-physical-mtce-physical-activity.17852/page-12 •Quote ME is a serious, chronic, and distressing disease, with minimal understanding of the underlying process and its causes, and no specific treatment or cure. • PEM is the key clinical feature of the disease, and understanding it and how to manage it (to the extent it can be understood and managed) is currently the main clinical means for reducing the overall impact of the disease. • Patients should remain as physically active and socially engaged as their symptoms allow, with a good safety margin, but not push themselves beyond that. This typically means a major, and sometimes extreme, reduction from pre-ME levels of activity and engagement. • Clinicians should help where they can with generic symptom management, support for accessing social services and dealing with medico-legal issues, and standard medical management for other existing or possible medical issues. • Reputable established patient groups and organisations can be useful sources of info and support, particularly early on	See Evidence reviews F,G and H for the evidence and committee discussions on the clinical and cost effectiveness of treatments and the evidence on the experience of interventions. The committee agree that self-help groups, support groups and other local and national resources for people with ME/CFS can provide useful information and include this in the information and support section of the guideline. *Training* The final recommendation in this section is clear that training should reflect current knowledge so that health and social care professionals can maintain continuous professional development in ME/CFS relevant to their role so that they provide care in line with this guideline. The development of training programmes by ME/CFS specialist services reflects the evidence in Evidence reviews A and B and the committee's experience that ME/CFS specialist services provide valuable training, information and support to non-specialists and people with ME/CFS. The recommendation includes that programmes should be developed with input from people with ME/CFS.

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				when the patient is first learning about the disease and how to live with it. This can be found on pages 145-147 of the Table (at link above), and is in response to a comment from Hope 4 ME & Fibro Northern Ireland. The same or similar sentences appear throughout the NICE response table, this is about the most comprehensive I've found (well done Hope 4 ME & Fibro NI) This is possibly the most obvious; A bit of a catch 22, or is it a chicken and egg, situation. **The current 'experts' needing retraining before they can advise on any training material.** **Patients should not be referred for 'specialist treatment' unless those administering it have been retrained.** Revision of existing training material is a problem when; a) (as Dr Muirhead found out) a lot of medical schools are unwilling to disclose the information. b) materials used are based on out-dated, un-evidenced theories that are still being disseminated and presented as 'evidence based' by 'the experts'.	
Local ME	Guideline	General	General	Members of the S4ME forum within LocalME endorse what Science For ME said: ↑ 1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why. We have proposed that it is essential, if this new guideline is to be effective that there be a change in orientation of multidisciplinary teams. CBT or OT run therapy focused teams providing individual and group multiple sessions based on a psychological and behavioural model will need to be closed down and their staff redeployed. New physician led medically focused teams will	Thank you for your comment. *Service design* This guideline focused on clinical recommendations and the committee did not comment on the delivery of services, which can be determined locally. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS. *Training* The section on Training for health and social care professionals recommends that all staff delivering care to people with ME/CFS

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				need to be set up, modelled on, and possibly in some instances sharing some staff and facilities with, those provided for other chronic disabling physical diseases such as MS and Parkinsons' disease, with a specialist nurses better qualified to assist patients with activity and symptom management and dealing with social and care needs. Can't see why there is any additional cost, certainly in the long run. If the psycho-behavioural approach is ineffective then surely it must also be uneconomic. 'Understanding', Expertise/testing and facilities /resources are/is also needed to assess the evidence for testing for physiological response to exercise, testing for mitochondrial dysfunction and other abnormalities in energy metabolism, oxidative stress, immune abnormalities, gastrointestinal abnormalities, imaging for cerebral blood flow deficits and intracranial hypertension, small fibre neuropathy, abnormalities in visual processing, abnormal gait pattern and so on. We believe that only a multidisciplinary compositional service will provide the expertise necessary to ensure that appropriate clinical assessment and treatment for ME, based on evidence from robust clinical and scientific research, are delivered as part of the guidelines **adoption by services**. Science For ME said: ↑ 2. Would implementation of any of the draft recommendations have significant cost implications? There will need to be initial significant redeployment and retraining as the skill set in	should have training relevant to their role so that they provide care in line with this guideline. To note the training recommendations have been edited. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. guideline highlights areas where resources should be focussed. Your comments will also be considered by NICE where relevant support activity is being planned. *National NHS initiative* A national NHS initiative is beyond the remit of NICE.

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				teams is reoriented away from a psychotherapeutic and behavioural model to a medical and activity management model. But the reduction in money wasted on long courses of ineffective CBT and GET therapies, and more effective management should lead to no extra increase in costs once the new teams are trained and established. Serious consideration should also be given to informing all past users of clinics based on the old CBT/GET treatments that the treatment they were given is now no longer recommended and has been recognised as ineffective and may in some cases have led to worsening symptoms. Similarly patients managed by GP's with advice to 'try to get more exercise' will need to be informed that this is inappropriate and offered support and up to date information. Just as with any medication that is withdrawn, the NHS has a responsibility to recall patients for a review and transfer to the new management approach. These will have significant costs, which will require allocation of extra funding for the transition phase. This is fully justified on the basis of the severity and long term nature of ME/CFS, and should, in the long run, save NHS money that has hitherto been wasted on late diagnosis and sometimes lengthy and ineffective therapies, which have led to worse long term	

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				outcomes and higher costs to the state in caring for people who were wrongly advised and became much sicker. Science For ME said: ↑ 3. What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.) A National NHS initiative to update all CCG's about the new approach and the new model of clinical team needed. National training courses for all staff deployed to implement the new model of care should be provided both online and in person, and new information materials written for clinicians and patients. National provision of materials and training courses for medical students, GP's and GP trainees with direct contact with all medical schools and GP practices to disseminate these. We suggest the education group of the CMRC and the MEA should play a lead role in providing such materials. This should not be left to local CCG's to produce their own training and materials, as most will not have appropriate staff with up to date knowledge, and there is a real danger that they will resort to assuming current providers of ME services will be willing or able to change their practices. It would also reduce the cost of unnecessary duplication of effort.	

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Local ME	Guideline	General	General	Fibromyalgia and Connective Tissue Disorders Latest: The 2nd International Virtual Congress on Controversies in Fibromyalgia 19-20 November 2020 Hutan, Nov 16, 2020 Latest: Genesis and dissemination of a controversial disease: chronic Lyme, 2020, Gocko et al cassava7, Nov 3, 2020 Endocrine: Thyroid, Adrenal, DiabetesImmune: Autoimmune and Mast Cell Disorders Latest: Mast Cell Activation Syndrome (MCAS) - discussion thread Mij, Nov 7, 2020 Latest: Epilepsy and non-epileptic or dissociative seizures (FND?) rvallee, Sep 27, 2020 Vitamin B12, D and other deficiencies ME and CFS as a reportable condition? .-'*Since April 2018, SNOMED CT UK Edition has been the mandatory terminology system for use in NHS primary care, replacing the Read Code (CTV3) terminology system, which is now retired. SNOMED CT UK Edition is scheduled for adoption across all clinical, secondary care and mental health settings from April 2020."* https://dxrevisionwatch.com/about/ **Further observations** A little backtracking and history here-and a pointer that we need to interrogate and understand the processes which result in 'People and Teams' & NICE, if things are to work in our favour..... **'NHS People and Teams'** (ie the remaining remnants of the **ME Services** roll out in 2004) - (some of which were steady pairs of hands, like Terry Mitchell's clinic in Norfolk& Suffolk and his regional steer in Cambs and Peterborough) -	Thank you for your comment and information. To note the text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) has been added to the context.

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				have essentially been wiped out in the various PCT/CCG's / NICE directed service requirement 2008 - and 2010 shake down of NHS Services by this Tory Government and Landsley 'reforms'. **BACME. and it's insidiousness** Most of the services and staff were/are steered by **BACME**. Those remaining services exist in a parlous state, if at all. Many services are delivered by **'Social Enterprise' arrangements** who operate essentially like private medicine care services constrained and exempt from FOI etc making decisions behind closed doors...... GPs and GP Federations likewise. We now have the perceived reversal of the 2010 Landsley 'reforms' - with the **Sustainability and Transformation programmes** - and **Alliance arrangements** which are responsible for contracting and commissioning services. Very few patient led, patient endorsed service development arrangements/working groups exist, or if they do, they are likely to be are fobbed off or forced into a waiting game [redacted] The journey in creating people and teams which can deliver what we want and need is fraught with hurdles and problems, NICE or no NICE! **The current flavour of the month** The current flavour of the month is 'covid services' and some funding available and an imperative. Likewise IAPT and FND and MUS....... apologies for acronyms. NICE is guidance and CCGs and Alliances will take it or leave	

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				it... if they choose to...... and many will. Don't get us wrong- I think the challenge to NICE and the BSP was an imperative and necessary. We have won the battle but the war is about to begin. **There are very few good clinical leads and precious few doctors will to put their heads above the parapet and chose ME and CFS in their career move**.	
Local ME	Guideline	General	General	**Our Situation from a Suffolk perspective** Here in Suffolk the patients' working group is already thinking on it's feet about the need to exert it's influence on the situation currently and to use NICE to our advantage. We are perhaps more fortunate than others in that we have some willing ears in the Commissioning and Contracts Teams at a senior level to influence the Board, Clinical Exec and the Alliance Strategy and Transformation work. We have laid some foundations for a proper MDT and service hoping that NICE would be the icing on the cake and justify our stance. So thank you to patients and other Guideline Committee members who have had to fight the fight on this.......We will soon know whether all the planning has paid off or if we need to go back to the drawing board for our Service Model in the future. Like long COVID, ME/CFS is an intractable, heterogeneous condition. Its causes are unclear, preventing long-term effective treatment. The urgent need for high-quality, imaginative and ambitious research should therefore not be undermined by downplaying the current impact of this condition on millions of people around the world. https://www.nature.com/articles/d41586-020-03136-0	Thank you for your comment and information.

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				In our quest to help people with long COVID, let's be candid in our portrayal of ME/CFS, the ongoing struggles of those with the condition, and its uncertain prognosis specifically testing for and excluding symptom-crossover conditions, which should be a starting point. At least our Norfolk & Suffolk 2009Patient Survey outcomes are now endorsed by NICE (in 2009 we were on the cusp of achieving our goal, a patient centred and endorsed MDT with a consultant) Stymied and snuffed out by the NHS reforms in 2010. BPS GET / CBT has always been the insurance lobby's projection, likewise the first recourse of many who would shortsightedly seek to cut costs without achieving the primary objective of attending to the sick with compassion, relieving suffering and promoting healing where possible. In fact the stakes are higher than ever for the insurance industry with the prospect of many thousands of Long Covid sufferers presenting benefit claims potentially costing billions over the next few years. **I expect the insurance parasites will spend whatever it takes to delay the new guidelines for as long as possible.** investigative journalism and scientific commentary, along with the work of our advocates and patients has at last highlighted the real problems. https://www.bbc.com/news/uk-scotland-54893317 Covid in Scotland: No clinics for thousands of 'long Covid' patients	

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				Thousands of Scots could be living with so-called "long Covid" with no early prospect of specialist treatment. A BBC investigation found no health boards in Scotland are offering dedicated long Covid clinics. Existing services such as physiotherapy are being used instead and only two health boards are working on long-term strategies. The Scottish government has said it is funding more research and guidance before finalising a treatment plan. [redacted], welcomed the proposed change in advice. 'Since the last guideline was published in 2007, a significant body of research has been published which highlight **the dysregulation of biological systems in ME/CFS. These changes cannot be explained by deconditioning, so our NHS service has for some time been moving away from a GET approach**	
Local ME	Guideline	General	General	**'Safeguarding** Training and experience in ME/CFS' is not sufficient. Health and social care professionals doing this work must have completed a course about ME/CFS that is consistent with this guideline. If they are not adequately informed, they can do a huge amount of harm. Add 'up to date' and 'in accordance with this guideline' to training and experience. And 'ensure that professionals are aware that ME/CFS is a medical, not a psychological or behavioural condition'.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. In the principles of care section of the guideline the committee raise awareness that ME/CFS a complex, chronic medical condition affecting multiple body systems.

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				Add 'involve a health professional of the patient's choosing' Or advocate or carer. Sadly for children this broadly reflects the status quo and is a very dangerous place- retraining of professionals is required, and for some, that is a huge paradigm shift.	The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.
Local ME	Guideline	General	General	**Co-morbidity /Co morbid conditions** Include a link to migraine, a common co-morbidity. Other comorbid conditions include IBS, and gastroparesis, particularly in severe patients (maybe seen as a complication of ME/CFS rather than a separte comorbidity POTS may also be seen as comorbid or part of ME/CFS orthostatic intolerance. ? does NICE refer to NHS advice pages if no NICE guideline exists? Mast Cell Activation Syndrome? small fibre neuropathy - research by Systrom. the patient's ME	Thank you for your comment and information. The discussion section of Evidence review D- Diagnosis includes a list conditions that commonly occur in people with ME/CFS and includes migraine. The NICE guideline on headaches in over 12s includes migraine. The NICE guideline on irritable bowel syndrome (CG61) has been added to the list of NICE guidelines for co-existing conditions.

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				specialist, as some treatments will need to be managed differently due to ME. Ideally those that are common comorbidities which can also be seen as part of ME, like POTS, could be diagnosed and managed by the ME specialist to reduce the number of hospital visits and interactions. **IBS Gastroparesis**- Isn't mentioned? IBS symptoms are quite common though. patients do have these as co morbid conditions. Gastroparesis seems to be mentioned more commonly in severer patients. There are meds & treatment for IBS or just for stomach cramps / diahorrea / constipation; shouldn't PoTS be listed as a co morbid condition? There's an orthostatic intolerance section in managing symptoms 1.11, but PoTS, NMH etc is a separate condition in its own right? So shouldn't GPs be aware of this as a co morbid condition? There is currently no NICE guideline for PoTS or orthostatic intolerance, and no advice there about how to get any kind of treatment for PoTS, or where to refer to. So GPs will be baffled and if patients are very ill or otherwise don't know, they won't get treatment. I didn't learn about the PoTS U.K. website until years later. PoTS U.K. is the only resource as far as I know with a list of doctors. At first I wasn't sure if this would be acceptable in the guidelines but I had a look at the actual NHS website for PoTS and even they signpost to it: "**When to get medical advice** See a GP if you think you have PoTS. could discuss a referral with a GP."	The managing co-existing conditions section of the guidelines only refers ot NICE guidance. *Orthostatic intolerance* The committee did not make any recommendations on the management of orthostatic intolerance noting that although this can be straightforward it this can involve advice on diet, carrying out daily activities and activity support and should be tailored to the person taking into account their other ME/CFS symptoms. The committee noted medicines usually prescribed for OI can worsen other symptoms in people with ME/CFS and should only be prescribed or overseen by a clinician with expertise in orthostatic intolerance. (see evidence review G). In the definition on orthostatic intolerance a sentence has been added to highlight the impact of severe orthostatic intolerance. *Add orthostatic hypertension.* These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added

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				So since the NHS website mentions it, I think it should be ok to include, in the absence a NICE guideline for **PoTS or orthostatic intolerance**. Or at the very least, tell GPs to refer to the NHS webpage for PoTS!" Is there any mention of mast cell activation syndrome as a common co-morbid condition, particularly in the more severely ill patient?. David Systrom mentions they find small fibre neuropathy in around half the patients he sees with ME - who invariably have preload failure. Dr Bansal in the Remember ME conference was talking about peripheral thyroid and adrenal resistance in ME. **Managing orthostatic intolerance** We are pleased to see this information included. Patients may have orthostatic intolerance that is not explained by easily measured heart rate and blood pressure abnormalities. (Can draw on the studies that have come out - Rowe on cerebral perfusion). In those with severe and very severe ME, orthostatic intolerance may be very severe, including not being able to sit up for more than a few seconds or minutes, or at all. (check - I think this was noted in an earlier section - might be redundant to repeat it) I think the Orthostatic intolerance section should include: • Patients may have orthostatic intolerance that is not explained by heart rate and blood pressure abnormalities. (Can draw on the studies that have come out). • In those with severe and very severe ME, orthostatic intolerance may be very severe,	

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				including not being able to sit up for more than a few seconds or minutes, or at all. This is very important to include because even doctors treating PoTS have been surprised / sceptical as to how little I can sit up. This is not caused by PoTS or NMH or OH. People with just PoTS can stay upright for more than a few seconds or minutes. They do not rapidly deteriorate if forced to stay upright for a few seconds more **Orthostatic intolerance types** - add orthostatic hypertension. Some people with ME/CFS experience orthostatic hypertension and the treatment is different to hypotension. 3 Many doctors are not familiar with treatment details related to orthostatic intolerance and may be unwilling to test for it and make a referral. Pacing with a heart rate monitor- Expert patients find this can be a very effective way to manage your symptoms and PEM. If you are considering dipping your toe into pacing with a heart rate monitor there are a lot of resources on the public HRM4Pacing page. neuropathic pain and headache guidelines "Treat pain to provide symptomatic relief and, if needed, investigate to rule out other conditions." 31, 38	
Local ME	Guideline	General	General	**No reference to NICE guideline on migraines. Migraine are very common and can often be effectively treated. Chronic daily migraine can be misdiagnosed as ME. Not specifically referring to this is an omission.** People with ME/CFS also experience other types of pain (e.g. ? - do we know if PEM body pain is neuropathic?) - there is no guidance on how other types of pain should be treated. 10	Thank you for your comments and information. *Pain* *Migraines* Migraines has been added to the list of differential and coexisting conditions in the Evidence review D-Diagnosis. *Types of pain*

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				People with ME/CFS deal with chronic pain and are often unable to engage in activities that could distract from the pain - this makes pain relief particularly important. Opiates are crucial for quality of life for some people with ME/CFS; access to these needs to be protected. The NICE pain guideline only refers to tramodol in rare acute cases. 12, 13 Managing nausea **Medicines** Dietary management and strategies Monitor people with severe or very severe ME/CFS who are at risk of malnutrition or unintentional weight loss because of: • restrictive diets • poor appetite linked with altered taste and smell • food intolerances • nausea or difficulty swallowing and chewing. Rest and Sleep **Managing nausea** **Training** I think there does need to be a lot more clarification on the retraining and how this can be implemented from what, from our perspective, is a starting point of below zero. Dr Murhead's module is as far as I know the only decent resource (UK based) and the situation with the existing network of fatigue clinics and specialist teams is basically one of institutionalised prejudice/bias against us. How do those medics snap out of the internalised messages they have been trained into and start to trust us, listen to us and respond with compassion and in the way they would if we had HIV, Parkinson's or cancer? We have all been on the receiving end of this sceptical and dismissive (at best) attitude, and know only too well the messages that doctors even outside of CFS services have taken on board. Due to their attitudes and our marginalised	The committee linked to NICE guidance that was relevant to people with ME/CFS, the committee acknowledged that this does not address all the type of pain that people with ME/CFS may experience. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate. Although pain relief was included in the protocol for pharmacological interventions no evidence was identified and the committee agreed they were unable to make any recommendations for specific medications. Training The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.

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				status many have not the first clue what our experience is and there is a massive amount of trust building to be done. I am pleased to see this somewhat acknowledged in the guideline, and the recommendation of the use of video of patient experience, but we need to be involved in the production of those. The Dialogues of a Neglected Illness videos are a great start. Can medical education be built around these two resources and will the NHS start there or ignore them? The following is from the 2007 GDL: "1.1.1.3 Healthcare professionals should be aware that – like all people receiving care in the NHS – people with CFS/ME have the right to refuse or withdraw from any component of their care plan without this affecting other aspects of their care, or future choices about care." Despite the above, families were being threatened with Social Services for withdrawing their youngsters from clinics, or even for letting them use their phones too much!! As you can imagine we've been asked on a number of occasions what this means for trusts and CCGs working with NICE guidance and quality standards. First of all, it doesn't change anything in relation to NICE technology appraisals. These still require funding to be made available within 3 months of the publication of the appraisal. This is reflected in the NHS Constitution, which states that patients have the right to drugs and treatments that have been recommended by NICE for use in the NHS, if their doctor believes they are clinically appropriate. There are rare circumstances when the 3 month period is extended. To help people understand more clearly what compliance means in relation to NICE technology appraisals we've recently produced a guide to compliance. This should prove	

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				really helpful to trusts and CCGs to understand how they can assess compliance with NICE technology appraisals.	
Local ME	Guideline	General	General	Specific points and comments about terminology - 1.1.8 Add to list Allergy intolerances possible Mast Cell activation - 1.1.9 Suggest use of Use of ICC and 'CC check sheet ''10 steps and severity scales' which were shared at the scoping meeting - 1.1.10 Personal care and support for people with severe or very severe ME- How when there are no domiciliary services and GP's don't do home visits? - 1.2.2 ~~psychological~~ wellbeing assessment -replace psychological with social, emotional, Quality of Life wellbeing assessment - 1.2.3 'fatigability' -replace severe physical & mental fatigue - 1.2.5 suggested reword -best practice precautionary approach redu - 1.2.7 'appropriate specialist' - What specialist -few exist! NO ME accredited training or focus in medical school. Inadequate CPD courses exist for up skilling. Those that are good (e.g. Invest in ME) are inadequately attended by GPs. - 1.2.8 refer them to a paediatrician - ME trained /new NICE compliant- write to the child or young person's place of education or training to advise about flexible adjustments or adaptations. Advising ME considered - disability recognised under legislation requiring suitable arrangements	Thank you for your comments. 1.1.8 These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added. 1.1.9 These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added. 1.1.10/1.5.5 The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The committee agree that there is variation in the delivery of home visits across the NHS but these recommendations will provide equity of access for this group, particularly for people with ME/CFS who have difficulty with leaving or are unable to leave their homes.. 1.2.2/1.5.1 After considering the range of stakeholder comments this has been edited to,'an assessment of the impact of symptoms on psychological, emotional and social wellbeing'

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				- 1.4 Diagnosis - 1.4.2 Diagnose ME/CFS in a child, young person or adult who has the symptoms in recommendation 1.2.3 that have persisted for 3 months. After a diagnosis, refer adults directly to a specialist team experienced in managing ME/CFS to develop a ~~management plan~~ Replace throughout with Care Plan or Education and Health Care Plan - 1.5.1 record a holistic assessment- NHS don't embrace holistic approaches! the impact of symptoms on ~~psychosocial~~ wellbeing -replace with social and emotional People with severe or very severe ME/CFS 1.5.5 Home visits- GP won't currently see patients face to face- They don't do domiciliary visits- nor do Primary care consultants and most paediatricians. 1.7 Safeguarding 1.7.1 Safeguarding assessments in people with confirmed or suspected ME/CFS should be carried out or overseen by health and social care professionals who have training and experience in ME/CFS -don't really get training - doesn't exist! 1.7.3 If an assessment under the Mental Health Act 1983 or the Mental Capacity Act 2005 is needed, - If people were trained properly this should never occur with ME and CFS-This is a contentious area as trained -Trained HCP don't exist - no training 1.7.4 Children and young people Caution if ME is considered or formally diagnosed 1.8.7 Maintaining independence – Social Care is virtually impossible to secure appropriatedl9 APPG Barriers to Access 2026/ Report	1.2.3 After considering the range of stakeholder comments this has been edited to, 'debilitating fatigue'. 1.2.5 The committee did not agree that your suggestion added any further clarity to the recommendation and has not been added. 1.2.7/1.2.8/1.7 The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services , to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS. 1.2.8 The section on supporting people with ME/CFS in work, education and training has further information on how adjustments and adaptions can be accessed.

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				1.9.4 Health and social care professionals should work with training and education services to: enact Disability and legal framework entitlement 1.9.5 Give parents and carers information about education, health and care plans and how to request one from their local authority - Care Education and Health care Plan 1.11 Managing ME/CFS Re phrase- Be aware there is no ~~current treatment or cure (non-pharmacological or~~ BUT pharmacological needs should be met for ME/CFS with symptom control for common presentations People with severe or very severe ME/CFS – endorse response by 25% group.	*Equality Act 2010* In the supporting people with ME/CFS in work, education and training section of the guideline there is direct reference to the Equality Act 2010 and how it could support people with ME/CFS. 1.4.2/1.5.1 Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) 1.9.5 In the section on *supporting people with ME/CFS in work, education and training* there is a recommendation to give parents and carers information about education, health and care plans (EHCPs) and how to request one from their local authority. 1.11 After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Local ME	Guideline	General	General	**This is all we had time for regrettably- we support 25% comments for severely affected** **Appendix A** Regarding Consultations,"Where it is appropriate, and enables meaningful engagement, conduct 12-week formal written consultations, with clear explanations and rationale for shorter	Thank you for your comment. The consultation period was the standard length for consultations on NICE guidelines as set out in Developing NICE guidelines: the manual. An e-mail was sent to all stakeholder groups in August 2020 to confirm the consultation dates when they were

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				time-frames or a more informal approach." The Compact (Cabinet Office 2010) para 2.4) https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/100807/file47158.pdf https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/255180/Consultation-Principles-Oct-2013.pdf 'Time frames for consultation should be proportionate and realistic to allow stakeholders sufficient time to provide a considered response and where the consultation spans all or part of a holiday period 2 policy makers should consider what if any impact there may be and take appropriate mitigating action. The amount of time required will depend on the nature and impact of the proposal (for example, the diversity of interested parties or the complexity of the issue, or even external events), and might typically vary between two and 12 weeks. The timing and length of a consultation should be decided on a case-by-case basis; there is no set formula for establishing the right length. In some cases there will be no requirement for consultation, depending on the issue and whether interested groups have already been engaged in the policy making process. For a new and contentious policy,12 weeks or more may still be appropriate. When deciding on the timescale for a given consultation the capacity of the groups being consulted to respond should be taken into consideration. However, longer and more detailed consultation will be needed in situations where smaller, more vulnerable organisations such as small charities could be affected. The principles of the Compact between government and the voluntary and community sector must continue to be respected 1 1. Where it is appropriate, and enables meaningful engagement, conduct 12-week formal written consultations, with clear explanations and rationale for shorter time-frames or	amended. We are grateful to your organisation for engaging with the consultation and for the comments you have submitted.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

10 November 2020 - 22 December 2020

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				a more informal approach." The Compact (Cabinet Office 2010) para 2.4) https://www.gov.uk/government/publications/consultation-principles guidance https://www.gov.uk/government/publications/consultation-principles-guidance (2012) https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/2695/code-practice-consultations.pdf https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/100807/file47158.pdf	
Local ME	Guideline	General	General	**LocalME Stakeholder -Final Statement under general comment** This is all we had time for regrettably. * We have serious concerns about NICE and their processes for consultation. * We support 25% comments for severely affected * Wish it known that absence of our comments in the form below does not mean agreement with the guideline as it stands as we support the S4ME comments in absence of our own through lack of time.	Thank you for your comment. The consultation period was the standard length for consultations on NICE guidelines as set out in [Developing NICE guidelines: the manual.](#) An e-mail was sent to all stakeholder groups in August 2020 to confirm the consultation dates when they were amended. We are grateful to your organisation for engaging with the consultation and for the comments you have submitted.
Local ME	Guideline	General	General	13 1.10 Multidisciplinary care 14 1.10.1 Provide care for people with ME/CFS using a coordinated multidisciplinary 15 approach. Based on the person's needs, include health and social care 16 professionals with expertise in the following:	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

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				Whereas the causes of ME are likely to be multiple, it is paramount that vector-borne infections have not been overlooked in ME patients, and referrals to infectious disease specialists should be a priority. There is a definite possibility that many or all symptoms of ME may be the result of bacterial or viral infections that have not been treated adequately, or not detected, and it is known that that some infections are hard to diagnose by present testing methods. It will be increasingly necessary to realise the financial implications to the NHS, and to individual doctors, of legal actions by patients pertaining to misdiagnosis. A class action lawsuit on behalf of Lyme disease patients has won substantial damages in November 2020 from the Infectious Disease Society of America (IDSA). Further actions are to be taken against 7 individual IDSA doctors due to missed or incorrect diagnoses and treatment of Lyme disease. Some infections, particularly vector-borne infections and parasitic infections, are presently regarded as being so rare that they are not routinely tested for. Failure to recognise their presence most often leads to chronic illness, including post-infection fatigue and many symptoms within the criteria for ME. The committee assumes that adequate criteria exist under NICE guidelines for diagnosing and treating Lyme and chronic infections, and thus assumes that Lyme and tick-borne infections have already been ruled out Page 58, Line 10: " tuberculosis, Lyme disease and post-Lyme syndrome, other chronic infections" https://www.nice.org.uk/guidance/gid-ng10091/documents/evidence-review-4	emphasise the importance of using clinical judgment when deciding on additional investigations. The same section of the guideline reinforces that where the interpretation of signs and symptoms is unclear the advice should be sought from a relevant specialist about referral. The discussion section of Evidence review D- Diagnosis includes a list of differential and co-existing conditions that commonly occur in people with ME/CFS including infections and infections – related disorders with Lyme disease listed.

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				But it is paramount that the committee acknowledge that, compared with the tools available for diagnosing the other conditions listed (page 58 above), Lyme disease diagnostics are not well established or straightforward. The NICE guidelines for Lyme disease are suitable for managing acute cases but do not encompass chronic cases, and rely completely on unreliable diagnostic tests. Also, it has not been a routine diagnostic procedure in practice to rule out Lyme disease in ME patients. The 2007 NICE Guidelines for ME/CFS did state that the physician must consider ruling out Lyme disease – but there was the caveat that testing was discretionary if the physician believed the patient had a low risk of encountering Lyme borreliosis. However, only a very low number of GPs and consultants have availed themselves of the CME tool on Lyme disease, https://www.rcgp.org.uk/clinical-and-research/resources/toolkits/lyme-disease-toolkit.aspx and when they go through this online CME training course, they will be linked to information from Public Health England stating that the estimated incidence of Lyme disease is only 3,000 cases per year, of which a mere 1000 cases are detected. This is a gross underestimate which has not been based on the most recent in-depth epidemiological reasoning. 3,000 cases a year would keep Lyme disease almost within the category of rare diseases, whereas 30,000 cases a year estimated by VIRAS, https://tinyurl.com/ybpmnuqf) and 132,000 cases a year (Cook and Puri 2020, (https://doi.org/10.1016/j.idm.2020.10.004) change the whole picture and reveal a disease of some significant risk to the public.	

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				The global incidence of tick-borne and other vector-borne infections has increased dramatically over the last 10 years, and even in urban areas in the UK, patients have been infected from a tick in their own back garden or local park. https://www.hackneycitizen.co.uk/2019/08/08/council-warnings-ticks-woman-lyme-disease-clissold-park/ The fact that the predicted incidence of Lyme disease cases could be up to 2 orders of magnitude higher that the number of cases actually recorded, should be a warning sign when considering the thousands of infected patients with no diagnosis, but who are suffering to various degrees with multiple symptoms, and that a high proportion of those patients will quite understandably meet the criteria for ME and/or Fibromyalgia. The hallmark skin rash associated with Lyme borreliosis, and pathognomic for the infection, may be seen in only 60% of cases. https://www.ncbi.nlm.nih.gov/pubmed/21117376 This could be an overestimate, as the original Connecticut epidemic in the 1970s reported that the rash occurred in only 25% of cases. http://www.ct.gov/dph/lib/dph/infectious_diseases/lyme/1976_circular_letter.pdf) It is impossible to know the true incidence of the rash, given that such a high proportion of patients with Lyme borreliosis are never examined in the first few weeks after a tick bite when the rash might appear, but other more serious symptoms have not become apparent. VIRAS has been regularly and constantly checking not only	

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				the biomedical research on ME, but also the social media platforms used by ME patients, for over 15 years. We have found that it is extremely rare for ME patients to have been tested for Borrelia infections, despite the diagnostic criterion listed in the 2007 guidelines. Even more rare is testing for Bartonella, Babesia Ehrlichia/Anaplasma, and Borrelia miyamotoi, all of which are known to be delivered by the same tick bite causing illness in Lyme patients. https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0004539#sec014 The term Lyme disease should more properly be known as Lyme borreliosis complex, due to the fact that expert doctors and research scientists have shown that 53% of tick-bite victims have at least 1 co-infection, and 30% have 2 or more pathogens as well as Borrelia causing their illness. https://www.lymedisease.org/lymepolicywonk-study-finds-coinfections-in-lyme-disease-common-2/ Two recent surveys of Lyme disease patients by VIRAS (https://www.mediafire.com/file/2wzd0ge3gokjsez/VIRAS_LB_Patient_Survey.pdf/file) and Fight Lyme Now (https://www.linkedin.com/pulse/fight-lyme-now-uk-disease-survey-diagnosis-treatment-cost-newton?fbclid=IwAR3Vg5OLvHXWzKzYDSD4o3Sv6IngrmsMWpvkFsgevQk9-GR66rcQebPxn-8) have shown that a high percentage of Lyme patients were previously diagnosed with ME, and many only discovered that they had Lyme and/or another tick-borne disease after a long time of illness. Their misdiagnoses were often only revealed after they had paid for private tests in highly-accredited but non-UK laboratories.	

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				Primary screening tests for Lyme borreliosis in the UK uses tests which have the disclaimer that a negative result does not rule out the presence of the infection. The sorry state of affairs with respect to Lyme tests in the UK and Europe is summarised by Leeflang et al, 2016 thus "the data in this review do not provide sufficient evidence to make inferences about the value of the tests for clinical practice. " https://doi.org/10.1186/s12879-016-1468-4 and by Cook and Puri, 2020, thus: "For early-stage/acute LD samples, the probability of a false-negative result is 80.3% for a single ELISA test and increases to 85.9% with the two-tier test. This indicates that in early-stage LD, false negatives are 65 times greater than for HIV testing. For late-stage LD, the two-tier test generated 16.7% false negatives compared with 0.095% false negatives generated by a two-step HIV test, which is over a 170-fold difference. Using clinically representative LD test sensitivities, the two-tier test generated over 500 times more false-negative results than two-stage HIV testing" https://doi.org/10.2147/IJGM.S131909 We therefore advise that a more rigorous process is set in place for the investigation of ME patients for vector-borne infections. This is reasonable, in view of the high probability that ME patients, and their doctors, will encounter difficulties with the lack of recognition that these infections are much more prevalent than is generally realised, and that obtaining an accurate diagnosis through the present NHS serology is not totally reliable. Physicians are unfortunately in a difficult position when they cannot rely on the standard serological tests, but they have a duty to avail themselves of the burgeoning information	

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				available from the published international literature by experts in the field of tick borne disease. The treatment and care of patients with ME may be better tailored to their needs, once the original infection from a tick bite has been identified, given that there is much evidence for subtle changes in the immune profile of patients with Lyme or post-treatment Lyme syndrome. https://doi.org/10.3389/fmed.2020.00568	
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	004 General	3 General	We are very concerned about the change in the name of the diagnosis as it is potentially confusing for patients who already have a diagnosis of "CFS/ME". It could also be confusing for families and those who support paediatric patients e.g. school staff. There does not appear to be an explanation for the change of the name of the diagnosis. The evidence base for any change in name should always be clarified for patients and health professionals.	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'*
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	009	21	We are surprised and concerned that there are no specific recommendations about the baseline screening blood investigations (in line with the current NICE Guidelines and best clinical practice) that need to be undertaken to rule out other causes of fatigue before diagnosing with CFS/ME. Clinicians find it incredibly helpful to have the basic list of blood results to begin the process of diagnosis, and we are concerned that not having this list will delay diagnosis because	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses and to tailor management appropriately. Taking into consideration the stakeholder comments the committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and

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				of the lack of clarity and direction. This is a particular issue for those who are not skilled/experienced in recognising CFS/ME and who have less understanding about the other possible causes of fatigue.	the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. In addition the committee have added that ME/CFS should be suspected if the, 'symptoms are not explained by another condition.
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	010	5	In practice, the advice regarding the management of symptoms should not be given if the diagnosis is only suspected (and not yet formally diagnosed). A diagnosis should be given following appropriate investigations supervised by a doctor prior to advice being given. Advice can then only be given once an assessment of the particular presentation of the individual has been conducted so that it is appropriate to the individual.	Thank you for your comment. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. See Evidence review D- for the evidence and committee discussion. However after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted for the following reasons: ○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis. • Further investigation/differential diagnoses. The committee agree it is important to exclude other diagnoses and

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					recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have added examples of investigations to be done when suspecting ME/CFS and have added that ME/CFS should be suspected if the 'symptoms are not explained by another condition.'
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	010	9	From our clinical experience and best practice it is not appropriate to write to an educational setting to give advice prior to a child being given a formal diagnosis.	Thank you for your comment. The committee disagree, in their experience and I the qualitative evidence early communication with schools and colleges is very important. The committee discussed the risks of an early diagnostic label and noted this recommendation refers to children and young people with suspected ME/CFS and the assumption should not be final diagnosis is ME/CFS. This recommendation is to raise awareness in the short term and allows for further communication when the diagnosis is confirmed.
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	011 General	9-11 General	We are concerned that the term "specialist team" has been used inconsistently throughout the document interspersed with Occupational Therapy and Physiotherapy only intervention. We feel that more consistency is needed. The use of the term "specialist CFS/ME MDT team" would be more appropriate.	Thank you for your comment. After considering stakeholder comments the committee edited specialist team to ME/CFS specialist team to provide clarification.
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline Supporting documentation - Children	015 General General	1-3 General General	We agree with this point but would like more emphasis throughout the document on the more positive outlook for paediatric patients to encourage engagement with the rehabilitation process.	Thank you for your comment.

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	and Young people				
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	018	10	We agree that ongoing communication and consideration of specific circumstances are important, however individual services need to respond to recurrent DNAs according to their Trust attendance and discharge policies, in order to ensure equitable services are maintained.	Thank you for your comment. The committee agree and in the recommendation it underlines the importance of discuss with the person why they could not attend and how the multidisciplinary team can support them.
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	024 General	10 General	Once again it is important to have a positive emphasis. Although it is correct to say energy management is not curative it is important to emphasise that it can facilitate recovery. "Not curative" is negative terminology and may discourage engagement in rehabilitation.	Thank you for your comment. The committee agreed to keep, 'is not curative' at the beginning of the recommendation. In the rationale for managing ME/CFS the committee outline why it is important that it is clear there are not any cures for ME/CFS.
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	024 General	14 General	We would prefer to see the term "assessed baseline" used instead of "Energy Envelope". If the term energy envelope is used we would like an emphasis on the potential for the energy envelope to expand and improve through treatment and rehabilitation. The term is recurrent throughout document.	Thank you for your comments. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	025	18	We are concerned that it is misleading to advise everyone to reduce activity as a first step. Sometimes this occurs but in practice it is critical to establish a baseline and maintain activity within a functional prescribed routine.	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to, agree a sustainable level of activity as the first step, which may mean reducing activity.'
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	026 General	1-7 General	We strongly suggest that this should be stated differently e.g. "Refer to Physiotherapy or Occupational Therapy in these circumstances for assessment of the appropriateness of a specific exercise programme to facilitate an increase in functional physical activity. "	Thank you for your comment. The following section on physical activity and exercise includes further detail about assessment and the programme that should be offered in these circumstances. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much

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				We are concerned that the term "physical activity" is misleading and too generalised. There should be a differentiation between the terms "physical activity" and "exercise" within this document. The use of the term "physical activity" here is misleading as it does not differentiate between functional activities of daily living and an exercise programmes prescribed by a Physiotherapist or an Occupational Therapist aimed at achieving a measurable goal.	repetition results in a guideline becoming unwieldy and unusable. This point is made later and then reinforced in the management section of the guideline and for this reason your suggestion has not been added to the recommendation. After considering the stakeholder comments this recommendation has been edited to include physical activity and exercise.
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	026	9	Change terminology to say refer people to a "specialist MDT team" rather than only Occupational Therapy & Physiotherapy to develop energy management plans.	Thank you for your comment. This recommendation refers to people with severe or very severe ME/CFS and the committee agreed that it was important that the expertise required here to provide support is a physiotherapist working within a ME/CFS specialist team.
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	027 028 028	24 1 8	We agree that exercise is not curative however we are concerned that the text is very misleading and could suggest to patients that they should not be advised to participate in physical activity or exercise at all. An emphasis on the benefits of exercise within a supervised programme monitored and reviewed by an MDT specialist team would be more appropriate and better practice. Immobility due to prolonged rest can have a significant impact on exercise tolerance and function. It is important that patients are given appropriate advice regarding secondary deconditioning. It is important to educate patients regarding how to maintain and increase muscle strength, muscle length and joint range of movement as deemed appropriate following assessment of their energy levels and health needs.	Thank you for your comment. After considering the stakeholder comments, the committee have added exercise into the recommendations on considering a physical activity programme to clarify where these apply to exercise. The recommendation describes the types of physical activity or exercise programmes that should not be offered to people with ME/CFS. The previous recommendation in the energy management section includes that people who would like to incorporate a physical activity or exercise programme into managing their ME/CFS (see the section on physical activity and exercise) should be referred to a physiotherapist or occupational therapist working in a ME/CFS specialist team. The following recommendation in the physical activity section reinforce this and include that if a physical activity or exercise programme is offered, it should be overseen by a physiotherapist in a ME/CFS specialist team.

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					To note after considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	028	12-15	We are concerned that this statement is once again misleading and may suggest to patients that they should not be advised to participate in physical activity or exercise at all. Advice should be based on a thorough assessment of an individual's energy levels and health needs by the specialist CFS/ME MDT team.	Thank you for your comment. After considering the stakeholder comments, the committee have added exercise into the recommendations on considering a physical activity programme to clarify where these apply to exercise. This recommendation is preceded by one in the energy management section that is to refer people who feel ready to progress their physical activity or would like to incorporate physical activity or exercise programme into managing their ME/CFS. To refer anyone would necessitate a discussion between the person and the healthcare professional. The guideline recommends a holistic personalised approach to the care and support of people with ME/CFS and as you note any discussion are specific to the individual.
Manchester Foundation NHS Trust - CFS/ME Service for Children and Young People	Guideline	028	28	We are concerned that this sentence is constructed poorly and should be change. We suggest that instead it should read: "Ensure a patient can maintain their initial activity management plan, which should be based on their baseline assessment, before increasing activity".	Thank you for your comment. This bullet point has been edited to,' maintaining this successfully for a period of time before attempting to increase it'.

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ME International	Guideline	General	General	It appears there is language that may protect patients from graded exercise therapy; however, we were disappointed they did not utilize information based on the International Consensus Criteria (ICC) or the International Consensus Primer (IC Primer). The draft guideline used the 2015 Institute of Medicine (IOM) Report from the US as a basis for its recommendation with some important changes. These changes Include reducing the time for diagnosis to 3 months and instead of PEM using the term post exertional symptom exacerbation (PESE). From draft guidance consultation evidence review: "ME/CFS should be diagnosed in people with the key features (debilitating fatiguability, post-exertional symptom exacerbation, unrefreshing sleep and cognitive difficulties) for 3 months." (Review D - pg 53) ME International does not support the use of the IOM Report for the diagnosis or treatment of people with ME and are concerned that basing the guideline in this report instead of the ICC and IC Primer may leave medical care for UK ME patients in a status quo continuing to provide inadequate care. The draft guideline leaves the more severe ME patients, who are homebound and/or bedbound, left without proper health care. Many of these patients deal with repeated episodes of paralysis, gastroparesis, sensitivities that leave them helpless in darkened rooms, etc. and require in-home care. Treatment guidance in the ME ICPrimer provides information that would help medical professionals give better care. In addition to the IC Primer, the materials created by Greg Crowhurst (https://www.stonebird.co.uk/) for caring for Severe ME patients would be a valuable resource to draw from both	Thank you for your comment. *Suspecting and diagnosing ME/CFS* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. For more detail on the committee discussion about the IOM criteria see Evidence review D-Diagnosis. The committee note in the rationale for suspecting ME/CFS that it is also the combination and interaction of the symptoms with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. *Access to care* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.

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				for the guideline and for medical professionals to work with ME patient caregivers. This link is ME International's Position Paper to clarify our position. https://www.me-international.org/uploads/1/2/7/6/127602984/mei_position_paper_201119_final.pdf Thank you for your consideration. Jim Lutey, President, ME International	
ME Letterforce	Guideline	General	General	ME-Letterforce has found it impossible to comment on the entire NICE Draft Guideline due to the time constraints imposed on us and having the Deadline just before Christmas. We support the "General" comments from Physios for ME 1, 2 and 3 (at the start of their submission) We support the submission from the Science for ME forum (S4ME) but cannot specify parts due to time constraint.	Thank you for your comment. The consultation period was the standard length for consultations on NICE guidelines as set out in Developing NICE guidelines: the manual. An e-mail was sent to all stakeholder groups in August 2020 to confirm the consultation dates when they were amended. We are grateful to your organisation for engaging with the consultation and for the comments you have submitted.

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ME Letterforce	Guideline		6-24	The heading "Energy Management" should be deleted and this section re-written. The techniques described here are APT from the PACE trial. There is no evidence that Energy Management (in the way it is described in the current Guideline) is safe, proven, or effective. There should be a separate section on REST The GP should discuss with patients and explain • It is not curative • That rest should be considered a priority • That they need to balance rest and activity in a technique called Pacing • Rest should not contain activity or stimulation • That they may have a daily rhythm or times when they function best during the day or night which may be different than how they were before. Planning rest for the non-productive times can help • That sleep can be important and sleeping during the day if needed may allow them to manage their symptoms more effectively • That some patients use rest before and after activities to try and cut down the post exertional effects • That rest taken lying down or with the feet up helps some patients • That they may need to do this for the rest of their lives as few people with ME/CFS recover • That deconditioning is not the cause of ME and we have no research to show that people with ME who rest are deconditioned	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS. There is a section on rest and sleep in the symptom management for people with ME/CFS part of the guideline.

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ME Letterforce	Guideline		4-5	We were very happy to see this included. However, the entire section on Management (as currently written) give the impression that Energy Management is really a treatment (although the word is not used), and that activity could be increased this way. It would be useful to mention here after Line 5 that REST and PACING are the two management techniques that patients report as most useful	Thank you for your comment. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Recommendation 1.11.3 includes the assessment and discussion on rest. In addition there is a section on rest and sleep in the symptom management for people with ME/CFS part of the guideline.
ME Letterforce	Guideline	024 - 026	Managing ME General	The Energy Management parts of this section need to be deleted and re-written. The "rational and impact section on managing ME" in this Guideline has no evidence of any successful clinical trials, published research or evidence on so called "energy management" techniques. It is not acceptable to people with ME that management techniques based solely on the experience of some members of the Guideline Development Group be offered which are not supported by good quality randomised trials. This section of the draft Guideline contains points which appear to come from the Manuals used in the PACE trial to deliver APT (Adaptive Pacing Therapy). These sections should be deleted as APT failed in the PACE Trial to improve outcome measures over SMC (Standard Medical Care) to any	Thank you for your comment. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

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				significant level. Removing GET because of the lack of robust evidence but keeping APT (Adaptive Pacing Therapy) which was also tested and failed in the PACE trial is inconsistent.	NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand

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					but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS.
ME Letterforce	Guideline	024 - 026	Managing ME General	This entire section "Managing ME/CFS" should be rewritten to include the management technique called PACING as it was originally developed by ME patients in the 1980's and 1990s. Classic Pacing is different from the APT technique. It requires no professional involvement, no potentially coercive or dangerous agreement plans and is completely within the control of the patient. Pacing (as practices by patients) is simply balancing rest and activity to try and minimise symptoms and relapses. It can be taught from paper handouts and/or internet tutorials and videos. Pacing has been shown as a consistently high ranking management technique in patient surveys. NHS Clinics offering APT and GET and GE could be closed with a saving to the NHS. By offering REST and Pacing to patients early in their disease and the support necessary to use them effectively, we would expect less long term and severely affected sufferers. Dr Melvin Ramsay (who researched and wrote about ME) said that his patients who could rest in the early stages had the best outcomes. REST needs to be recommended as a specific management technique.	Thank you for your comment. Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. *Pacing*

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					The committee discussed the use of the term pacing agreed that it means something different to different people with many different versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it. *Rest* Section 1.12 includes recommendations on rest and sleep.
ME Letterforce	Guideline	022 - 023	Multidisciplinary Care General	The lack of services in England and Wales for people with ME should be considered a national emergency and measures put in place to address this. Some people with ME feel ill-treated, excluded and have been discharged from the current NHS clinics worse than when they started. There are house-bound people with ME who have never seen a Bio-medical Specialist for their disease. The NHS core key principles have not been applied to this group. There is no safe, assessable Multidisciplinary care for people with ME in England or Wales. We propose that a National Centre of Excellence for ME (NCEME) is set up providing multidisciplinary care and the current ME/CFS clinics are closed. The NCEME should be modelled on Multiple Sclerosis Centres with extra services as needed. It could provide a remote and travelling service for people with ME who have no services in their area. In addition we need special wards where patients can be treated for short and medium stays.	Thank you for your comment. The committee agree there is inequity in access to ME/CFS services and throughout the guideline have made recommendations to improve access to care however it was not within the committee's remit to make specific recommendations on service design and delivery. See evidence review I multidisciplinary care for the committee discussion on ME/CFS services.
ME Letterforce	Guideline	0	20-22	It would be more efficient if the aids and adaptations are provided once the initial diagnosis is made. There may be long delays before they are seen and a "management (prefer SUPPORT) plan developed"	Thank you for your comment. IN the section on aids and adaptions the committee recommend access to aids and adaptions that are identified in the person's social care needs assessment without delay.

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					To note management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) and hope this clarifies the approach of the planning.
ME Letterforce	Guideline	004	General	We welcome the recognition of the severe impact of ME/CFS and the trauma caused by the disbelief and stigma, and recognition of the ineffectiveness of GET and CBT based on deconditioning	Thank you for your comment.
ME Letterforce	Guideline	004	16-21	It would be helpful to include that many people with ME are house and bedbound and have been for decades. Many of these have not had access to normal medical care or access to a doctor with bio-medical training in their disease.	Thank you for your comment. The section on people with severe and very severe ME/CFS includes that symptoms of severe or very severe ME/CFS may mean that people are housebound or bedbound.
ME Letterforce	Guideline	004	7-9	It would be more accurate to say that ME "does" have a significant impact	Thank you for your comment. The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes.. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS.
ME Letterforce	Guideline	004	10-12	Would be better placed before lines 7-9 to reinforce that this is a physical disease	Thank you for your comment. The bullet point on impact has been moved to the second bullet point. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to

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					reflect the range of impact that can be experienced with ME/CFS.
ME Letterforce	Guideline	004	13-15	Gives the impression that ME can be a mild disease. However, given that in the diagnostic section of this guideline (page 8 . lines 14-16) says that people with ME have a significant reduction in functioning should reflect this severity.	Thank you for your comment. The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes.. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS.
ME Letterforce	Guideline	004	5-6	Because ME is classified by the WHO as a Neurological Disease the word "Disease" should replace "Condition". It would help to say that multiple body systems can be affected and result in a large number of different symptoms.	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change condition to disease. Reference to the ICD10 classification has been included in the context section of the guideline. The section on suspecting ME/CFS highlights the different symptoms that people with ME/CFS may experience.
ME Letterforce	Guideline	005	1-8	Please include that health services need to be available remotely as many patients are house bound and bedbound. Patients who appear ambulatory can suffer post exertional symptoms after medical appointments and will need to be seen at home for that reason.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as

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					online communications may be more appropriate depending on the person's symptoms.
ME Letterforce	Guideline	005	12-14	Please change "regular appointments" to "finding solutions" to their symptoms. Given that some patients may have a number of different symptoms priority needs to be given to the most urgent first. Do not assume that Fatigue is the most severe or the major problem. We support the comments made by Physios for ME Regular monitoring needs to include whatever symptom is dominant at any time and causing the greatest loss of physical functioning or of concern to the patient. This may need to be done remotely to avoid post exertional symptoms after a medical appointment	Thank you for your comment. The review in primary care section of the guideline provides further information and includes review of symptoms. The committee agree that flexibility in accessing services is important to all people with ME/CFS and this is address in the access to care section of the guideline and in the care of people with severe and very severe ME/CFS.
ME Letterforce	Guideline	006	General	This will likely cause confusion. People with ME can have a variety of symptoms regardless of their level of severity. It is the number of and severity of the symptoms that creates the distinction and the further complications from these symptoms. The impression given here is that these are symptoms solely confirmed to the Severe and V ery severe Group but as these are common ME symptoms found in the various definitions of ME and can occur at any level of severity. Someone with "mild" ME may experience these symptoms and then more severely if they have PEM exacerbation.	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Taking into account the range of stakeholder comments on the descriptions of severity in the guideline the committee have moved the recommendations on people with severe and very severe ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. The following section on suspecting ME/CFS includes the symptoms that all people with ME/CFS experience and those symptoms that are commonly associated with ME/CFS and now precedes this section.

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				It would be helpful to explain that as symptoms can fluctuate during the day and a person with ME could have symptoms classed as "severe" in the morning and "mild" in the evening. The mistake being made here is that symptoms are confined to one patient group when it should be the severity of the symptoms and their effect on the patients function. We run the risk of creating two patient groups. Those with "Mild or Moderate ME" with fatigue and PEM and"severe and very severe" with common ME symptoms found in other diagnosis criteria.	
ME Letterforce	Guideline	006	General	If a 4 category system is used (mild, moderate, severe and very severe) the GP should be aware that there can be considerable overlap between these in one patient. It can fluctuate in one day or over a period of time with (as an example) the person with ME in the Severe category for most of the day and then the Moderate category at night. The person with ME should be categorised where they spend the majority of their time and not assumed to be in the mild category (as an example) because they can attend a medical examination (and then spend the next week in bed).	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The committee note that definitions of severity are not clear cut.
ME Letterforce	Guideline	006	7-27	Change this heading to "Awareness of ME/CFS and its impact" as these are common symptoms and can affect all levels of ME/CFS Add • Flu-like symptoms may be recurrent or chronic and typically activate or worsen with exertion • Susceptibility to viral infections with prolonged recovery periods	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Taking into account the range of stakeholder comments on the descriptions of severity in the guideline the committee have moved the recommendations on people with severe and very severe ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS

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				• Variability and fluctuation of both symptoms and physical findings in the course of a day • Tender, enlarged lymph nodes, sore throats • Loss of thermostatic stability • Intolerance of extremes of temperature • Alterations of sleep rhythm or vivid dreams, or both • Muscle pain, cramps, or twitching • Muscle tenderness and weakness • Loss of stamina	were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. The following section on suspecting ME/CFS includes the symptoms that all people with ME/CFS experience and those symptoms that are commonly associated with ME/CFS and now precedes this section.
ME Letterforce	Guideline	006	7-27	We suggest that a new heading " Severe to Very Severe ME" is created and includes • Usually confined to their home or bed or unable to stand for more than a very short time if at all • May not be able to use a conventional toilet or can only walk short steps to one • May not be able to bathe and need cleaning in bed or can bathe only with help • May be Tube fed or need a liquid diet (unable to eat or digest food) • May be unable to prepare fresh food • May be unable to swallow • May have Contractures • May have muscle wastage • May have Difficulty communicating • Is unlikely to be able to attend hospital but may be able to do so in a stretcher by ambulance and needing a bed or a stretcher in the clinic	Thank you for your comments. After taking into consideration the comments from stakeholders the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. The examples included in this section are based on the committee's knowledge and experience of people with severe and very severe ME/CFS and are the examples are not meant to be an exhaustive list. The committee note that the examples you have are included throughout the guideline.

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				• May be able to use an electric wheelchair for a short time or one that allows them to lie flat only	
ME Letterforce	Guideline	006	7-27	We support the comment by Physios for ME that a risk analysis must be done for every interaction with a severely affected person to weigh the benefits and that specialised Severe nurses etc trained and used.	Thank you for your comment.
ME Letterforce	Guideline	007	7	Add Vibration and chemicals and perfume	Thank you for your comment. Hypersensitivity and the examples you mention are included in the previous recommendations on symptoms people with ME/CFS may experience. These are examples in the recommendations and as with any examples these cannot be exhaustive for this reason your suggestions have not been added.
ME Letterforce	Guideline	007	8	(inset at the line) may vary in ability to use a wheelchair (electric or manual) or mobility scooter	Thank you for your comment. After considering the range of stakeholder comments this has been edited to, 'are housebound or bed-bound and may need support with all activities of daily living, including aids and adaptions to assist mobility and independence in activities of daily living (for example wheelchairs)' The section on aids and adaptions provides further information. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
ME Letterforce	Guideline	007	26	Add at the end "with their permission"	Thank you for your comment. 'if appropriate' has been added to the recommendation.

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ME Letterforce	Guideline	008	10-16	Please Include an acute viral onset. Because ME often starts with a virus the GP needs to be looking for this onset and not dismissing people with ME as "just having a virus". The viral symptoms can continue for years in some people. ME and Post Viral syndrome share a WHO code and it is important to include this.	Thank you for your comment. The committee discussed the inclusion of triggering events but decided not to include reference to this as it is not clear what causes ME/CFS and the inclusion of any examples of triggers may be taken as an absolute list. The context section notes that in many cases, symptoms are thought to be triggered by an infection.
ME Letterforce	Guideline	008	5-9	Please include a Neurological examination	Thank you for your comment. This recommendation has been edited to include,' a medical assessment (including relevant symptoms and history, comorbidities, overall physical and mental health) and a physical examination.' This would include all appropriate assessments.
ME Letterforce	Guideline	008	8	Any Psychological Wellbeing Assessment should have a light touch at this stage. They will probably have more pressing medical / work / home issues that need to be addressed first.	Thank you for your comment.
ME Letterforce	Guideline	008	17 Box 1	We support post exertional symptoms exacerbation as a symptom. It does however need explanation further in this document as most doctors will have not been trained in what this means. It should also be explained that people with ME call this "PEM" post exertional malaise	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM). The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. The link to the definition of PEM in the terms used in the guideline is included here
ME Letterforce	Guideline	009	1-16 (insert after)	Add a new point "fluctuating nature during the day. Sometimes with seasonal fluctuations"	Thank you for your comment. The committee discussed the other symptoms you suggested should be on the list and they agreed these describe the nature of the symptoms and the impact of ME/CFS and these are addressed elsewhere in the guideline.

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				Add a new point "Unable to walk short distances or use a manual wheelchair" Add a new point "Gait disturbances, clumsiness" Add a new point "Secondary infections and other complications after an acute viral onset such as tonsillitis, sinus infections, a continual hacking cough, inflamed ribs"	The committee note that infections are listed in the examples of differential diagnosis or co-existing conditions in evidence review D.
ME Letterforce	Guideline	009	2-3	Add to the end of the current sentence "Bear in mind that Orthostatic intolerance does affect the vast majority of ME patients and can cause severe Post Exertional Malaise"	Thank you for your comment. This recommendation lists the associated symptoms, evidence review D and G have more information on orthostatic intolerance and the occurrence in people with ME/CFS.
ME Letterforce	Guideline	009	13-14	add taste, add perfume and chemicals, add drugs	Thank you for your comment. The committee discussed your suggestions and agreed to add taste, they considered the other suggestions were covered in the current examples given. The committee note that any list of examples is not intended to be exhaustive.
ME Letterforce	Guideline	009	Line 1 Box at the top of the Page	Please add as a separate line in the box "Neurological symptoms – temperature changes, pins and needles, twitching" Please add to box– "Pain in muscles" Please add to box "post viral syndrome or ongoing viral symptoms such as sore throat, swollen glands, fever". (ME shares a WHO code with Post Viral Syndrome)	Thank you for comment Box 1 includes the key symptoms for the diagnosis of ME/CFS. The committee did not identify your suggestions as key symptoms but note they are included in the following recommendation on associated symptoms. See evidence review D – diagnosis for the committee discussion on the diagnostic criteria.

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ME Letterforce	Guideline	009	4	add "breathlessness" Add " some patients may not be aware of any of the above symptoms while standing, but suffer PEM later"	Thank you for your comment. These are examples of symptoms that people may experience and the committee note that any list of examples is not intended to be exhaustive. The definition linked to gives further explanation about orthostatic intolerance.
ME Letterforce	Guideline	010	11-21 (general)	This should include advice to recuperate from a viral illness if they have the same symptoms as at the acute viral onset or if the viral symptoms keep reoccurring. Convalescence should be recommended. The GP needs to explain post exertional malaise at this stage. People with suspected ME need specific information on rest and activity at the critical start of the disease as REST here may mean a less severe form later on. Home help should be offered with no delays as an urgent priority and as a medical need (i.e. not means tested) There should be a specific warning to never to push self but to stop, rest and pace, not 'exercise' at this important early stage of the disease. they should be told to cut down on activity and not push themselves They may not be able to see their "energy limit" and it may change from day to day. If PEM is delayed 24-72 hours after the activity then the patient will not see the link and they will continue with potentially harmful behaviour during the early part of the onset.	Thank you for your comment. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term. The committee agreed that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and this advice would not result in harm to anyone. Rest and convalescence is included in the advice. *Energy envelope* After considering the stakeholder comments the committee agreed that this concept might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. This they agreed applied to PEM. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. The committee agreed that people should be given personalised advice about managing their symptoms and recommend this in

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					the advice for people with suspected ME/CFS section of the guideline. * To note that after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit Energy envelope to use energy limits.
ME Letterforce	Guideline	010	12-15	isn't adequate as it refers to a section that doesn't include managing specific symptoms commonly found in ME/CFS. We need to delete the current content in that section which is from the Adapted Pacing (APT) model (one arm of the PACE trial)	Thank you for your comment. Taking into account the stakeholder comments the committee agreed to delete this text on the basis that this section refers to people with suspected ME/CFS. The committee agreed it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and this advice should not result in harm to anyone. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies).

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					Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS.
ME Letterforce	Guideline	010	17-20	Insert "explain post exertional malaise or exacerbation of symptoms "	Thank you for your comment. After considering the stakeholder comments the committee agreed that this concept and energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on PEM PEM and energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. * To note that after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit Energy envelope to use energy limits.
ME Letterforce	Guideline	010	17-20	Include ' keep a diary of main activities including periods standing still can help see main triggers for PEM	Thank you for your comment. After considering the stakeholder comments the committee agreed that this concept and energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on PEM and energy limits* may not be helpful. At such keeping a diary at this stage may not be appropriate. The committee amended the recommendation to

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					advise people to manage their daily activity and not push through symptoms. * To note that after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit Energy envelope to use energy limits.
ME Letterforce	Guideline	010	17-20	Include 'ensure support is in place for them to convalesce, home visits if needed, or help at home as a medical need to prevent further deterioration . Any barriers to this need to be discussed and practical solutions found. The patient's family may need to be involved in their convalescence.	Thank you for your comment. This section refers to a short time period (6 weeks) and for people that are suspected to have ME/CFS as such the advice here is general. The section does start by being clear that care should be personalised as such access to care would be considered by the healthcare professionals providing care.
ME Letterforce	Guideline	010	9-10	We support the comments by Physios for ME	Thank you for your comment.
ME Letterforce	Guideline	010	19-20	We support the comments from Physios for ME	Thank you for your comment.
ME Letterforce	Guideline	010	20	Include Sleep as much as they need	Thank you for your comment. The discussion section of evidence review E notes that the committee did not make a recommendation on daytime sleep or naps due to a lack of evidence and a lack of agreement in the committee on a strategy that was suitable for all people with suspected ME/CFS. The committee are aware that in the early stages or acute phase of the illness some people find daytime sleep or naps beneficial, allowing for more meaningful activities to be achieved during the day; while other people have found daytime sleep/naps to be unrefreshing, potentially affecting the quality of sleep at night and contributing to sleep-wake reversal which can be difficult to regulate in the future. For this reason your suggestion has not been included.

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ME Letterforce	Guideline	011	9-12	Young people with ME should not be referred to any team that promotes harmful psychosocial treatments.	Thank you for your comment.
ME Letterforce	Guideline	011	1-2	A person with ME who has an acute viral onset may not be well enough to attend a GP clinic for a review. A telephone number should be provided and appointments at the patients home. The patients family or named advocate should be a contact if the person with ME is unable to use a telephone	Thank you for your comment and information. The recommendation includes that people should be told who to contact. This section refers to a short time period (6 weeks) and for people that are suspected to have ME/CFS as such the advice here is general. The section does start by being clear that care should be personalised as such access to care would be considered by the healthcare professionals providing care.
ME Letterforce	Guideline	011	7-8	People with ME should only be referred to Bio-Medical specialist in their condition. Given, however that we have very few of these at the moment and that immediate advice to rest and sleep is needed the GP should trained in PEM andpassing on this advice People with ME should not be referred to the current "CFS" clinics that are operated using the harmful Psycho-social approach or private doctors who use these methods. They should not be referred to Clinics that use Adaptive Pacing, graded exercise or any activity management program. After Diagnosis the person with ME should be given information on PACING and REST by the GP The GP should assess the urgent medical needs of the person with ME and try as best to deal with the symptoms The GP may need to write reports to the person's employer, school or the benefits agency and examine any barriers to PACING and REST that the person may have	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. Based on the evidence (Evidence reviews A.B,C & D) and the committee's experience referral to specialist care was recommended for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. ME/CFS specialist teams where seen as the most appropriate place for people with ME/CFS to access support. In the guideline primary care has a role in ongoing care and review once a personalised care and support plan has been agreed and developed.

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ME Letterforce	Guideline	012	10-30	Replace the term "management plan" with "Support plan" Using "management plan" can give the impression of a fixed and inflexible set of agreements and may be overwhelming to someone newly diagnosed. This section could be named "How to support the person with ME"	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
ME Letterforce	Guideline	012	1-9 general	Daily living should be assessed here as a separate point – can the patient bath, can they cook, is anyone able to cook for them. Can they operate a car safely. The patient's home should be assessed. Can the patient get up and down stairs now. Is the bath accessible, can they stand in a shower. Mobility and all activities should be assessed to consider the time(s) the person with ME is at their worst and the cumulative effects. As an example a person with ME should not be asked if they can have a bath and cook a meal in a tick box exercise. They may be able to do one but not both on the same day. Work and Education need a separate point here. Can they still function or get to their place of employment. Do they need a report for their employer. Do they need a report to obtain financial help from insurance or a state benefit.	Thank you for your comment. The recommendation includes the minimum areas to be considered in the assessment, the list is not meant to be exhaustive and does not exclude the areas you have mentioned.
ME Letterforce	Guideline	012	7-9	include new food intolerance, digestion problems	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
ME Letterforce	Guideline	012	21-22	This should be renamed PACING and REST. The energy management strategies in the current Guideline are from the	Thank you for your comment. *Energy management*

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				PACE Trial "Adaptive Pacing Therapy" model. The APT approach was shown to be ineffective in the PACE Trial.	Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS.
ME Letterforce	Guideline	012	23-24	General information better suited to the general population should be avoided. It is pointless to give a person with ME information (as an example) on general cardiovascular health as they are unable to exercise and may have a diet which is limited as they rely on a food delivery service or have severe food intolerances. Physical Maintenance advice could be given later on in the disease once the demands of their new disability, work and financial concerns are addressed and this	Thank you for your comment The committee agree, at the top of the symptom management section and in the section of co-existing conditions it is clear that the management of symptoms and other conditions should take into account the sections on principles of care for people with ME/CFS, access to care and the energy management in this guideline.

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				needs to be targeted to their disability. The Physical Maintenance advice must be tailored to the patient and their abilities.	
ME Letterforce	Guideline	012	4	should include being unable to work or finish education	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
ME Letterforce	Guideline	013	Information and Support	We welcome the inclusion of this section	Thank you for your comment.
ME Letterforce	Guideline	013	1-3	We would prefer the words "support plan". The newly diagnosed person with ME should be given a "Support plan" which shows how they will be helped to overcome any barriers This should include any barriers in the way of their REST and PACING, who will be handling this and how to contact them. There should also be a MEDICAL support model where the patient can prioritise their symptoms and who will be helping with these.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) The multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.

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ME Letterforce	Guideline	013	11-13	People with ME should have a home visit if needed. The Assessment is likely to be long. People with severe and very severe may need to have a family member present. They need to be sent details of the assessment in writing to consider before the visit. They may need to have the assessment broken down into chunks.	Thank you for your comment. The committee agree and this is included in the section on access to care for people with severe or very severe ME/CFS. The committee note that this might take more than one visit and the support of their family or a carer where appropriate.
ME Letterforce	Guideline	014	19-24	This needs to be evidence based. People with ME need to understand that both recovery and remission are uncertain. Recovery rates are estimated at between 3-5%. Remission rates are not known. Some patients improve over time and some deteriorate or remain stable. The Dubbo study in Australia reported that the severity of onset could influence recovery	Thank you for your comment. After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS. See evidence review A for the committee discussion on information about the long term outlook for people with ME/CFS.
ME Letterforce	Guideline	014	25-27	The word "can" should be changed to "Has". It is impossible that a disease that causes a substantial reduction in daily functioning, when people with ME find it hard to combine work with any social life or else have lost their careers and education could not cause anything other than a major impact.	Thank you for your comment. After considering the range of stakeholder comments on this recommendation it has been edited to,' varies widely in its impact on people's lives, and can affect their daily activities, family and social life, and work or education (these impacts maybe severe)'. This is to reflect the experience of all people with ME/CFS. See evidence review A for the committee discussion.
ME Letterforce	Guideline	014	30-31	It should be made clear that any self-management techniques have no proven success of improving symptoms and are not a cure. Pacing is designed to try and stop further decline due to over activity. Patients may have very little control over their symptoms in reality as the demands of daily living may mean that some live in a perpetual post exertional malaise state.	Thank you for your comment and information.
ME Letterforce	Guideline	014	Line 18 (insert after)	There may be a pattern to the symptoms over the day or weekly or with seasons and some patients find it better to live within their pattern	Thank you for your comment and information.

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ME Letterforce	Guideline	015	General 11-22	We welcome the inclusion of Social Care in the Guideline. Social Care should be considered part of the patients Medical Care if it will help the patient to REST and PACE. It should not be subject to means testing and should be at a level the patient needs in order to cut down on post exertional symptoms.	Thank you for your comment and information.
ME Letterforce	Guideline	015	16-18	There should also be an offer of a written report to show which area the person with ME needs help with unless the OT's has had specific training in ME as many have unhelpful ideas about activity and exercise. The report should also include what the patients daily symptoms burden is and when they can be contacted. It should be explained that Social Care assessments may need to be carried out in a series of small appointments at appropriate times of the day to avoid the patient deteriorating and spaced at an appropriate level. OT's may not have experience of how severe ME can be and this needs to be made clear.	Thank you for your comment. It is not within NICE'S remit to make recommendations about healthcare professionals providing medical reports to supporting applications for assessments. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
ME Letterforce	Guideline	015	6-7	Care should be taken that people with ME are not given "resources" that are based on factually incorrect information or self helps groups that encourage exercise therapies and Adaptive Pacing	Thank you for your comment.
ME Letterforce	Guideline	015	3	Add … but is still serious	Thank you for your comment. This recommendation does not suggest that ME/CFS is not serious in children and young people and as this point does not add any further clarity it has not been added.

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ME Letterforce	Guideline	015	8	People with ME should be given written reports to support benefit applications. This should be considered part of medical care.	Thank you for your comment. It is not within NICE'S remit to make recommendations about healthcare professionals providing medical reports to supporting applications for benefits.
ME Letterforce	Guideline	015	12	It may be a good idea to remove "sensitively" here. All contact with patients and families should be performed in a sensitive manner.	Thank you for your comment. The committee agree that all contact with patients and families should be performed in a sensitive manner. 'sensitively' was added here to reflect recommendation 1.1.2 and that some people may have had negative experiences with social care services.
ME Letterforce	Guideline	016	Safeguarding	We welcome this topic being in the Guideline.	Thank you for your comment and information.
ME Letterforce	Guideline	016	11	Add Self harm (as in mistaken for)	Thank you for your comment. This recommendation does not include specific examples and for that reason your suggestion has not been added.
ME Letterforce	Guideline	016	11 (insert new point after)	Add a point that some people with ME may need to be admitted to a hospital Ward or Centre which specialises in their disease if they are unable to care for themselves temporarily at home or if carers cannot cope. They should not be admitted to a Psychiatric ward purely because there is no where else to put them	Thank you for your comment. This section is about safeguarding and not about the access to hospital care, this is addressed in the access to care section where there are recommendations to facilitate admission to hospital.
ME Letterforce	Guideline	017	20-22	We welcome this section in very useful section the Guideline	Thank you for your comment.
ME Letterforce	Guideline	018	General	Ideally Patients should be able to see a team of Bio-medical doctors who specialise in their disease rather than being referred to multiple clinics to investigate the multiple symptoms patients have (which causes complications due to lack of co-ordination). People with ME should not be threatened with a treatment or investigation being denied because they have had to cancel	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be

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				appointments at short notice (and multiple times) or it would cause PEM. They should not be denied a service because they cannot commit to an appointment with a set time frame that a hospital insists on. That hospitals or clinics provide an email address for questions or appointment problems. People with ME will not always be able to plan or to speak clearly or use a telephone. Referrals by the GP need to include specific instructions for the time of day the person can be seen and any other limitations on appointments. If a person with ME (as an example) can attend a hospital but only in the afternoon that needs to be in the referral. It would save a great deal of time and effort trying to re-arrange appointments and all the resource waste from that.	available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee recognised certain parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. The committee agree that people with ME/CFS should not be discharged for missing an appointment without discussing the reasons why and have made a recommendation addressing this. The committee agree that flexibility in accessing to services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult The committee note in the recommendations that other methods, such as online communications may be more appropriate depending on the person's symptoms.

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ME Letterforce	Guideline	018	19-24	This should be applied to all People with ME as symptoms fluctuate	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments and hospital stays can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. The committee agreed that it was important to raise awareness about the challenges that people with severe and very severe ME/CFS have. Access for all people with ME/CFS is addressed in the first recommendation in this section.
ME Letterforce	Guideline	018	1	Appointments being co-ordinated by a named person that a person with ME is not faced with multiple telephone calls to rearrange appointments	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
ME Letterforce	Guideline	018	15	Please change 'fear' to 'likelihood' of relapse. The chance of a relapse or symptoms intensifying is part of the disease.	Thank you for your comment. After considering stakeholder comments about the word fear this recommendation has been edited 'risk that their symptoms will worsen may prevent people from leaving their home'.
ME Letterforce	Guideline	019	Inpatient Care General	We welcome this good advice. Ideally it should be explored before a hospital stay if the treatment could be done at the patients home and hospital stays thus avoided The language could be further improved as hospital is likely to be a problem for people with ME at all levels	Thank you for your comment and information.
ME Letterforce	Guideline	019	1	Change "whether" to "which aspects"	Thank you for your comment. This recommendation refers to all people with ME/CFS and as such 'whether' is appropriate.
ME Letterforce	Guideline	019	4	Hospital stays should be scheduled when there is a private room for the patient	Thank you for your comment.

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ME Letterforce	Guideline	019	7	Please add food and perfumes (smells needs to be more understandable). Some NHS equipment smells of artificial perfume. If in a ward, the smell of artificial scents from other patients and staff will be a problem for some.	Thank you for your comment These are examples in the recommendation and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
ME Letterforce	Guideline	019	8	This should be changed to all levels of ME	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments and hospital stays can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. The committee agreed that it was important to raise awareness about the challenges that people with severe and very severe ME/CFS have.
ME Letterforce	Guideline	019	28	should read "a temperature suitable for the patient" as many people with ME have temperature control failure. Please add close to a window that the patient can control with blackout blinds.	Thank you for your comment These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
ME Letterforce	Guideline	019	29	Please add perfumes and artificial scents on staff and in bathrooms and equipment. Placing a person with ME close to a window that opens may be useful for that reason	Thank you for your comment These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
ME Letterforce	Guideline	020	1-18 General	People with ME should have access to non-means tested grants for equipment that they need for health reasons. They may need to move from a house with stairs to a bungalow or fit a stair lift or wheelchair lift. We should not expect the patient or their family to shoulder the burden of caring for them at home. This should be considered as a medical need and supplied.	Thank you for your comment and information.

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				If we expect people with ME to live with their activity limit then the physical items they need should be provided as medical care.	
ME Letterforce	Guideline	020	**26-30**	This should apply to all levels of ME/CFS. The work "risks" should not be used as it could be misconstrued into "deconditioning" which was one of the earlier justifications for denying Aids earlier.	Thank you for your comment. The committee agree that access to aids and adaptions are important for all people with ME/CFS and this is highlighted in the first recommendation on access to assessment. The committee agreed that it was important to highlight people with moderate to very severe ME/CFS recognising the challenges they have. The committee note there are risks and benefits to all strategies to support people with ME/CFS managing their symptoms and any risk, if any, will be individual to the person and should be discussed.
ME Letterforce	Guideline	020	23-25	If the patient has a medical need for home adaptation then this should be funded. The health benefits would be that the patient would have less PEM.	Thank you for your comment and information.
ME Letterforce	Guideline	021	11-14	We welcome this point. Please include post exertional exacerbation of symptoms specifically in the information on ME as this is such a unique hallmark of the disease that most employers will simply not understand. Please remove the words "agreed management plan" as this could be potentially coercive . Any plan or assessment that the patient has should be kept confidential and not disclosed to an employer unless there are portions of it the patient would like disclosed. Potentially if we use "agreed management plan" a patient could chose to change their plan and then have to	Thank you for your comment. This recommendation does not give any detail on the information to be given as this would be personalised, agreed with the person with ME/CFS and consent given for it be shared. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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				justify that to an employer. The person with ME should remain in control. We would recommend that interaction with the employer should consist of providing information about ME/CFS, to explain how this affects their job and to ask for adjustments needed No confidential information or plans should be shared as this is a breach of the patients right to privacy and to control their treatment.	
ME Letterforce	Guideline	021	8-10	We welcome the information about the Equality Act	Thank you for your comment.
ME Letterforce	Guideline	021	4-5	Surveys from patient groups show that most have had to give up work. We need to give reasonable expectations. We suggest that it is changed to "They may not be able to continue with work or education" and "they may need a long period of convalescence".	Thank you for your comment. After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support.
ME Letterforce	Guideline	021	6-7	This is misleading as it gives the impression that work, education is not "activity" and will not cause PEM. All people with ME will find working full time a huge struggle as the disease places a huge burden on them. We should not trivialise the symptoms even a "mild" person with ME has We suggest that this is changed to "going back to work, school or college is likely to cause post exertional symptoms and it may be impossible to safely keep safely within your activity limit unless accommodations are made"	Thank you for your comment. After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support.
ME Letterforce	Guideline	022	17-22 General	This should include REST and Pacing (instead of energy management). Energy management should be avoided as there is no evidence that this is a safe and efficient approach to use. Pacing has been shown by patient surveys as the	Thank you for your comment. Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee

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				preferred option. APT should be avoided as this was one of the arms of the PACE trial and was not shown to be effective. Using REST and pacing as a management technique is reported by People with ME as being helpful in patient surveys. We need this as a separate special category here. Home based services should include dentistry, ultrasound, small simple operations, cervical smear, cancer check-ups and investigations and treatment, birth control and foot care. Managing chronic infections should be included Reactions to drugs should be included	concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS. Recommendation 1.11.3 includes the assessment and discussion on rest. In addition there is a section on rest and sleep in the symptom management for people with ME/CFS part of the guideline.
ME Letterforce	Guideline	022	13-16	The emphasis needs to be on Bio-medical care and this should be explicit in the description. Care should include remote services for housebound people with ME, services in their own homes and hospital wards suitable for the severely affected when needed.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS

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					results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). Throughout the guideline the importance of ME/CFS specialist services is reinforced and where access to these services is required. They have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. *Access to care* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be

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					difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
ME Letterforce	Guideline	022	19	Should be "managing fluctuating symptoms and relapses"	Thank you for your comment. After considering the range of stakeholder comments on the wording of flare the committee edited flare to flare ups. The description of flare up in the terms in the guideline includes that a flare up is a worsening of symptoms.
ME Letterforce	Guideline	022	22	Should include Food intolerances	Thank you for your comment. This list is a top-level overview of the minimum expertise a person with ME/CFS should be able to access and each bullet point could include many examples of areas of expertise and it would not be exhaustive. The committee agreed that expertise in diet and nutrition would include food intolerance.
ME Letterforce	Guideline	023	1-2	It would be better to split these as they are not always related. Mobility, avoiding post exertional symptoms and access to aids such as electric wheelchairs Avoiding falls, loss of dexterity, clumsiness, weakness Rehabilitation should only be carried out by those trained in PEM. May need admittance to a specialised wards. This should not include exercise programs that cause PEM.	Thank you for your comment. This list is a top-level overview of the minimum expertise a person with ME/CFS should be able to access and each bullet point could include many examples of areas of expertise and it would not be exhaustive. This list is not meant to be exhaustive and for this reason your suggestions have not been included.
ME Letterforce	Guideline	023	5-6	GP's due to their lack of training and time constraints may find it hard to manage care. We would like to see more training for medical professionals such as the 2020 CPD course featuring Dr Nina Muirhead.	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the

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					recommendations in the training for health and social care professionals section of the guideline. We will pass this information to our resource endorsement team. More information on endorsement can be found here: https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme .
ME Letterforce	Guideline	023	5-6	We recommend a Centre of Excellence be set up to train and support GPs / Local Consultants. This should be a Biomedical Team with specialists in different symptoms in different bodily symptoms.	Thank you for your comment. Setting up a centre of excellence to train and support GPs and local consultants is beyond the remit of NICE.
ME Letterforce	Guideline	023	5-6	We agree with the "general comments" by Physios for ME at the end of their submission on the training of Physiotherapists on the move away from exercise based treatments.	Thank you for your comment.
ME Letterforce	Guideline	024	6-24 General	The next section should be "PACING". It is important that the distinction is made between Pacing (as reported useful in Patient surveys) and APT which is a regimented form of activity management used in the PACE trial and shown to be ineffective The GP should explain that • Pacing is balancing rest and activity • Post Exertional Symptoms occur when the person with ME has exceeded their limit of activity • Activity includes all energy expenditure physical, emotional and mental. This includes simple household and self-care tasks that the person could easily perform previously • The goal of Pacing is to stop extra symptom exacerbation from over exertion	*Thank you for your comment.* *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or

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				• That patients find there is an energy limit that in times of better functioning activity may increase naturally and at other times it may shrink • That the "energy limit" cannot be measured and can change over time in an unpredictable way • Pacing requires no Professional involvement and can be learned from printed or internet resource • That it is completely in the hands of the person with ME • Some people find a symptom diary, useful as post exertional symptoms can take up to 72 hours to develop • Some people find an activity diary useful with main activities including periods of standing still • That some people with ME report being permanently worse after exceeding their activity limit • Young people and those who find it hard to judge their activity limit can be referred to a Professional trained in this field • That there may be specific barriers stopping it being more effective (and these will be assessed) The GP should provide the person with ME with a written guide to Pacing and told where other information can be found. Family members can be involved if needed so they can support the Person with ME. It may be difficult for them to understand that REST is important.	downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS. The committee note that much of your bullet points are included in the energy management section of the guideline. *Pacing* The committee discussed the use of the term pacing agreed that it means something different to different people with many different versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it.
ME Letterforce	Guideline	024	1-3	This is unlikely to be helpful in practise as a GP would find it difficult to search for ME symptoms and find them in other separate NICE Guidelines.	Thank you for your comment.

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				As an example, there is no guidance for "temperature intolerances causing patients to be stuck in "hot" or "cold" with low and hot body temperature or Chronic infections or the Cognitive problems people with ME face and existing guidelines are likely to be inappropriate in their treatment. NICE Guidance tends to be written for Medical Conditions with symptoms specific to it or for Symptoms with an emphasis on a known medical condition related to it. A person with ME presenting with a chronic sore throat with an infection that reoccurs every few weeks or a sinus infection that never goes away should not be treated by current NICE guidance on Acute infections that resolve. Advice from a Bio-Medical ME Specialist with experience may be needed if there is no NICE Guidance, that Guidance is designed for an acute illness and not the chronic problems people with ME face or if exercise is recommended. Current NICE Guidelines may not include advice or treatments suitable for people with ME as many will need investigations at home or be sensitive to drugs and treatments in an unusual way.	The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist with ME/CFS and these should be investigated and managed in accordance with best practice. This section also lists related NICE guidelines and recommends the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions and the associated symptoms in people with ME/CFS.
ME Letterforce	Guideline	025	15-29	Needs to be deleted. This is the APT model from the PACE Trial manual. The useful items here will be covered in the REST and PACING sections.	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have

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					while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS.
ME Letterforce	Guideline	025	7-14	The Assessment should include • What are the barriers to rest and sleep • Does the person with ME already have a working knowledge of where their "energy limit is" (other terms patients may use include "threshold" or "energy envelop")? • How severe does their ME get. Consider the severity during the day and when in PEM or through seasonal changes • What ability is there to undertake daily activities • What are the work or education demands • What other roles do they have i.e. are they a carer for a partner, parent or children	Thank you for your comment. This recommendation provides an overview of what should be included in a discussion when developing a plan for energy management. The areas you mention are included within the topics included in overview. The beginning of the recommendation also includes, discuss, 'along with anything else that is important to the person'.

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				• What support can they call on from partner and family • What mobility do they have and what aids could help with this. People with ME need to be encouraged to conserve energy so aids like Electric Wheelchairs should be considered. • What are the main health concerns and symptoms that they would like addressed. This should include dentistry, birth control etc. • Do they have any co-morbidities or other diseases • Are they usually able to come to a GP clinic or will they need appointments at home • Any other issues or concerns important to the person	
ME Letterforce	Guideline	025	1-3	needs to be deleted. The word “tolerance” should not be used in the Guideline. This is from the deconditioning model of GET. It also implies a “sensitivity” that needs to be overcome and there is no evidence that this is the case and “tolerance” achieved.	Thank you for your comment. After considering the stakeholder comments tolerance has been deleted.
ME Letterforce	Guideline	025	4-6	Needs to be an Assessment only (without an energy management plan). Ideally this should be done before the section on REST and PACING). There is no evidence that having an energy management plan is safe and effective for patients. This was part of the APT arm from the PACE trial and the evidence from that does not support its inclusion in this Guideline.	Thank you for your comment. This is an assessment for the energy management plan, a holistic assessment for the care and support plan is set out in section 1.5. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that

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					supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS. .
ME Letterforce	Guideline	025	21	We support the comment from Physios for ME	Thank you for your comment.
ME Letterforce	Guideline	026	1-7	should be deleted. A patient survey by the ME Association showed that an activity program led by a Physiotherapist was one of the most damaging to people with ME. Most NHS Physiotherapists have no training in ME/CFS and until they are re-trained should be avoided for exercise or activity programs. There is a wide spread belief in deconditioning, sensitisation in Physiotherapy which can make them a danger to patients. The words "ready to progress" are misleading and should not be used. They imply a state that can be measured and is safe to exceed.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews A, G and H) and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the

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				The words "would like to incorporate a physical activity program" should not be used. They imply that there is a proven, safe physical activity program available.	balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
ME Letterforce	Guideline	026	16-22	Should be re-considered in any as it may be pointless to a group of people who cannot exercise or make major lifestyle changes. The GP should consider balancing Physical Maintenance and PEM / demands of daily living / quality of life and other priorities that the patients may have. This should be considered if there is health issues raised by the patient or if all the patients current health issues are dealt with and they have enough activity quota /flexibility to consider it.	Thank you for your comment. The committee agreed it was important that people with ME/CFS who have periods of long term immobility should include strategies to maintain and prevent deterioration of physical functioning and mobility in their care and support plan. In addition, 'Strategies need to be carried out in small amounts and spread out throughout the day' has been added to the recommendation to clarify this is in the context of the priorities that people may have.

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					After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.
ME Letterforce	Guideline	026	8-11	People with severe or very severe ME Severe and very severe patients should not be offered "energy management programs" as they have not been shown to be safe or effective. They should be offered advice on REST and PACING from a Specialist with experience in the group and only If it is judged as being tolerated. words "management plan" be changed to "support plan" and be focussed on all the things the person with ME needs help with. The GP should consider balancing Physical Maintenance and PEM / demands of daily living / quality of life and other priorities that the patients may have. This should be considered if there is health issue in this area specifically raised by the patient.	Thank you for your comment. Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that all people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. The additional recommendations on people with severe to very severe ME/CFS are to ensure that additional caution is taken including the plan being developed by a physiotherapist or occupational therapist working in a ME/CFS specialist team. *Rest and sleep.* The committee agreed that rest was an important part of managing activity in people with ME/CFS. The role of rest and sleep are further addressed in section 1.12 and the rationale provides further information on this. *Pacing*

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					The committee discussed the use of the term pacing agreed that it means something different to different people with many different versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it.
ME Letterforce	Guideline	026	12-15	The current text in this point "any increases (if possible) much slower" gives the impression that the only way is up. This is misleading. Levels can go up and down. People with ME can lose quality of life trying to increase activity if the methods taught fail. An experienced Neurological Physiotherapist with training in bedbound patients may be of benefit here to the severely affected. Although they may need extra training to recognise and avoid causing post exertional symptoms.	Thank you for your comment. The additional recommendations on people with severe to very severe ME/CFS are to ensure that additional caution is taken. The committee included (if possible) to emphasise that any increases may not be possible and the plan should be developed by a physiotherapist or occupational therapist working in a ME/CFS specialist team.
ME Letterforce	Guideline	026	17-18	Change "management plan" to 'support plan' as it can become a non-productive burden. People with ME (who have other more pressing health issues and) who cannot exercise, change their diet or their lifestyle in many cases. A management plan can be coercive forcing the patient into making agreements in order not to upset their medical practitioner or at a time when they don't understand the disease. It has the potential to cause conflict. We recommend that the words "management plan" be changed to "support plan" and be focussed on all the things the person with ME needs help with.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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ME Letterforce	Guideline	027	3-9	We welcome the inclusion of this section. Osteoporosis investigations will need to be carried out in the patients home or by stretcher to hospital for scans in some cases. If patients are very severe and unable to attend a hospital, give advice on preventative treatment.	Thank you for your comment and information. The following recommendation includes that advice should be given on how to recognise and prevent possible complications of long-term immobility.
ME Letterforce	Guideline	027	14-19	We support the comment from Physios for ME on Post Exertional Symptom exacerbation	Thank you for your comment.
ME Letterforce	Guideline	027	20-23	This may cause confusion as it contradicts other advice in the Draft Guideline. People with ME should be advised not to undertake any exercise program (regardless of structure). There is no exercise program which has been developed that has proven safety and efficiency. We support the comment from Physios for ME and this may be the place to include their comments on and explanation of the abnormal physiology of ME, the research findings and how they impact.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews A, G and H) and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
ME Letterforce	Guideline	028	Physical Activity General	We welcome the advice in this section. It will make a difference to new patients who will no longer have their health potentially made worse by exercise programs.	Thank you for your comment.

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				We support the comments made by Physios for ME	
ME Letterforce	Guideline	029	Physical Activity General	We support the comments made by Physios for ME 1-5 and 6-13	Thank you for your comment.
ME Letterforce	Guideline	029	1-16	We ask for this to be deleted. This describes a graded exercise program. There Is no evidence that any exercise or physical activity program is safe and effective for patients. Patient surveys have shown that physical activity or exercise programs are responsible to the most harm. Changing the name but offering the same advice is not acceptable to people with ME.	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This

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					has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. This not what is set out in recommendations 1.11.20-1.11.21. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed it was important people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.

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ME Letterforce	Guideline	029	17-22	We welcome the inclusion of REST and SLEEP. However, they should be separate larger topics due to their importance. In patient surveys patients report that REST is the most useful strategy that they have. It would be useful to include 1. Patients report REST as being the highest ranking useful strategy that they use 2. When a person with ME has overdone activity the first option should be to REST until they feel better 3. That they should consider REST as a priority over activity 4. That the benefits of REST out way any potential de-conditioning that the patient could experience. That research has shown people with ME are no more deconditioned than other sedentary people. 5. That SLEEP is important and people should sleep as much as they feel they need to and at time they need to 6. The SLEEP can be useful if the patient has particularly severe symptoms at a time of the day or night. As an example if POTS, weakness, nausea etc is worse in the early mornings then the patient may benefit from sleeping through that time 7. Dr Melvin Ramsay who was an early expert who researched ME and wrote on the topic, said that the patients who did best were the ones who were able to REST during the start of the disease. 8. REST and SLEEP should be considered especially recuperative if someone with ME has ongoing viral symptoms after an acute onset of that type. Patients	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.

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				should be encouraged to think of this as convalescence.	
ME Letterforce	Guideline	030	3-11 Managing OI General	We support the comments made by Physios for ME And would like to add People with ME need to know • What the symptoms of OI are. They may not realise that dizziness, nausea or fainting is due to this. • That standing still can, in some people, result in OI symptoms. It may not be noticeable moving from sitting to standing but standing still in a queue (as an example) can cause severe symptoms and then PEM • It would be very helpful to mention here that the cause of OI is not known and is not caused by deconditioning or too much rest It would be useful at this point to explain to medical professional that OI and POTS can in some cases be investigated easily at the patients home by using the "poor man's tilt table test" and the GP can carry this out. This would cut down on costs and make this simple pre- test available to people with ME who are housebound. Please include that OI can also manifest as Postural Hypertension	Thank you for your comment and information. In the suspecting ME/CFS section of the guideline orthostatic intolerance is identified as one of the symptoms that are commonly associated with ME/CFS. The committee made a consensus recommendation to raise awareness about this. The guideline is about the diagnosis and management of ME/CFS and for this reason the committee was unable to make more detailed recommendations on the causes or diagnosis of orthostatic intolerance. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
ME Letterforce	Guideline	030	13-16	It would be helpful to add here	Thank you for your comments. Although pain relief was included in the protocol for pharmacological interventions no evidence was identified and the

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				• Please discuss pain medication as pain is a symptom of ME • Pain can stop people with ME being able to REST and SLEEP. This barrier should be treated as a priority and addressed early. • Pain can be a symptom associated with over activity and PEM • People with ME may experience different types of pain at the same time or at different times. Pain medication may need to be prescribed of different types and dosages to treat the variety of different pain types • One drug may not be enough to treat pain. The approach may be to layer pain medication • Consider prescribing patches or topical pain relief if the person with ME has stomach problems • Consider other types of pain relief if medication causes complications or fails. People with ME can have adverse reactions to drugs and may need other types of symptomatic relief. • Pain Clinics can be inappropriate for people with ME as they have no training in physiology of the disease and may operate from dangerous models associated with exercise programs such as deconditioning and sensitisation.	committee agreed they were unable to make any specific recommendations for medicines or prescribing. The committee have provided general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS. The committee linked to NICE guidance that was relevant to people with ME/CFS, the committee acknowledged that this does not address all the type of pain that people with ME/CFS may experience. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate. In addition the managing co-existing conditions of section of the guideline recommends that the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS.
ME Letterforce	Guideline	030	10-12	Needs to be deleted as it conflicts with lines 7-9. People with ME should be referred to a Specialist if OI/POTS is a concern they want addressed. It should not be underestimated how debilitating OI can be in addition to ME. However, care should be taken to ensure that the Specialist they see has had	Thank you for your comment. The recommendations are not conflicting, the first advises on referral when prescribing medication and the second when symptoms are worsening.

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				training and will NOT prescribe an exercise program. People with ME and OI are likely to be different to other people with standalone OI in their response to exercise programs used.	The managing co-existing conditions of section of the guideline also recommends that the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS.
ME Letterforce	Guideline	031	1-4	There are a large number of drugs available to treat nausea and finding the right one could make a big difference to someone with ME. Nausea as an ongoing symptom of a n acute onset viral (stomach bug) or food poisoning should be considered. It might be useful to mention here that nausea can be a symptom of POTS	Thank you for your comment. The evidence for any pharmacological interventions for ME/CFS was inconclusive with limited evidence for any one medicine and this was supported by the committee's clinical experience and consensus view. As a result the committee could not confidently recommend any medicines. To note the recommendation on nausea has been moved to the section on dietary management and strategies.
ME Letterforce	Guideline	031	5-6	This could be confusing and stop GPs from treating symptoms. Please change the wording to "do not offer any medicines or supplements to treat or cure ME but offer as needed for symptoms"	Thank you for your comment. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.' The committee note the following subsection in the guideline is 'medicines for symptom management' and provides advice for prescribers. The discussion section of Evidence review F: Pharmacological management recognises some people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and this should be discussed on an individual basis.
ME Letterforce	Guideline	031	13-14	Add "trying a different brand of a drug if the person with ME has reactions to ingredients such as fillers used" Add "discontinuing drug treatment if adverse reactions noticed and do not tell People with ME that this is normal and will improve as they take the drug"	Thank you for your comment. The committee have included in the other considerations section of Evidence review F:Pharmacolgical management that it is important that medicines management is tailored to the person

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					with ME/CFS and as a result could not provide detailed advice on how to manage intolerance.
ME Letterforce	Guideline	032	15-20	Discuss why someone with ME is taking vitamins first. The reason some people with ME take individual supplements is some find they can tolerate them better and that by trial and error they help symptoms. Multivitamins may be less well tolerated. If a person with ME finds a vitamin helps a symptom then do not recommend that they stop.	Thank you for your comment. The committee agree that any information given would be preceded by a discussion about what vitamins someone is taking and why. Recommendation 1.12.24 recognises it is the person's choice to take vitamins or supplements but that this should be an informed choice with an awareness about potential side effects.
ME Letterforce	Guideline	032	2-3	Discuss with the person their food intolerances and allergies first. Be aware that new ones may appear at the onset of ME	Thank you for the comment. The committee agree and dietary assessment is included in the assessment and care planning recommendations.
ME Letterforce	Guideline	032	23	Add "explain that exercise cannot be used as part of weight control if it causes PEM" Add "slow stomach emptying can also be a symptom of POTS"	Thank you for your comment. The committee discussion section of Evidence review G- non pharmacological management includes that addressing weight gain in people with ME/CFS may require different strategies to those addressing weight gain in people without ME/CFS, in particular exercise may not be appropriate. 'Slow stomach emptying can also be a symptom of POTS" is not a reason for referral or a dietary strategy and has not been added to the recommendations.
ME Letterforce	Guideline	033	3-5	Ask people with severe ME if they would like a dietician assessment in their own home. Do not assume that the diet a person has is limited or poor through choice or lack of education.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home

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					visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The recommendations for people with severe and very severe ME/CFS are comprehensive and include referral to a dietician with a special interest in ME/CFS and recognise there are many reasons why a person's diet is limited.
ME Letterforce	Guideline	034	**Psychological therapies** **General**	This section should start with "Do not offer CBT or Psychological therapies as a cure or treatment for ME/CFS". This will bring it into the same format and warning level as per exercise as a cure.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).

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ME Letterforce	Guideline	034	2-26	2-26. As there is no evidence that CBT is effective or safe for people with ME this section should be deleted. CBT was one of the arms of the PACE Trial and we know from that it is not useful. We would like this section replaced by "Supportive counselling" for people with ME who request it.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).
ME Letterforce	Guideline	034	5-11	We prefer a "Support Plan" which contains what a person with ME needs. A "Management plan" where the patients has to agree to a course of action can be potentially coercive and controlling. The person with ME should be in complete control of their sleep, activity and rest. They are the best people to determine this and can adjust as they see fit and when.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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				A CBT therapist is not an appropriate trained individual to determine appropriate rest, activity and sleep. They have no medical training in exercise physiology related to ME.	The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness and if chosen by the person with ME/CFS delivered as part of the care and support plan and energy management plan. The CBT therapist would work with the other healthcare professionals that specialise in ME/CFS.

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ME Letterforce	Guideline	034	3-4	Discussing a Person with ME's personal understanding of symptoms may not be useful. People with ME have a right to their own thoughts and feelings and a therapist should not be judging if these are appropriate. In particular CBT therapists (who are not medical doctors with an understanding of ME) are not qualified to judge patients symptoms and what causes them.	Thank you for your comment and information. The guideline specifically states that CBT in this context 'takes a non-judgemental, supportive approach to the person's experience of their symptoms.
ME Letterforce	Guideline	036	Managing Co-existing conditions	We support the comments made by Physios for ME	Thank you for your comment.
ME Letterforce	Guideline	036	5-6	It would be useful here to add "Doctors should consider the number and cumulative effect on the Person with ME who have Co-Existing Conditions. The disease burden and knock on effect on the person's functioning and quality of life should be considered"	Thank you for your comment. The NICE guideline on Multimorbidity linked to in this section directly address this point.
ME Letterforce	Guideline	037	2-5	Replace the word "Flare" with "increase in Severity". Remove the reference to "usually lasts for a few days"	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse. This section has been reformatted to aid clarity in reference to you point about usually, 'usually' has been deleted. In the definition describes further the length of time of a flare up and includes that they will typically resolve after a few days in the comparison to a relapse that will last longer.
ME Letterforce	Guideline	037	21-24	21-24 Add consider medication or other treatment for new symptoms 21-24 Add consider medication or treatment for chronic or new infections	Thank you for your comment. The recommendation includes as a minimum what would be reviewed in the care and support plan after a relapse and is not meant to be exhaustive. This does not exclude the areas you

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					have mentioned and as with any review it would be personalised to the individual.
ME Letterforce	Guideline	037	15-17	15-17 Relapse. This should be defined as a exacerbation of symptoms that continues past the person with ME's normal PEM recovery time. "Management plan" needs to be removed. The extra stress on to a person with ME who is suffering a relapse of trying to impose a management plan would add to their disease burden.	Thank you for your comment. Flare ups and relapse are further defined in the terms used in the guideline with flare up recognising that flare ups usually occur as part of PEM anda relapse as a sustained and marked exacerbation of symptoms lasting longer than a flare-up.
ME Letterforce	Guideline	037	10-11	Monitor symptoms if patient wishes as phone calls or visits can cause further PEM.	Thank you for your comment and information. Monitoring symptoms here refers to the person and monitoring their symptoms, to be aware of worsening symptoms indicating a possible relapse.
ME Letterforce	Guideline	037	12-13	Should be deleted as this refers to an exercise program. The person with ME should be left to monitor their symptoms and to continue to REST and PACE	Thank you for your comment. This refers to physical activity and not an exercise programme and for this reason has not been deleted.
ME Letterforce	Guideline	037	1	The Word "Flare" can gives the wrong impression. It sounds like something short and intense. Given that Post Exertional exacerbation of symptoms can take up to 72 hours to develop and weeks if not months and longer to resolve we need to find a better way of describing this. Please consider "Managing Fluctuating Symptoms, Relapses and Increases in Severity" as the heading for this section	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse. Flare ups and relapse are further defined in the terms used in the guideline with flare up recognising that flare ups usually occur as part of PEM andis transient with a relapse as a sustained and marked exacerbation of symptoms lasting longer than a flare-up.
ME Letterforce	Guideline	037	9	Add temporarily reducing activity levels and recommending they REST, SLEEP and use classic PACING as needed.	Thank you for your comment. The recommendation includes general strategies for people with ME/CFS, specific strategies would be individual to the person with ME/CFS and discussed as part of their care and support

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					plan. The risk of including examples in a recommendation is that they cannot be exhaustive and there is the risk these are taken as the only options available.
ME Letterforce	Guideline	038	12-16	Delete this section as it refers to a Management Plan and activity/exercise which should be avoided	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) This refers to the person's overall care plan.
ME Letterforce	Guideline	038	6-9	If a relapse is not responding to REST, SLEEP and PACING the person with ME should receive support as needed from a Specialist. This should only be a person with experience in Biomedical treatment of symptoms. This may need to be offered in the patient's own home as a visit to a clinic may make a relapse worse. They may request supportive counselling to be delivered in their own home as well.	Thank you for your comment. The committee agree and throughout the guideline the importance of ME/CFS specialist services is reinforced and where access to these services is required. They have recommended that certain interventions should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. The committee agree that flexibility in accessing to services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
ME Letterforce	Guideline	038	3-5	This should be deleted as no management plan should be needed.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans

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					https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) This refers to the person's overall care plan.
ME Letterforce	Guideline	038	17-19	Remove the word "flare" We welcome the opportunity for people with ME to discuss what they learn from a Relapse and what can be done in the future to stop this happening	Thank you for your comment. This applies to a flare up as well and for this reason has not been deleted.
ME Letterforce	Guideline	038	1-2	Consider the language and intent here. It is not reasonable to ask a person with ME and / or family members to "agree" to any plan. It is up to the person with ME, (with involvement of their family if appropriate and a medical professional) to determine with support they need with REST, SLEEP and PACING needs. The person with ME may ask for help to communicate and explain their new needs to their family or carers. The control must rest with the patient.	Thank you for your comment. The recommendation is to discuss and agree. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
ME Letterforce	Guideline	038	10-11	Remove the word "flare"	Thank you for your comment. This applies to a flare up as well and for this reason has not been deleted.
ME Letterforce	Guideline	038	20-21	Remove the word "flare"	Thank you for your comment. This applies to a flare up as well and for this reason has not been deleted.
ME Letterforce	Guideline	039	2-4	Please add to this section "Patients should be given a way of formally requesting a review when needed"	Thank you for your comment. The committee agree that people with ME/CFS should have access to care when needed. Throughout the guideline the

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				Remove the word "management plan". This should be a review of their care and what issues the patient needs addressed. Please add that this may need to be done at a series of appointments at the patients home. They should not face further PEM attending a clinic if that is a problem.	committee have reinforced the importance of personalised collaborative care and in addition in the multidisciplinary section of the guideline the recommends everyone with ME/CFS has a named contact in their primary care and/or ME/CFS specialist teams to help them access services. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. As noted access to services is reinforced throughout the guideline and for this reason your suggestion has not been added to the recommendations here. The care and support plan should underpin the person's care and should be reviewed at least annually to assess if any changes need to be made to the plan or the person's care. For this reason review of the plan has not been removed. To note management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The committee note that the review

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					here is based in primary care and this would reduce the need for travelling to specialist centres.
ME Letterforce	Guideline	039	5-7 8-12 16	These reviews need to be offered in the patient's own home as required. The person with ME should not face further PEM by being forced to attend a clinic for this. Please remove the word " management plan " from this section. Remove "Activity" as people with ME should not be undertaking "Activity programs"	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The committee note that the review here is based in primary care and this would reduce the need for travelling to specialist centres. The care and support plan should underpin the person's care and should be reviewed at least annually to assess if any changes need to be made to the plan or the person's care. For this reason review of the plan has not been removed. To note management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) Activity has been edited to energy management plan.
ME Letterforce	Guideline	040	General	We support the comments made by Physios for ME	Thank you for your comment and information. We will pass this information to our resource endorsement team. More information on endorsement can be found here

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				We welcome the inclusion of this very important topic. In particular we would like to highlight the excellent CPD training course with Dr Nina Muirhead. We propose that because there are few doctors left in England and Wales who have experience in treating people with ME and who have a Biomedical approach, training needs to be developed as a matter of urgency and with their involvement.	https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme
ME Letterforce	Guideline	040	11-15	This should include research finding on specific physical abnormalities in people with ME. Because we don't understand what causes ME we need to concentrate on the research findings that help to explain symptoms. This should be bio-medical. The emphasis on Psychosocial biased training has led to poorly educated GP's who are not comfortable with patients and so not understand their physical symptoms. it would be useful here to include "International" as research in the UK has in some ways been lagging behind the rest of the world	Thank you for your comment. The committee discussed the level of detail that should be included in training programmes and agreed on a general description to avoid a prescriptive interpretation of the content allowing the recommendations to remain relevant as research in the area develops. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
ME Letterforce	Guideline	040	17-18	The "specialist services" needs some more qualification. Current NHS clinics based on Psychosocial methods should not be providing training. We need Education developed by doctors and other professionals e.g. Physios and OTs with experience in what ME is and how best to treat patients.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.

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ME Letterforce	Guideline	041	9-11	Please add "activity includes standing still and can cause disproportionately far worse PEM compared to (e.g.) walking for same length of time. Patients need to know this as some may not be aware of any symptoms of OI. Note - Orthostatic intolerance affects the vast majority of ME patients and is not caused by deconditioning.	Thank you for your comment. The definition of activity includes physical activity, the committee decided not to include examples of any activity (physical, cognitive, emotional or social) as any list of examples cannot be exhaustive and there is the risk these are taken as the only options available.
ME Letterforce	Guideline	042	17-18	Remove "hypervigilance during sleep" as there is no evidence and this may be interpreted as a psychological problem	Thank you for your comment. Hypervigilance has been removed.
ME Letterforce	Guideline	043	3-8	3 8 Please remove "management plan" and the lines underneath. Replace with "Support Plan" and define this as the actions needed to support the patient and the areas Remove CBT, insert "Supportive Counselling if requested" Remove "Physical Maintenance" Add "Convalescence", "REST" and "Sleep" Remove Energy Management and Physical Activity and add "PACING" (but ensure this is not APT) Add "Symptom treatment priorities" Add "Investigations needed" Add "work or educational support" Add "reports needed for state benefits or insurance" Add "Aids needed"	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans. https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) The definition is a summary and includes an overview of what is within the care and support plan, it is not meant to be exhaustive. For this reason you suggestions have not been added.

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				Add "other support needed"	
ME Letterforce	Guideline	043	9-13	11. Change "Most are.." to "some are" 12. Add a new sentence after "Social pursuits" that reads "Work can be part time or limited to a sedentary job only" then "may need special transport to work or school" and "may need help in the home or with cooking" and " may need a wheelchair to be able to work and pace their energy and strength" 13 Add … "or use holidays" 13 Add at the end that they may have difficulty attending medical appointments as work uses all their energy	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. As noted above the definitions are not clear cut and they provide a guide to the level of impact of symptoms on everyday functioning. For these reasons your suggestions have not been added.
ME Letterforce	Guideline	044	6-17	Remove or rewrite this section. It is unlikely that People with ME will have the energy left over from the demands of daily living to engage in what is an exercise program. Any exercise program will trigger post exertional symptoms. They may have more urgent issues to spend this energy on. They may prefer to use this to have a social life or something else if they did.	Thank you for your comment. After considering the range of stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility. The committee agreed this was very important for people with ME/CFS with prolonged limited mobility.
ME Letterforce	Guideline	044	4-5 6-17	Remove the reference to the WHO guide to Physical Activity as it contains no ME related information Remove or rewrite this section. It is unlikely that People with ME will have the energy left over from the demands of daily living to engage in what is an exercise program. Any exercise program will trigger post exertional symptoms. They may have	Thank you for your comment. The committee agreed it was important to have this definition and have included at the end that that for many people, physical activity has a health benefit but in people with ME/CFS physical activity may make their symptoms worsen'. *Physical maintenance*

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				more urgent issues to spend this energy on. They may prefer to use this to have a social life or something else if they did.	After considering the range of stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility. The committee agreed this was very important for people with ME/CFS with prolonged limited mobility.
ME Letterforce	Guideline	045	17-20	Please include that sleep can feel deep but is still unrefreshing. It is not just a feeling of a light sleep for all. Some people with ME wake up feeling worse than when they went to bed/sleep	Thank you for your comment. After considering the stakeholder comments, this definition has been edited to,' Unrefreshing sleep means that is non-restorative. Even after a full night's sleep people do not feel refreshed. People with ME/CFS often report waking up exhausted and feeling as if they have not slept at all, no matter how long they were asleep.' to aid further clarity.
ME Letterforce	Guideline	045	3-4	It should be clear that severely affected people are not likely to use a self propelled wheelchair to a great extent and will need to be pushed or to use an electric wheelchair. In some cases a lie-flat wheelchair is needed	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
ME/CFS Parents UK	Guideline	General	General	Pregnancy is not mentioned in the guidelines. • There are variable affects. Some are more well during pregnancy but some are worse. As well as first trimester tiredness an awareness is needed that during the 3rd trimester women with ME often have more fatigue and symptoms again. They may need	Thank you for your comment. The committee agree this is an important area with very little information available for clinicians and pregnant women with ME/CFS. The evidence in this area is sparse and none was identified to support the committee in developing any recommendations.

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				more support or home visits. Home visits should be more available throughout pregnancy. - There needs to be understanding about limited energy during hospital check-ups, with provision for wheelchair access, being able to lie down, home visits where needed and to be able to have partner/carer present. There also needs to be understanding of sensitivities to medications. Consultants need understanding that PEM can be a major factor in births.	The committee hope that the focus in the guideline on personalised care and regular review of care would prompt the necessary planning required for pregnant women through to and including the post-natal period. In the recommendations on Access to care the importance of providing care that reflects the person's needs is emphasised. To highlight the lack of information available additional text has been added to the other considerations sections of Evidence review A:Information for people with ME/CFS, Evidence review B: Information and support for health and social care professionals, and Evidence review C: Access to care. To raise awareness of this gap in the evidence pregnant women and women in the post-natal period have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations. *Home visits* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
ME/CFS Parents UK	Guideline	General	General	Post-natal:	Thank you for your comment. The committee agree this is an important area with very little information available for clinicians and pregnant women with

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				• A side room at hospital should be offered so it is quieter. Keep disturbance in room to minimum to allow mother to rest and recover. • May need more support in hospital from partner, allow to stay with them in carer role to help care for baby if needed. • May need home visits from health visitors or other health care advisors for longer than normally provided. • Breastfeeding support as often reduces symptoms, but also support using alternative feeding if that suits the family better. • Blood tests should be run if the mother deteriorates after birth. B12 especially, if gas and air was used during labour. • Partner, if partner has ME further rest /support needed and more support perhaps during child birth. Rest area needed... (page 14, line 29).	ME/CFS. The evidence in this area is sparse and none was identified to support the committee in developing any recommendations. The committee hope that the focus in the guideline on personalised care and regular review of care would prompt the necessary planning required for pregnant women through to and including the post-natal period. In the recommendations on Access to care the importance of providing care that reflects the person's needs is emphasised. To highlight the lack of information available additional text has been added to the other considerations sections of Evidence review A:Information for people with ME/CFS, Evidence review B: Information and support for health and social care professionals, and Evidence review C: Access to care. To raise awareness of this gap in the evidence pregnant women and women in the post-natal period have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations. *Home visits* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.

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ME/CFS Parents UK	Guideline	General	General	Parent • Understanding with school that ME is disability and may require assistance with parking space close to school or alternative support getting child to school either from council or school staff collecting from car so parent doesn't need to walk. • Alternative offers to in person parent consultations • Social services care may be needed for child care support to allow parent sufficient rest. Also help may be needed to enable parents to get out with their children and enjoy recreational activities such as baby and toddler groups, day trips etc. • Ensure professionals respect competency of mother /father and that being severe or single does not necessarily equate to not being able to home educate your child or to be able to look after them sufficiently (often though with the right support needed as often support may likely be needed). • Empower disabled parents with ME with as much choice and respect as other parents and do not discriminate or presume upon their parenting abilities, based on their disability, or their support system based on if they are a single parent. • Enquire politely and respectfully if any concerns and support requirements queried, but understand the right to privacy as much as any other non disabled parent is afforded (Page 15, line 12). • Parents often need more support with home maintenance and cleanliness, shopping, gardening, transport.	Thank you for your comments. The recommendations in the guideline apply to all people with ME/CFS and include that health and social care professionals should treat people with empathy and understanding about how their ME/CFS affects them. The committee agree that access to social care is important and has made recommendations to support access to social care. In the maintaining independence section there is a section on access to and the provision of aids and adaptions. These include examples such as a blue badge that could help people maintain their independence and improve their quality of life The committee hope these recommendations help to address some of the challenges that parents with ME/CFS face.

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				• Parents may require a lot of support during baby and toddler stages.	
ME/CFS Parents UK	Guideline	General	General	Therapy/treatment • Understanding that pacing is more challenging when you have childcare responsibilities.	Thank you for your comment. The committee have recommended that care should be personalised and collaborative and should take into account the individual circumstances of the person with ME/CFS.
ME/CFS Parents UK	Guideline	General	General	Child: • May need more support from school, especially if the parent is severe or single. • May need emotional support. • offer a homework club as homework tasks can be very draining for parents. • Access to child carer groups • Recognising that the childs social life and access to clubs may be limited by the parent's health. Have an awareness that this does not mean that a child is a young carer , although some may be, but having suportive open polite, respectful discussions, can target support areas that are needed and support accordingly (Page 16, line 3).	Thank you for your comment. The committee discussed the impact on children having a parent with ME/CFS and noted that the recommendations and advice to families and carers applies to children as well and they should not be overlooked. The committee agree that not all children with parents that have ME/CFS will be young carers but for those that are a young carers needs assessment could be helpful.
ME/CFS Parents UK	Guideline	General	General	There does appear to be a high prevalence of ME parents and ME children and genetic links could be recommended research. Also genetic counselling pre pregnancy, If possible, could be useful.	Thank you for your comment. The prevalence of ME/CFS, links in families and genetic counselling was not evaluated in the guideline and not an area the committee were able to develop research recommendations for.
ME/CFS Parents UK	Guideline	General	General	Some parents with ME choose to home educate because of the difficulties with school runs /access /timetabling and also because of being forced out of the school system either because of these reasons or inappropriate safe guarding reasons, when their child develops ME and finds it difficult to attend school.	Thank you for your comment and information. *Safeguarding*

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				It is very concerning the large number of parents of children with ME that are have unfounded accusations of FII and find themselves forced out of the education system and CFS clinics due to difficulties with attendance. This is especially after a child has been made worse after being pressured by local authorities and school head teachers' pressure to attend more than is possible, within that child's current capability (Page 15, line 19). Also ME/CFS clinics have harmed children, as well as parents, through inappropriate rehabilitative physiotherapy, or even harming during first basic assessment, with for example core after core exercise. This is without appropriate assessments or understanding of capacity, or the effects of exercise on patients with ME. Then patients are either discharged or social services contacted due to missed appointments or not able to meet the desire or schedule of the CFS team or the CFS team not recognising the harm of exercise or the need for rest after relapse (Page 17, line 15). Often the parent also has ME themselves and involving social services and safe guarding assessments unnecessarily, has caused extreme distress and often relapse, for both the children and parent. There does appear to be a high prevalence of ME parents and ME children and genetic links could be recommended research. Also genetic counselling pre pregnancy, If possible, could be useful. Alternative therapies that have been helpful, in ME population and people would like to see funded and further research in to the benefits of - Acupuncture, Osteopathy - Perrin technique in particular, Chiropractor, B12, Mitochondrial supplements, such as coq10, acetly l carnitine and alpha lipoic acid, d ribose..	The committee agreed the topic of safeguarding was very important and agreed to include a separate section in the guideline addressing this. *Education and work* Evidence review A highlights the challenges that children and young people can have in accessing education and adults can have at work this was supported by the committee's experience. To address this the committee made recommendations to supporting people with ME/CFS in work, education and training (section 1.9). *Delivery of care* The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. *Prevalence in families* The prevalence of ME/CFS, links in families and genetic counselling was not evaluated in the guideline and not an area the committee were able to develop research recommendations for. *Osteopathy* After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. However no evidence was identified to support recommending treatments and osteopathy services for people with ME/CFS (Evidence reviews G,H and I) and the committee

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				Please note that lightening therapy is not osteopathy and should not be linked as such in the same sentence or context.. (Page 28, line 10). We have heard of harm from the lightening therapy, as well as from graded exercise therapy/exercise therapies. Many have found it hard to access the wheelchair /social support necessary or disabiity / inability to work benefits that should be able to support them and need far more support from their doctors for these. Direct care payments can help in maintaining independence and help with parenting roles and preferred lifestyles. Access to work can be helpful for support in maintaining or starting work (Page 21, line 8) . However, many with ME find it hard to work, especially if the work place is not flexible and will not support fairly reasonable adjustments. In particular, many parents often find it very hard to sustain working, as well as being a parent. This impacts upon available money and an increase in risk of poverty and maintaining quality of life , especially if they are not able to access benefit support, or a single or unsupported parent.	agreed they could not include any recommendations for treatments based on osteopathy. *Access to social care* The committee agree that access to social care is important and has made recommendations to support access to social care and signposting to benefits. In the maintaining independence section there is a section on access to and the provision of aids and adaptions. These include examples such as a blue badge that could help people maintain their independence and improve their quality of life.
ME/CFS Parents UK	Guideline	014	29	Birth: • Caesarean section may be best for some mothers, especially more severe, but recovery can be longer than in healthy parents. Vaginal births are possible and well tolerated. Fatigue may lead to interventions such as assisted births being needed. Medication is not always well tolerated as some people with ME are sensitive to medications. • PEM may affect births, especially if they are long. The partner may need to be the mother's advocate.	Thank you for your comment and information.

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NHS England and NHS Improvement	Guideline		Throughout	The explicit mention of dieticians/referrals is welcome to help people understand the need for referral in more complex situations – might it be appropriate to be more explicit about the roles and responsibilities of physiotherapists and occupational therapists within the document too, appreciating that they may be interchangeable at points? (CH)	Thank you for your comments. The section on multidisciplinary care recommends the expertise people with ME/CFS should have access to. This section lists the expertise that is required and not specific professions recognising that members of multidisciplinary teams particularly in specialist teams work holistically supporting many elements of care. As you note where expertise is required from a specific professional this is explicit. Referral to a physiotherapist or occupational therapist is explicitly recommended in the recommendations on physical activity and for developing energy management plans for people with severe and very severe ME/CFS.
NHS England and NHS Improvement	Guideline			**Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why.** Having a named person in primary care if that is the GP may be a challenge due to capacity, however the developing roles of AHPs in primary care may be an enabler to achieving this in practice. (CH)	Thank you for your comment. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as flexible access to care, to implement some recommendations in the guideline. guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned.
NHS England and NHS Improvement	Guideline			**What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.)** Employer forums to enable employers to understand and educate re. condition and how they can support users to maintain their employment, reducing occupational deprivation; Utilising an outcome measure that helps the user to see the progress there are making e.g such as the Patient activation measure; Good practice Case studies - Services in Devon – Exeter are delivering services in response to NICE guidelines, including carer forums/group sessions to help the users overcome	Thank you for your comment and suggestions. We will pass this information to our local practice collection team. More information on local practice can be found here**:** https://www.nice.org.uk/localPractice/collection?page=1&pageSize=10&type=&published=&filter=ME+.

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				challenges. The feedback and outcomes achieved from have carers group sessions has had very positive impact . (CH)	
NHS England and NHS Improvement	Guideline	General		To align with the NHSEI comprehensive model for personalised care, we would suggest use of the term "personalised care and support plan" rather than "management plan". (PC)	Thank you for your comment. Management plan has been edited to personalised care and support plan.
NHS England and NHS Improvement	Guideline	General	General	Chapter 1 In general terms, this is a highly unusual guideline in that it appears to dismiss almost all the evidence existing relating to the diagnosis, management and treatment of ME/CFS. The first chapter on identifying and diagnosing ME/CFS dismisses existing diagnostic criteria; they assert that ME/CFS is highly individual, unpredictable and variable in its symptoms and severity; it often runs a fluctuating and variable individual course; and then they conclude that: *" the committee agreed to consider the evidence based on inclusion criteria that did not include PESE [post exertional symptom exacerbation] as a* ***compulsory*** *feature for diagnosis as "indirect", on the basis that it was difficult to be sure if the population consisted only of people with ME/CFS".* This is really quite an extraordinary conclusion which is unjustified by any evidence, but is clearly the view of the guideline committee or some dominant views within the committee. This kind of conclusions/assertions, based on no evidence and derived from the 'views of the committee', runs through the rest of the guideline. **(TK)**	Thank you for your comment. *Dismissed evidence* All NICE guidelines follow the process for evidence synthesis as set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. Accordingly no study has been excluded that met the review protocols. If the studies did not have any of the outcomes listed in the protocol then they would have been excluded. The process for quality rating used in NICE guidance is an internationally agreed process and it is not unusual for evidence to be graded as low or very low quality. This does not mean it cannot be used to make recommendations but affects the strength of recommendations. PESE/PEM is widely acknowledged in ME/CFS specialist practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just do not know how many if the information is not reported.

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					Where this is the case, the trial population could include people that do not have ME/CFS and this makes it difficult for the committee to be confident of the benefits and risks of the interventions on people with ME/CFS. Using GRADE and CERQual the committee agreed that evidence without this information would be 'indirect' (relevance in CERQual) acknowledging this uncertainty about the population. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and CERQual. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative and qualitative evidence and the application of indirectness and relevance. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee included members with clinical and personal experience of children and young people with ME/CFS.

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					When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed).
NHS England and NHS Improvement	Guideline	General	General	Chapter 2 and 3 The next two chapters, based on no relevant or appropriate evidence except the views of the guideline committee, states there are no tests and nothing clear about the illness, but the conclusion from chapter 1 remains (that ME/CFS has a single COMPULSORY feature – PESE). As such, this guideline is no longer a guideline on ME/CFS, but on PESE. They have created a new illness which, no doubt, overlaps with ME/CFS. And they have done so on no convincing evidence at all; but have, in the process, eliminated key trials with significant evidence for the benefits of psychological treatment, for example the Oxford trial. In my view, what the guideline makers should have done is what was done for NICE in another area with a controversial diagnosis: ADHD. The then GDG did a pretty extensive look at the evidence supporting and contradicting the existence of ADHD using the Washington criteria, which are the criteria most commonly used to establish the existence of a separate/new illness category. It is fair to say that this could be	Thank you for your comment. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The four symptoms (debilitating fatigue, PEM, unrefreshing sleep and cognitive difficulties) were agreed by the committee as the best basis for identifying people with ME/CFS and as essential to a diagnosis of ME/CFS. The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail).

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				done with many conditions as very few have "gold standard" diagnostic tests, including those which have clear physical pathology, such as diabetes. **(TK)**	
NHS England and NHS Improvement	Guideline	General	General	Chapter 4 onwards The rest of the guideline then ignores any quantitative study which doesn't fit this new disease – PESE; and, instead, the committee base most of their recommendations on an analysis of qualitative evidence. And all the quantitative evidence cited is systematically downgraded until they conclude that there is no cure nor any treatment for PESE, just self-management, with the option to do some psychological work because people like it. I don't think I have read a guideline which recommends that patients must be told that there is no cure and no treatment for people with the condition. When this guideline is compared to the guideline on the management of chronic pain, it becomes obvious that the two guidelines (ME/CFS and the Management of Chronic Pain) had used entirely different methods, different language and came to very different conclusions about the role of psychological treatments. There is therefore a strong impression that the ME/CFS guideline committee are not in favour of psychology or psychiatry in general, hence the exclusion of certain pieces of evidence. It is my view that the guideline needs to be redone to include the evidence base that this guideline committee have sought to systematically exclude. There are doubts that the existing guideline committee would be able to approach the evidence without bias and to admit that some of the best evidence for treatment and help for people with ME/CFS is psychological treatment (and exercise). We have doubts that the existing guideline committee would be able to approach the evidence without bias and to admit that some of the best evidence for treatment and help for	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis as set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. Accordingly no study has been excluded that met the review protocols. If the studies did not have any of the outcomes listed in the protocol then they would have been excluded. The process for quality rating used in NICE guidance is an internationally agreed process and it is not unusual for evidence to be graded as low or very low quality. This does not mean it cannot be used to make recommendations but affects the strength of recommendations. PESE/PEM is widely acknowledged in ME/CFS specialist practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just do not know how many if the information is not reported. Where this is the case, the trial population could include people that do not have ME/CFS and this makes it difficult for the committee to be confident of the benefits and risks of the interventions on people with ME/CFS. Using GRADE and CERQual the committee agreed that evidence without this information would be 'indirect' (relevance in

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				people with ME/CFS is psychological treatment (and exercise). **(TK)**	CERQual) acknowledging this uncertainty about the population. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and CERQual. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative and qualitative evidence and the application of indirectness and relevance. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee included members with clinical and personal experience of children and young people with ME/CFS. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through

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					discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). The NICE Policy on declaring and managing interests for NICE advisory committees sets out the processes for : • what interests need to be declared and when • how declared interests should be recorded • when a declared interest could represent a conflict of interest and the action that should be taken to manage this. As with any other guideline this Policy has been applied to this guideline. The Interests Register for the committee is published on the NICE website (https://www.nice.org.uk/guidance/indevelopment/gid-ng10091/documents) . The register has been updated throughout the development of the guideline and includes the decisions and actions made on the interests declared.
NHS England and NHS Improvement	Guideline	General		Has it been considered where a young person with Long Term Condition in the midst of transitioning to adult health services, diagnosed with ME may need a tailored approach? Query relates also to whether the transition process be paused and if not, would there be any special measures put in place to ensure smooth transition. (ND)	Thank you for your comment. The guideline recommends a personalised approach thought out the guideline and there is a recommendation in the Multidisciplinary care section of the guideline that links to the NICE guideline on transition from children's to adults' services for young people using health or social care services.
NHS England and NHS Improvement	Guideline	General		For clinic appointments….is the app 'Attend' anywhere used for individuals in this group? and/or are young people expected to physically attend the clinic? Need to consider other flexible ways of working (ND)	Thank you for your comment. The committee recognised there are such challenges with people with ME/CFS and in the access to care section of the guideline recommends that care should be provided flexibly such as by phone or video conferencing or making home visits.

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NHS England and NHS Improvement	Guideline	General		Helpful to have information included to highlight the links to an integrated approach to health for these individuals especially where there are numerous conditions that may be being managed at one time. Coordination is key to avoiding people explaining themselves multiple times. The role of a coordinator, specialist nurse or named professional may be useful to outline. (ND)	Thank you for your comment. The committee agree and this is emphasised in the multidisciplinary care section of the guideline, included in here is a recommendation for a named contact to support people with ME/CFS to coordinate management plan, help them access services and support them during periods of relapse.
NHS England and NHS Improvement	Guideline	General		**Holistic** assessment and management is vital - recognising multisystem involvement and impact (KC)	Thank you for your comment and information. The committee and have made recommendations that holistic assessment and management is vital.
NHS England and NHS Improvement	Guideline	General		Involvement of **occupational health** support in MDT assessment/management could be helpful	Thank you for your comment. The multidisciplinary section of the guideline includes a list of expertise that people with ME/CFS should have access to and this includes support to engage in work.
NHS England and NHS Improvement	Guideline	General		If a new symptoms arises, important not to necessarily attribute it to CFS as it could be coincidental different pathology (KC)	Thank you for your comment. The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a change in symptoms are investigated and not assumed to be due to the person's ME/CFS. This should ensure that changing or new symptoms are not overlooked and appropriate investigations are done. This is also reinforced in the flare up and relapse section of the guideline.
NHS England and NHS Improvement	Guideline	General		Access: need to address the issue of equity of access to different communities and those with protected characteristics as well as the impact of the care they then receive (KC)	Thank you for your comment. When evaluating all the evidence the committee considered all the groups identified in the Equality Impact Assessment, the applicability and generalisability of the evidence was considered by the committee in their discussion of the evidence. Very little specific evidence was identified for any of the groups and the committee agreed that the recommendations should equally apply to all groups, and did not discriminate against any

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					particular group and separate recommendations were not thought necessary for any of these groups. The committee agree these factors need to be considered when delivering care and have added, 'Be sensitive to the person's socioeconomic, cultural and ethnic background, and faith group, and think about how these might influence their symptoms, understanding and choice of management.' to recommendation 1.1.3.
NHS England and NHS Improvement	Guideline	004	17	Really important point to bring out: "feel stigmatised by people who do not understand their illness" (KC)	Thank you for your comment.
NHS England and NHS Improvement	Guideline	004	21	Include recognition that people may have invested in alternative interventions for which the evidence base is weak, as per Evidence review G - Non pharmacological management (PC)	Thank you for your comment. This is addressed in the managing ME/CFS section of the guideline and recognised in the rationale and for this reason your suggestion has not been added to this recommendation.
NHS England and NHS Improvement	Guideline	005	Section 1.1.3	"Health and social care professionals should:" suggest 1.1.3 section inc acknowledgement is a must as good practice when supporting anyone with a confirmed or suspected LTC. (ND)	Thank you for your comment. Must is used in a recommendation when there is a legal duty to apply a recommendation. This is not the case here and no changes have been made to the recommendation.
NHS England and NHS Improvement	Guideline	005	6	Using a person-centred approach to assess people's needs is vital. Good to emphasise that it is not just about the symptom per se but what they want to be able to do in life. (KC)	Thank you for your comment.
NHS England and NHS Improvement	Guideline	005	10	"Early and accurate diagnosis so they get appropriate care for their symptoms" - knowledge on how to do this might need re-inforcing (KC)	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.

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NHS England and NHS Improvement	Guideline	005	13	Really important to highlight the relapsing-remitting nature of the condition (KC)	Thank you for your comment.
NHS England and NHS Improvement	Guideline	005	16	The management plan should be positioned as a plan that is agreed with the person so they have some choice and control of the care and support they will receive. To decline the plan would suggest they were not involved in agreeing it in the first place. (PC)	Thank you for your comment. This recommendation is supported by the evidence and the committee's experience. Some people with ME/CFS reported negative reactions from health and social care professionals when they did not want to follow the advice given (see Evidence review A, Appendices 1 and 2). The committee agreed it was important to make a recommendation supporting people's choices and involvement in their care. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.).
NHS England and NHS Improvement	Guideline	006		Are there different symptoms affecting different groups that healthcare/social care professionals need to be aware of in order to assess and manage? (KC)	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Taking into account the range of stakeholder comments on the descriptions of severity in the guideline the committee have moved the recommendations on people with severe and very severe ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. The following section on suspecting ME/CFS includes the symptoms that all people with ME/CFS experience and those symptoms that are commonly associated with ME/CFS and now precedes this section.

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NHS England and NHS Improvement	Guideline	006	7	Important to state that this is a **multisystem** condition - not only limited to fatigue (as the name CFS implies - do people with lived experience think this is still the right term to use?) (KC)	Thank you for your comment. The first recommendation in the guideline highlights that ME/CFS is,' a complex, chronic medical condition affecting multiple body systems'. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'*
NHS England and NHS Improvement	Guideline	006	8	"may experience some of the following symptoms that significantly affect their emotional wellbeing, communication, mobility and ability to interact with others and care for themselves" wording may confuse, suggest "can" instead of "may" and put "maintain or provide" in front of "care for themselves". (ND)	Thank you for your comment. The committee agreed that your suggestions did not add further clarity to the recommendation and for this reason your suggestions have not been added.
NHS England and NHS Improvement	Guideline	006	28	Suggest section 1.1.9 is reframed to show ability and not disability especially "have problems accessing information" which may be seen as blame attributing. (ND)	Thank you for your comment. This section highlights the difficulties that people with severe or very severe ME/CFS may have and is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these difficulties and the support that may be needed to manage their symptoms.

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					The following part of the sentence explains why people with severe or very severe ME/CFS may have problems accessing information and it is clear this is not blame attributing.
NHS England and NHS Improvement	Guideline	007	21	Suggest there needs to be reference to these individuals having the relevant skills, training and expertise also. (ND)	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training in line with this guideline and this is included in the recommendations in the training health and social care professionals section of the guideline. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable for this reason your suggestion has not been added to the recommendation.
NHS England and NHS Improvement	Guideline	007	22	Risk assessment with person with severe ME still should involve the person where appropriate. (ND)	Thank you for your comment. 'if appropriate' has been added to the recommendation.
NHS England and NHS Improvement	Guideline	008	4	Suggest inclusion of line to explain to person that despite the "lack of test" this will not/should not impact their ability to access timely and effective care. (ND)	Thank you for your comment. Recommendation 1.14 in the principles of care section of the guideline includes that people with ME/CFS need timely and accurate diagnosis so they get appropriate care for their symptoms. In addition the section on suspecting ME/CFS also includes a recommendation that while waiting for a diagnosis people should be given advice on managing this symptoms and links to the section on advice for people with suspected ME/CFS.
NHS England and NHS Improvement	Guideline	008	15	May be some variation in application where stating "significantly reduced" and need to ensure this isn't unwarranted. How will this be measured? (ND)	Thank you for your comment. While agreeing that the application of significantly is subjective to the individual the committee note that it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important when suspecting and in the diagnosis of ME/CFS and not seeing each criteria in isolation. It is anticipated

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					that over the period of 6 weeks and then at 3 months this would result in a significant reduction in a person's ability compared to the pre-illness levels and this is generally accepted description of the impact. The IOM 2015 describes, 'a substantial reduction or impairment in the ability…'.
NHS England and NHS Improvement	Guideline	009	19	"give the person advice about symptom management" needs to be expanded in generic terms to reflect there is also offers of support and information more widely that is included in the following sections. (ND)	Thank you for your comment. This has a link added to the section on advice for people with suspected ME/CFS. The committee agree that although here this is referring to people with suspected ME/CFS much of the information in the access to care section of the guideline is good practice in how to enable access health and social care. The NICE guideline on patient experience is referenced in the information and support section of the guideline.
NHS England and NHS Improvement	Guideline	010	9	"write to the child or young person's place of education or training to advise about flexible adjustments or adaptations." Suggest this needs to identify also how the child or family are included in this process (as identified later in the guidance). (ND)	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan.
NHS England and NHS Improvement	Guideline	011	8 and 12	Any management plan should be agreed with the patient, so rather than 'develop' could this say 'agree'? (PC)	Thank you for your comment. This has been edited to, 'develop and agree'. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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NHS England and NHS Improvement	Guideline	012	10	To align with the NHSEI comprehensive model for personalised care, we would suggest use of the term "personalised care and support plan" rather than "management plan". This would focus the discussion around what matters to the person and the health and wellbeing outcomes that they want to achieve. This is particularly helpful for people with ME/CFS due to the varied nature of the condition and how this will impact on the person's life. The criteria used by NHSEI for a personalised care and support plan are: 1. People are central in developing and agreeing their personalised care and support plan including deciding who is involved in the process 2. People have proactive, personalised conversations which focus on what matters to them, paying attention to their needs and wider health wellbeing 3. People agree the health and wellbeing outcomes they want to achieve, in partnership with the relevant professionals 4. Each person has a sharable personalised care and support plan which records what matters to them, their outcomes and how they will be achieved 5. People have the opportunity to formally and informally review their care plan. (PC)	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
NHS England and NHS Improvement	Guideline	012	29	As well as health and social care professionals who are supporting the person, there may be a wider support network including peer support and mentors, voluntary and community services that should also be reflected in the plan. (PC)	Thank you for your comment. This is included in the information and support section link in the first bullet point.
NHS England and NHS Improvement	Guideline	013	2	Suggest adding in that the plan could be developed by the person themselves if they wish to. (PC)	Thank you for comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans

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					https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.). In line with this the bullet points have been deleted as this is reflected in the aims of a care and support plan. The personalised care and support plan is based on the person's needs and includes the areas listed. The plan is developed in collaboration with the person with ME/CFS and explores their aims *and the management of their health and well-being within the context of their whole life and family situation. It should be proportionate, flexible and coordinated and adaptable to a person's health condition, situation and care and support needs.* The recommendation is clear that the person is in charge of their care and support plan and this would include developing it themselves.
NHS England and NHS Improvement	Guideline	013	4	If we are talking about a personalised or person centred approach to planning then we would suggest that this bullet point should be amended to say 'what matters to the person and the support they may need' rather than preferences and needs. (PC)	Thank you for comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.). In line with this the bullet points have been deleted as this is reflected in the aims of a care and support plan. The personalised care and support plan is based on the person's needs and includes the areas listed. The plan is developed in collaboration with the person with ME/CFS and explores their aims *and the management of their health and well-being within the context of their whole life and family situation. It should be proportionate, flexible and coordinated and adaptable to a person's health condition, situation and care and support needs.*

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NHS England and NHS Improvement	Guideline	013	10	It might be useful to add in that a copy of the management plan should be held as part of a shared record, so it can be accessed by all involved in the person's care without them having to repeat their story over and over again. (PC)	Thank you for your comment. The review in primary care section of the guideline states that there should be access to the care and support plan and any clinical communications from the ME/CFS specialist team. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
NHS England and NHS Improvement	Guideline	013	12	Are home visits only available to this group? Also what other flexible approaches are available and promoted? (ND)	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
NHS England and NHS Improvement	Guideline	013	14	Information in **different languages** too - are ethnically diverse communities as aware of the support that is available? (KC)	Thank you for your comment. ' and if possible in the person's preferred language' has been added to the recommendation.
NHS England and NHS Improvement	Guideline	013	17	Suggest adding something about the importance of being aware of people's levels of health literacy when providing information. (PC)	Thank you for your comment. As with all examples in recommendations they are not meant to be exhaustive and the link to the NICE guidelines on patient experience in adult services has further information on communication.
NHS England and NHS Improvement	Guideline	013	17	"Provide information to people with ME/CFS and their families and carers in a variety of formats" suggest needs to identify	Thank you for your comment. As with all examples in recommendations they are not meant to be exhaustive and the link to the NICE guidelines on patient

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				that it is about giving information in a way the person understands not just about variety. (ND)	experience in adult services has further information on communication.
NHS England and NHS Improvement	Guideline	014	1	For young people, what method/s used to communicate effectively? Need to consider the range of communications available from virtual learning and environments and apps through to more traditional routes etc (ND)	Thank you for your comment. Digital media, for example video or interactive apps are included in the examples.
NHS England and NHS Improvement	Guideline	014	22	This is really important to emphasise, as there is a great deal of misunderstanding about recovering from ME/CFS. May be helpful to explain that ME/CFS is categorised as a long-term condition. (PC)	Thank you for your comment. After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS.
NHS England and NHS Improvement	Guideline	015	6	Could also include peer support networks, mentoring, and health and wellbeing coaches. Could also reference social prescribing schemes that could help people access practical support with finances and employment, or to connect in with community groups to help address people's wider wellbeing needs. (PC)	Thank you for your comment. The committee agreed on a broad recommendation on where to access information and not to add examples of organisations. As with any list of examples these cannot be exhaustive and there is the risk these are taken as the only options available.
NHS England and NHS Improvement	Guideline	015	12	If including this statement in 1.6.8 add…. Adopting a strengths-based approach (e.g. focusing on the persons strengths as per the care act 2014) discuss sensitively with the person and their family members or carers how they can access support to optimise health and wellbeing including, community groups, voluntary sector and social care support. Explain that community support can help the person living with ME/CFS as well as provide a rout to support for families and carers through carer support services including a carers assessment. (CH)	Thank you for your comment. This recommendation directly addresses the evidence (see evidence reviews A and C) and committee's experience that some people with ME/CFS have had poor experiences accessing health and social care services. This recommendation is to raise awareness in healthcare professionals that this might be a sensitive area and to reassure people with ME/CFS that this is an option to access support The committee discussed the use of the term 'strengths based' and recognised that this term is not recognised as helpful by all

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					disability groups. The committee agree that it is important to for health and social care professionals to work collaboratively to identify the strengths a person has and to build on these but also that there is a balance where people are able to access support for a disability without feeling like they have failed. For this reason the term strengths based approach has not been used.
NHS England and NHS Improvement	Guideline	015	16	Explain to people their families and carers how to self-refer for a social care needs assessment from the local authority, if their needs cannot be met by signposting to community support networks and voluntary sector. Offer to make the referral for them, if they prefer or where applicable. (CH)	Thank you for your comment. This section directly addresses how to access social care for formal support and how some people may find this difficult as a result of previous experiences. As social prescribing is a less formal form of support it is not as relevant to this section. For this reason these suggestions have not been added.
NHS England and NHS Improvement	Guideline	015	17	"Offer to make the referral for them if they prefer" suggest helpful here to explain the relationship between services and how information will be shared to support effective care. (ND)	Thank you for your comment. This section addresses how to access social support and the committee agree that this information would be useful if the person pursues a referral but that this point does not add any further clarity to the recommendation and has not been added.
NHS England and NHS Improvement	Guideline	015	22	This is the first point in the document where reference is made to ME/CFS as a disability. This could be introduced with more detail on page 14, line 22, making links to the 2010 Equality Act Guidance which lists ME amongst "impairments with fluctuating or recurring effects". (PC)	Thank you for your comment. In the supporting people with ME/CFS in work, education and training section of the guideline there is direct reference to the Equality Act 2010 and how it could support people with ME/CFS.
NHS England and NHS Improvement	Guideline	017	8	"Recognise that the following are not necessarily a sign of abuse or neglect in children and young people with confirmed or suspected ME/CFS" suggest this is ambiguous and runs the risk of reaffirming poor safeguarding practice, a change in terminology might be helpful here. (ND)	Thank you for your comment. These recommendations are to raise awareness about the difficulties that some children and young people and their families have experienced when safeguarding concerns have been raised. The importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative

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					consequences particularly for children and young people, and their families. The committee disagree these recommendations are ambiguous and are contrary to safeguarding practice and training. Recommendation 1.7.5 is 'that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability.' The NICE guidelines on child maltreatment and child abuse and neglect are cross referred to. This is clear that if a professional has concerns they should be addressed in the same way as with any person Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
NHS England and NHS Improvement	Guideline	018	1	Information about the best times for appointments etc with a person with ME/CFS should be recorded in the management plan so all can see. (PC)	Thank you for your comment. These are examples of how to improve access to care for people with ME/CFS AND for this reason your suggestions have not been added.
NHS England and NHS Improvement	Guideline	018	25	"Hospital care" - is this also "inpatient services"? (ND)	Thank you for your comment. This refers to inpatient care but not directly to specialist ME/CFS inpatient services.
NHS England and NHS Improvement	Guideline	020	23	Proposal to change working to - Utilising a strengths-based approach, where applicable, enable prompt assessment for access to home adaptation. If their person is not eligible for support, continue to offer information and support in arranging home adaptations. (CH)	Thank you for your comment. The committee discussed the use of the term 'strengths based' and recognised that this term is not recognised as helpful by all disability groups. The committee agree that it is important to for health and social care professionals to work collaboratively to

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					identify the strengths a person has and to build on these but also that there is a balance where people are able to access support for a disability without feeling like they have failed. For this reason the term strengths based approach has not been used.
NHS England and NHS Improvement	Guideline	020	2	Please include 'adopting a strengths based approach' e.g. If a person with ME/CFS needs support at home, **adopting a strengths based approach**, conduct an assessment, record and provide information and support on.	Thank you for your comment. The committee discussed the use of the term 'strengths based' and recognised that this term is not recognised as helpful by all disability groups. The committee agree that it is important to for health and social care professionals to work collaboratively to identify the strengths a person has and to build on these but also that there is a balance where people are able to access support for a disability without feeling like they have failed. For this reason the term strengths based approach has not been used.
NHS England and NHS Improvement	Guideline	020	2	The assessment does not need to be a social care assessment, this information may have already been gathered by the individual in health services and this information can be shared with social care, where applicable, to reduce duplication and the need for the individual to tell their story more than required. (CH)	Thank you for your comment. This section is supported by the evidence (Evidence review A))and the committee's experience that people with ME/CFS have found it challenging to access social care support. The committee agreed it was important to raise awareness about this and recommend that a social care assessment should be done if needed.
NHS England and NHS Improvement	Guideline	020	16	Could also include support in making applications for benefits, more than just how to claim. People with ME/CFS often face difficulties in successfully applying for benefits. (PC)	Thank you for your comment These are examples in the recommendation and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added
NHS England and NHS Improvement	Guideline	021	3	Flexible working or reduced hours could also be explored. (PC)	Thank you for your comment. Additional text on work has been added to the committee discussion in evidence review A and includes that adaptions and adjustments should be discussed and gives examples including flexible working.

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NHS England and NHS Improvement	Guideline	027	8 and 14	"advice and support" needs to state "information" also as this is key to good decision-making. Also information may need to stimulate not just the signs and symptoms but what to do if concerned, where to get ongoing support etc. (ND)	Thank you for your comment. Information has been added to these recommendations.
NHS England and NHS Improvement	Guideline	028	19	This supports a shared decision making conversation, but suggest also adding the risks and benefits of doing nothing so they understand the implications of immobility and can decide what course of action is best for them. (PC)	Thank you for your comment. This recommendation refers to the risks and benefits of a physical activity or exercise programme. Earlier in the assessment and planning section of the guideline there is reference to physical functioning and mobility. To note after considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing
NHS England and NHS Improvement	Guideline	031	2	"Encourage people with ME/CFS who have nausea to keep up adequate fluid intake and advise them to try to eat regularly, taking small amounts often." There are several strategies that can be applied locally to minimise ongoing nausea, suggest this section needs expanding. (ND)	Thank you for your comment. This recommendation has been moved to the dietary management section and this section includes more advice on how to minimise complications caused by gastrointestinal symptoms.
NHS England and NHS Improvement	Guideline	032	11	"they spend a lot of time indoors" as this is an example this may need to be identified as one to ensure this isn't generalisation. (ND)	Thank you for your comment. The recommendation has been edited and 'because they spend a lot of time indoors' has been deleted.
NHS England and NHS Improvement	Guideline	037	19	"and discuss" suggests this needs to be explicit in a discussion with the person (ND)	Thank you for your comment. The earlier part of the recommendation includes that the care and support plan is reviewed with the person.
NHS England and NHS Improvement	Guideline	040	16	Training should also highlight the shift in approach away from recommending GET and CBT as primary interventions. (PC)	Thank you for your comment. The committee discussed the level of detail that should be included in training programmes and agreed on a general description to avoid a prescriptive interpretation of the content

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					allowing the recommendations to remain relevant as research in the area develops.
NHS England and NHS Improvement	Guideline	041	5	Terms used in this guide – if above recommendations accepted in relation to adopting a strengths based approach – it would be helpful to add 'strengths based approach' definition to this section to ensure people understand the need to promote wellbeing, independence and community connection, before creating dependency on care and support. A strengths-based approach would help to achieve the right balance with care and support as references on page 53 line 14-18 (CH)	Thank you for your comment. ' Strengths based approach' has not been used a term in the guideline so has not been added into this section. The committee discussed the use of the term 'strengths based' and recognised that this term is not recognised as helpful by all disability groups. The committee agree that it is important to for health and social care professionals to work collaboratively to identify the strengths a person has and to build on these but also that there is a balance where people are able to access support for a disability without feeling like they have failed. For this reason the term strengths based approach has not been used.
NHS England and NHS Improvement	Guideline	048	24	This may require a training resource to ensure this shift in thinking is made by the health & care workforce. (PC)	Thank you for your response. Your comments will be considered by NICE where relevant support activity is being planned'.
NHS England and NHS Improvement	Guideline	060	9	For information The research suggestion in relation to outcome measures is welcome. For information, The CFS/ME service in Exeter has been successfully utilising the Patient activation Measure to evidence patient activation/progress/outcomes. (CH)	Thank you for this information.
Oxford University Hospitals NHS Foundation Trust	Guideline	General	General	Oxford University Hospital NHS Foundation Trust has delivered a highly regarded service for patients with ME/CFS (to use the Guideline terminology*) for many years. The Trust is most concerned at the evidence review and recommendations, which are at striking variance from our clinical experience on observing patients improve with both CBT and GET.	Thank you for your comment. *Excluded trials* See evidence review D-diagnosis for the evidence and committee discussion on the diagnostic criteria. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a

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				Having contributed patients to clinical trials in this area we are also concerned about the way the clinical trial data has been handled. In particular, excluding trial finding because they did not explicitly require patients who had post exertional symptom exacerbation – on the one hand most patients report this, including those who participated in the clinical trials, which should therefore not have been disregarded – on the other hand we are unconvinced by the committees opinion that only patients with this symptom have ME/CFS. We would not therefore find these guidelines helpful. Our Trust also runs chronic pain services. We welcome the draft guidelines for the management of patients with chronic pain – many of whom have both fatigue with post exertional symptom exacerbation – which recommend exercise and CBT, and are perplexed by the striking contradiction between these draft guidelines. We are extremely concerned that if these guidelines were to be implemented as is, they would lead to an increase in patients whose symptoms deteriorate over time and a greater burden on our health and social care systems. If these draft guidelines are agreed, it will make it hard if not impossible to deliver GET and CBT as treatments in our service. This would threaten the continued purpose, viability and funding of our service, leaving patients with no specialist service in our Trust. **we have used the guideline terminology ME/CFS throughout this document, but we prefer and use the term CFS, or CFS/ME in recognition of the fact that ME continues to be*	criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. The committee no evidence that met the inclusion criteria for the review protocols was excluded. After considering the stakeholder comments the committee agreed to revisit the quantitative and qualitative evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) *Post exertional symptom exacerbation/post exertional malaise* The committee agree these symptoms are seen in other conditions, but note it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS. *Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline

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				used by some patients and support groups, but is not medically accurate.	could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. As such the difference between the guidelines is not a problem. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that when managing any co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account. *Terminology* The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'* The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3)' has been added to the context. *CBT and GET*

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					The management sections of the guideline include recommendations: • to support people with energy management • to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or programme into the management of their ME/CFS. • to offer CBT to help people manage their symptoms and to reduce the distress associated with having a chronic illness and are options for the management plan where appropriate. To accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. See evidence reviews G and H for the evidence and the committee discussion on these recommendations. After considering the stakeholder comments about the lack of clarity around what the guideline recommends on energy management and physical activity and exercise the committee made the following edits: • on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. • the section on physical activity now includes exercise • Made clear that a personalised collaborative physical activity or exercise programme includes making flexible adjustments to their physical activity (up and down as needed).

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					The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity and exercise programmes. This guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Oxford University Hospitals NHS Foundation Trust	Guideline	General	General	1.9.1 Consider re-ordering this section. It presents an overly pessimistic view of the condition. Patients should be advised that people with ME/CFS are often able to continue with their studies and work with support and some degree of adaption to their studies and work. Specialist services are well placed to advise on this in individual cases.	Thank you for your comments. Taking into account your comments this section has been reordered to place the recommendations that focus on support at work at the beginning of the section.
Oxford University Hospitals NHS	Guideline	010	018	1.3.1 The term 'Energy Envelope' (defined in the document as 'the amount of energy a person has to do all activities without triggering an increase in their symptoms') and referred to	Thank you for your comment. After considering the stakeholder comments the committee agreed that this concept and energy envelope might not always

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Foundation Trust				multiple times throughout the guideline is strongly associated with Adaptive Pacing Therapy – an approach that has an insufficient evidence base to support its recommendation with a NICE guideline. The use of the term suggests that people with ME/CFS have an objective and finite amount of energy. The term 'envelope' suggests something that is fixed with static boundaries and the way the term is used also infers that it is an evidenced phenomenon in people with ME/CFS. This could be very misleading to patients and clinicians. Energy is a complex factor in understanding and managing fatigue. Certain activities can cause considerable fatigue and other activities can be experienced as energising. The way in which different activities effect energy levels in different people with ME/CFS also varies from person to person and to apply to term 'energy envelope' therefore seems reductive and does not support an individualised approach. An individualised approach to understanding the way in which different activities impact fatigue differently, the way in which breaks, rests and activity variety can support energy levels, and understanding ways to reduce 'boom and bust' patterns of activity (stabilise activity) are all key in clinical practice to helping people manage their activity levels and fatigue.	be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on PEM and energy limits* may not be helpful. At such keeping a diary at this stage may not be appropriate. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits. *Re Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies).

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Oxford University Hospitals NHS Foundation Trust	Guideline	010	020	1.3.1 There is no evidence that patients with ME/CFS should always 'rest when they need to'. The document goes on to suggest an individualised approach to treatment – this may include working with the patient to determine the most helpful approach to rest, which might involve 'resting *before* they need to'. It ought to be noted that excessive rest and sleep can cause a deterioration in fitness and stamina which are associated with physical and cognitive/psychological symptoms.	Thank you for your comment. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term. The committee agreed it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and this advice would not result in harm to anyone. As you note the committee recommend a personalised approach and this would include discussing with the person with suspected ME/CFS about how much rest is appropriate.
Oxford University Hospitals NHS Foundation Trust	Guideline	013	006	1.5.3 There is evidence that living according to values, and value-based action, are important in other chronic conditions e.g. improvements in values-based action have been associated with improvements in outcomes (McCracken and Yang 2006 doi.org/10.1016/j.pain.2006.02.021; Vowles & McCracken 2008 10.1037/0022-006X.76.3.397; Vowles & McCracken 2011 doi.org/10.1016/j.brat.2011.08.002). Values could be added to this point.	Thank you for comment and information. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.). In line with this the bullet points have been deleted as this is reflected in the aims of a care and support plan. The personalised care and support plan is based on the person's needs and includes the areas listed. The plan is developed in collaboration with the person with ME/CFS and explores their aims *and the management of their health and well-being within the context of their whole life and family situation. It should be proportionate, flexible and coordinated and adaptable to a person's health condition, situation and care and support needs.*
Oxford University	Guideline	014	016	1.6.4	Thank you for your comment.

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Hospitals NHS Foundation Trust			22 & 23	ME/CFS is poorly understood. No medical or non-medical causal factors have been established. It appears to be a complex condition affecting people in different ways. The development of difficulties and history vary greatly person-to-person and so too the possible contribution of medical and non-medical factors. For some people symptoms are variable, for others less so. It is not well established how many people recover, given wide variations in diagnostic criteria, there are even less consensus about what constitutes recovery. Saying a 'small proportion' recover is not only conjecture, but presents a pessimistic and fatalistic outlook to patients. A significant proportion of patients who receive treatment in the OUH fatigue service report significant increases in functioning and wellbeing that point toward recovery. We hold a large database of documented patient testimony that attests to self-assessed 'recovery'. We need to also acknowledges that the concept of recovery is complex. While people with CFS may not experience full remission of all symptoms, they often experience a sense of being recovered in that they are able to re-engage with their lives in meaningful ways.	After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS.
Oxford University Hospitals NHS Foundation Trust	Guideline	018	012	1.8.2 Conversely people with ME/ME who suspect they may not be able to attend an appointment should give as much notice as possible, or ask someone else to communicate on their behalf, to limit wasted service provider appointment time, which could be used for someone else on this occasion.	Thank you for your comment. This recommendation is supported by the evidence that people with ME/CFS reported that some health and social care professionals did not understand ME/CFS and difficulties they may sometimes have in attending appointments (see evidence review A and C). This was supported by the committee's experience and they agreed that the relationship with health and social care services is collaborative.

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					This recommendation highlighted the difficulties people with ME/CFS have had in accessing services. After considering the range of stakeholder comments the committee edited this recommendation to, 'an appointment' and deleted,' contact the'' to recognise that it is a collaborative relationship between the healthcare professionals and the person with ME/CFS and it could be the person with ME/CFS that contacts the service.
Oxford University Hospitals NHS Foundation Trust	Guideline	020	020	1.8.9 Not all service providers have the capacity to provide aids and adaptations so rewording required to include "or refer to appropriate service to provide aids and adaptations identified in the person's management plan".	Thank you for your comment. These recommendations refer to the social care needs assessment and the aids and adaptions identified as part of that assessment. This has been made clearer in the recommendations.
Oxford University Hospitals NHS Foundation Trust	Guideline	023	007	1.10.3 Specialist teams within the NHS do not have the resources to support people with ME/CFS indefinitely, so it is an unrealistic expectation to support individuals during future periods of relapse after discharged from treatment. One of the benefits of CBT is that post-treatment the person with ME/CFS is better able to manage their relapse than before treatment.	Thank you for your comment. The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no one single model of care. Some of the committee members described experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support.
Oxford University Hospitals NHS Foundation Trust	Guideline	024	General 21-24	1.11.2 The phrase 'energy management' appears to almost wholly be a description of Adaptive Pacing Therapy – an unproven approach that is recommended by some patient support groups. It would be more accurate to summarise the points of agreement between the therapies that have been explored in ME/CFS for which there is some supporting evidence. Whilst we agree that it is not helpful for activity to be automatically progressed in predetermined fixed increments,	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits.

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				following this guideline could lead to a 'boom and bust' pattern where people with CFS significantly increase their activity in better phases leading to a worsening of symptoms and a subsequent decrease in activity. This does not allow for stabilising activity levels and can be self-perpetuating as it creates a cognitive, emotional and behavioural vicious cycle. The advice is therefore likely to be unhelpful to patients.	This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). After considering the stakeholder comments the committee agreed to clarify that, 'energy management uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse).' It is now clearer that this avoids the 'boom and bust' pattern Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS.
Oxford University Hospitals NHS Foundation Trust	Guideline	025	025 - 026	1.11.6 Some degree of fluctuation in daily energy levels is inevitable (you would also expect to see this in people that do not have ME/CFS) so it does not seem helpful to recommend reductions in activity based on this, as it could lead to progressive declines in activity and progressive disability. The degree and impact of fluctuation also needs to be considered before deciding to reduce activity levels.	Thank you for your comment. After considering the stakeholder comments this has been edited to,' Advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).'

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Oxford University Hospitals NHS Foundation Trust	Guideline	025	018	1.11.4 The 'boom and bust' concept is a well-established and commonly used phrase to describe unbalanced patterns of activity. Some people with ME/CFS "over-do" and some "under-do", therefore generalising that all people with ME/CFS should reduce activity as a first step is neither personalised or patient-centred.	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to, agree a sustainable level of activity as the first step, which may mean reducing activity.'
Oxford University Hospitals NHS Foundation Trust	Guideline	026	006	1.11.8 'incorporate a physical activity programme into'; This appears to be using alternative phrasing to capture the fact that patients may wish to work towards increasing their level of physical functioning – which is a key component of rehabilitative approaches for ME/CFS. The guideline should be mentioning that some patients gain benefit from increasing activity levels within a package of specialist care.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews A, G and H) and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.

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Oxford University Hospitals NHS Foundation Trust	Guideline	027	002	1.11.11 Respiratory health should be addressed. Reduced mobility is known to affect respiratory function, especially those with respiratory comorbidities. See Guidelines for the physiotherapy management of the adult, medical, spontaneously breathing patient (2008) Thorax, Volume 64, Issue Suppl 1 http://dx.doi.org/10.1136/thx.2008.110726 British Thoracic Society guideline on pulmonary rehabilitation in adults: accredited by NICE (2013) Thorax, Volume 68, Issue Suppl 2 http://dx.doi.org/10.1136/thoraxjnl-2013-203808	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Oxford University Hospitals NHS Foundation Trust	Guideline	028	001	1.11.16 Evidence from the OUH CFS service indicates that Graded Exercise Therapy is helpful to the majority of patients who receive it. There is no documented evidence of harm from this individualised treatment approach. This experience is at clear variance from the guidelines which is concerning. Extract from service evaluation carried out in 2019 of 56 patients who received Graded Exercise Therapy: "These analyses show that there is a significant difference between pre-treatment and post-treatment scores for CFQ (Chalder Fatigue Questionnaire), SF-36 (physical functioning subscale), self-efficacy, and HAD(A) and HAD(D) (Hospital Anxiety and Depression Scale) outcome measures for those who received GET alone. The proportion of patients with clinically significant improvements in fatigue and physical functioning were 83% and 66% respectively. These data are comparable to that for the previous service evaluation by Zahl	Thank you for your comment and information. *Treatment or cure* After considering the range of stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. After considering the stakeholder comments, the committee have added exercise into the recommendations on considering a physical activity programme to clarify where these apply to exercise. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C),

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			 6-7	et al (2014)[1], (clinically significant improvements in fatigue and physical functioning were 86% and 59% respectively).” Conflicts with statements: 1.10.1 states care should provide “support to engage in work, education, social activities and hobbies” which may involve physical activity and exercise to achieve these aims 1.11.11 questionable how to “include physical maintenance…joint flexibility, muscle strength and endurance, bone health, cardiovascular health” in a manageable plan without physical activity or exercise? 1.11.14 supporting someone with their physical maintenance and mobility, and the factors listed in this point, by its very nature includes physical activity and exercise **Suggest removing the words “ treatment or”** We are concerned that the guideline grossly misrepresents GET. GET as practiced in OUH does not advise fixed incremental increases in physical activity or exercise. It is flexible, adapts to the experience of the individual with ME/CFS and is collaborative. In addition to impacting on individuals yet to come through treatment, we are also concerned that this framing of GET may cause undue distress to people with ME/CFS who have previously received this treatment. (see also p.63 L13-15 which asserts that GET is based on deconditioning as the cause of ME/CFS. This also misrepresents the GET approach, which sees deconditioning as one potential maintaining factor, not causative).	diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or

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				This should be corrected.	that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS *Underrepresentation of people who have benefited from GET.* The committee membership had a broad range of professional and personal knowledge about the different experiences of people with ME/CFS and this was discussed and considered at all stages of the decision making. There is little representation in the qualitative literature of people who have benefited from GET and the committee hope that where this can be published it will be as this can only further inform the care and support of people with ME/CFS.
Oxford University Hospitals NHS Foundation Trust	Guideline	028	008	1.11.21 Access to support from specialist services will unlikely be timely enough to give advice to manage current flare up. Advice from specialist services can help manage future flare-ups.	Thank you for your comment. The committee agree that advice for a flare up should be planned and this is included in the previous recommendation. Recommendation 1.11.21 refers to support that might be needed after the flare up.
Oxford University Hospitals NHS Foundation Trust	Guideline	028	028	1.11.20 States "a physical activity programme should be personalised and should be possible to maintain it successfully before attempting to increase 28 physical ability" – this is the essence of GET which the guidelines also ban. We are perplexed.	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS.

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					This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this

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					option. Where this is the case the committee agreed it was important people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Oxford University Hospitals NHS Foundation Trust	Guideline	030	001	1.11.23 There is evidence that endogenous body clocks are important for physiological rhythms and energy metabolism (Brown et al 2006) so could also include keeping a regular sleep schedule, as this is known to aid reductions in daytime sleepiness. This should be included. Manber R, Bootzin R, Acebo C, Carskadon M. (1996) The Effects of Regularizing Sleep-Wake Schedules on Daytime Sleepiness. Sleep 19; 5:432–441. https://doi.org/10.1093/sleep/19.5.432	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Oxford University Hospitals NHS Foundation Trust	Guideline	030	016	1.11.27 There is no reference to the NICE guidance for managing chronic pain. This guidance would be more appropriate for a ME/CFS patient group than the guidance referenced for neuropathic pain and headaches.	*Thank you for your comment.* *Neuropathic pain and headaches* The committee disagree these references are inappropriate, people with ME/CFS report many different types of pain, neuropathic pain and headaches included. These are examples of NICE guidelines on pain and is not intended to be an exhaustive list of the types of pain people with ME/CFS may experience. *Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply.

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					The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that any when managing any co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account.
Oxford University Hospitals NHS Foundation Trust	Guideline	034	005	1.11.43 The statement 'Do not offer CBT as a treatment or cure for ME/CFS' is misleading and could create unhelpful perceptions of the treatment approach. CBT is not offered as a 'cure' for CFS but it can be part of an overall treatment plan which aims to work collaboratively with people to benefit wellbeing and functioning (see also comment 4 regards broader views of recovery). Whilst no intervention in any domain can ever 'guarantee' improvement, it is our clinical experience that both objective and patient-perceived improvement is the norm in our service and it is important that a sense of hope is not lost in the guideline. The guideline should be changed to address this point.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.
Oxford University Hospitals NHS Foundation Trust	Guideline	040	017	1.15.2 This recommendation will be challenging in practice because many departmental training budgets are limited and, as noted on page 70, there are few such training opportunities and competency frameworks available for ME/CFS.	Thank you for your comment. The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. A strong theme from the evidence was the lack of understanding about ME/CFS and training in health and social care professionals and the committee agreed it was important to make recommendations about training. Your comments will also be

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					considered by NICE where relevant support activity is being planned.
Oxford University Hospitals NHS Foundation Trust	Guideline	047	001	Research recommendations Sleep is neglected. Kallestad et al (2015) suggested that insomnia severity may be a maintaining factor in chronic fatigue. They reported that improvement in insomnia in CFS patient (using an ACT-based approach) predicted improvement in fatigue, independently of age, gender, improvement in pain intensity, depression and anxiety. Vethe et al (2018) also concluded that long-term improvement in insomnia severity is significantly associated with long-term improvement in chronic fatigue (again using an ACT-based programme). Therefore treatments targeting insomnia severity in a CFS population should be further investigated. Russell et al (2017) state that that future research should explore the effectiveness of sleep components within interventions, and sleep specific interventions, using comprehensive outcome measures that fully capture the range of sleep difficulties experienced in CFS. There is evidence that sleep specific interventions targeting pre-sleep arousal, perceptions of sleep and negative mood on waking, have also been suggested to improve fatigue in ME/CFS. These could also be recommendations for research. Kallestad H, Jacobsen H, IngeLandrø N, Borchgrevink P, Stiles T. The role of insomnia in the treatment of chronic fatigue. Journal of Psychosomatic Research. 2015; 78(5):427-432 Vethe D, Kallestad H, Jacobsen H, Landrø N, Borchgrevink P, Stiles T. The Relationship Between Improvement in Insomnia Severity and Long-Term Outcomes in the Treatment of Chronic Fatigue. Front. Psychol. 2018 doi.org/10.3389/fpsyg.2018.01764	Thank you for your comment and information.

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				Russell, C., Kyle, S. and Wearden, A. Do evidence based interventions for chronic fatigue syndrome improve sleep? A systematic review and narrative synthesis. *Sleep Med. Rev.* 2017; 33, 101–110. doi: 10.1016/j.smrv.2016.05.001 Russell C, Wearden A, Fairclough G, Emsley R, Kyle S (2016) Subjective But Not Actigraphy-Defined Sleep Predicts Next-Day Fatigue in Chronic Fatigue Syndrome: A Prospective Daily Diary Study. SLEEP; 39, 4: 2016	
Oxford University Hospitals NHS Foundation Trust	Guideline	059	007	Having a single point of contact within a specialist care team would be impractical as people with ME/CFS cannot be under their care indefinitely. The single point of contact would be the GP as for other long term conditions.	Thank you for your comment.
Oxford University Hospitals NHS Foundation Trust	Guideline	065	013	Question why the committee did not also refer to the NICE guidance for managing chronic pain, which seems more relevant than the NICE guidance for neuropathic pain.	Thank you for your comment. *Neuropathic pain* The committee disagree, people with ME/CFS report many different types of pain, neuropathic pain is one of them. These are examples of NICE guidelines on pain and is not intended to be an exhaustive list of the types of pain people with ME/CFS may experience. *Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. As such the difference between the guidelines is not a problem.

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					The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that any when managing any symptoms or co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account.
Oxford University Hospitals NHS Foundation Trust	Guideline	034, 067	General	1.11.43-1.11.50 The guideline on psychological support (and subsequent section on why the committee made the recommendations) focuses on CBT with the exclusion of any other comment on serving the broader psychological needs of people with ME/CFS. The guideline focuses on managing the impact of the condition itself rather than acknowledging the whole individual (including their historical context). Research evidence (for example: Heim et al. (2006) Early Adverse Experience and Risk for Chronic Fatigue Syndrome. *Arch Gen Psychiatry* 63 (11); Kempe et al. (2013) The Prevalence and Impact of Early Childhood Trauma in Chronic Fatigue Syndrome. *Journal of Psychiatric Research* 47 (5)) and our clinical experience, indicate that past adverse experiences are prevalent amongst people with CFS. Acknowledging, understanding and working with the relationship between past complex adverse experience and managing fatigue and its impact can be a fundamental part of a successful therapeutic approach with people with ME/CFS. To reflect the research evidence and experience of fatigue services, the guideline should acknowledge the need for psychological provision to be able to sensitively formulate and manage these factors within the context of working with	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). The guideline takes a holistic approach and this is explicit in the assessment and care planning section. The committee have edited the management plan to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.). This further supports the guideline's emphasis upon being centred on the person's needs and wishes and adopting a holistic approach. The personalised care and support plan supports the person's aims and the management of their health and well-being within the context of their whole life and family situation.

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				individuals with ME/CFS. This should include acknowledging that past adverse experiences increase the risk for developing CFS and that services should be able to adequately manage the potential impact of this within its work with people with ME/CFS. This is likely to involve the need for suitably experienced practitioner psychologists to be embedded within services in both therapy and supervisory roles.	
Parents of Children with ME/CFS Support Group	Guideline	General	General	This response has been produced by sharing and discussing the draft NICE ME/CFS guideline with the members of the Parents of Children with ME/CFS support group. This is a national group with 1,476 members [as of 21/12/2020] whose children have a diagnosis of ME/CFS and cover the whole range of severities.	Thank you for your submission.
Parents of Children with ME/CFS Support Group	Guideline	General	General	Now that the guideline names the illness as ME/CFS how will this be reflected on patient diagnoses? How will healthcare professionals update their records to show that patients have ME/CFS? Will all patients will a diagnosis of CFS/ME or CFS be written to with a new, correct diagnosis? It has taken far too long for the hugely damaging and misrepresentative label of 'CFS' to be changed and it is vital that patients receive the correct diagnosis which fully represents their illness.	Thank you for your comment. It is beyond the remit of this NICE guideline to advise how medical notes should be kept. To recognise that myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) this information has been added to the context section of the guideline.
Parents of Children with ME/CFS Support Group	Guideline	General	General	Can NICE please investigate and give assurance that any research based on the false epistemology of ME/CFS as a biopsychosocial illness will be halted immediately? Can they further provide assurance that future trials will only be funded if they follow a biomedical model and have been recommended as areas for further research by the committee who have developed this guideline?	Thank you for your comment. The halting of trials and the funding of future trials is beyond the remit of NICE guidance. The committee hope the research recommendations identified as areas for research will be considered by research funders. NICE research recommendations are reviewed regularly by the NIHR to help facilitate their funding and uptake.
Parents of Children with	Guideline	General	General	We call upon NICE to issue a public apology for the harm caused to patients with ME/CFS in the past, acknowledge that mistakes have been made in recommending treatments based	Thank you for your comment. The 2007 guideline recommendations were based on the available evidence at the time and reflected the committee's

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ME/CFS Support Group				on poor or very poor research and confirming that ME/CFS is to be treated as a serious, biomedical, long-term illness in the future.	understanding of that evidence. The guideline was clear that any course of treatment should always be delivered as a result of a shared decision after discussion of the potential benefits and risks.
Parents of Children with ME/CFS Support Group	Guideline	General	General	We think that the management plan will be challenging to implement, as they should only be written by health care professionals who have been trained in the new guideline.There is a real risk that paediatric management plans could be written by large tertiary services who follow an outdated model of paediatric ME/CFS. There is also a risk that parents of children with ME/CFS could wrongly be seen as obstructive if their child is not able to follow every aspect of the plan due to an increase in symptoms.. We would prefer to see the terminology **"Co-produced care plan"** used rather than a "Management plan". This wording would then reflect the need for children and their parents to have input into the plan rather than it being written solely by a healthcare professional. We have used the phrase "Management plan" for consistency in our response, but our comments reflect the need for this plan to be created as a co-produced document.	Thank you for your comment and information. To note management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) and hope this clarifies the approach of the planning.
Parents of Children with ME/CFS Support Group	Guideline	008 - 009	17 Box 1	• It is vital that the diagnostic criteria, especially as applied to research, are tightened. The development of an accurate test for ME/CFS can only be achieved if there are agreed research diagnostic criteria. • Add: Post-exertional symptom exacerbation **may be** delayed in onset by hours or days **(typically 12-72 hours) but can sometimes occur straight away**.	Thank you for your comment. The committee agree there is a need for validated diagnostic criteria but recognised the importance of clear and informative guidance to assist clinicians, who may not be experts in ME/CFS, in identifying people with ME/CFS Recognising the absence of a validated diagnostic criteria they made a research recommendation to develop validated criteria (see the. committee discussion in evidence review D).

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				● Change:" Unrefreshing Sleep" - a more accurate term for this is "**Sleep disturbance**" ● Change: "Cognitive difficulties (sometimes described as 'brain fog'), including problems finding words, ~~temporary~~ dyslexia or dyscalculia, slurred speech ……." The word 'temporary' in front of dyslexia or dyscalculia needs removing. ● Add: **"These cognitive difficulties may be present consistently, as with some severely/very severely affected people, or may present variably as part of the PESE."** ● The words exertion and activity appear to be used interchangeably in this section, yet they are not synonymous. Can the use of these words please be tightened, or a definition of exertion also given as part of the glossary to clarify their meaning in the guideline?	The committee have made the following edits to Box 1 and hope this has added some clarity for readers. *PESE/PEM* The committee note that post exertional malaise is usually described as delayed in onset with it typically delayed 12-48 hours after activity, but recognised that some people with ME/CFS report PEM in a reduced (or later) time and have added 'can typically' to the definition. To note after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM). The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS. *Unrefreshing sleep* After considering the stakeholder comments on the description of sleep symptoms the committee edited the bullet points to, 'unrefreshing sleep and /or sleep disturbance, which may include: • feeling exhausted, feeling flu-like and stiff on waking • broken or shallow sleep, altered sleep pattern or hypersomnia.

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					The committee have also edited the definition in the terms used in the guideline section. *Cognitive difficulties* After considering the stakeholder comments on the description of cognitive difficulties the committee made these edits: Cognitive difficulties (sometimes described as 'brain fog'), including problems finding words or numbers, slurred speech, difficulty in speaking, slowed responsiveness, short-term memory problems, and difficulty concentrating or multitasking. The section on people with severe and very severe ME/CFS expands on the cognitive difficulties people with severe or very severe ME/CFS experience. There is a definition of activity in the terms used in the guideline and this is linked to in Box 1.
Parents of Children with ME/CFS Support Group	Guideline	004	5	The word 'neurological' needs adding to this to say that ME/CFS "is a complex, chronic medical **neurological** condition affecting multiple body systems". The rationale for this is that ME/CFS is included amongst the neurological conditions by the WHO and, more importantly, on the NHS website (under variable neurological conditions).	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to add neurological. To note reference to the ICD10 classification has been included in the context section of the guideline.
Parents of Children with ME/CFS Support Group	Guideline	004	12	Add: **This variability means that some people have symptoms and incapacity that does not necessarily fit exactly into the severity scale, so their symptoms cross a boundary between moderate and severe.**	Thank you for your comment. The committee agree there is a wide range of impact that exists along a continuum. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS.

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Parents of Children with ME/CFS Support Group	Guideline	004	17	Add: "feel stigmatised by people **and medical professionals**"	Thank you for your comment. This has been edited to include 'family, friends, health and social care professionals and teachers'. This reflects the similar recommendation in the additional principles for the care of children and young people.
Parents of Children with ME/CFS Support Group	Guideline	005	26	In addition to the harm caused by the previous guideline for CFS/ME to patients, there was also significant harm caused to parents of children with ME/CFS. We strongly recommend that this is also added to the recommendations for delivering care for children and young people. Parents play an important mediating role as carers for their ill children and it is vital that they are included as stakeholders in all principles of care. Add: **"Be aware of the impact on parents of children and young people with ME/CFS who have been inappropriately threatened with or subject to court action for childrens' non-attendance or wrongly given child protection orders or diagnosis of FII, and who may find it difficult to trust health and social care services.."**	Thank you for your comment. This recommendation focuses children and young people and for this reason your suggestion has not been added. The committee agree that parents and carers have an important role in the care of their children with ME/CFS and this is reinforced throughout the guideline. The supporting families and carers of people with ME/CFS section of the guideline has advice on accessing support.
Parents of Children with ME/CFS Support Group	Guideline	006	7	We are concerned that some of these characteristics/impacts of severe or very severe ME/CFS are also present in children, young people with moderate ME/CFS. We would be happy as a group to support the development of an accurate severity scale of ME/CFS for children and young people.	Thank you for your comment. The committee agree that any of the symptoms included here can affect anyone with ME/CFS, the aim of this section is to highlight symptoms can occur with such severity that they significantly affect the lives of people with severe or very severe ME/CFS.

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Parents of Children with ME/CFS Support Group	Guideline	006	16	Add: "extreme weakness, with severely reduced movement, **with paralysis or near paralysis for some people with very severe ME/CFS"**	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Parents of Children with ME/CFS Support Group	Guideline	006	18	Add: "cognitive difficulties, causing a limited ability to communicate and take in written or verbal communication, **and memory problems"**	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Parents of Children with ME/CFS Support Group	Guideline	006	22	Add: "'gastrointestinal difficulties such as nausea, incontinence, constipation and bloating **and abdominal pain"**	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Parents of Children with ME/CFS Support Group	Guideline	007	8	Add: "need aids such as wheelchairs **or electric wheelchairs**"	Thank you for your comment. After considering the range of stakeholder comments this has been edited to, 'are housebound or bed-bound and may need support with all activities of daily living, including aids and adaptions to assist mobility and independence in activities of daily living (for example wheelchairs)' The section on aids and adaptions provides further information. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Parents of Children with ME/CFS Support Group	Guideline	007	26	It is our experience that children and young people with severe or very severe ME/CFS are often disbelieved or wrongly diagnosed. It is important to flag to medical professionals that children and young people can be affected	Thank you for your comment. This section refers to people with ME/CFS and as such includes children and young people.

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				by severe or very severe ME/CFS so that this can be considered within approaches to care. Add **"Recognise that children and young people may have severe or very severe ME/CFS."**	
Parents of Children with ME/CFS Support Group	Guideline	008	3	It is very disappointing and an ongoing concern that there is no diagnostic test for ME/CFS. We need urgent, biomedical research to develop a test, and for NICE to be ready to urgently approve a test and make it available to patients in England.	Thank you for your comment. The committee agree and have a research recommendation for the development of clinical and cost effective diagnostic tests.
Parents of Children with ME/CFS Support Group	Guideline	008	8	It is our experience that anything requiring an assessment of psychological wellbeing in children and young people equates to a referral to CAMHS. This has been and would continue to be detrimental to the care of children and young people, as they would then get stuck in a long waiting list to see a service which does not have the training and experience to help them. Add information relating to children and young people here: **"For children and young people this does not require a referral to CAMHS."**	Thank you for your comment. The committee note that the assessment recommended describes the routine examinations and assessments when a patient has an undiagnosed illness. At this stage the person has not been diagnosed with ME/CFS or any other condition and it is important to investigate the possibility of other diagnosis and co-existing conditions. Any referrals would be based on the outcome of an assessment not the because the assessment has been done.
Parents of Children with ME/CFS Support Group	Guideline	008	9	The phrase "Baseline investigations" is very vague. What does this mean? Can the baseline investigations be listed here? Our preference is for baseline investigations such as those listed in the Chronic Fatigue Syndrome Myalgic Encephalomyelitis Primer for Clinical Practitioners 2014 Edition"	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.

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Parents of Children with ME/CFS Support Group	Guideline	009	21	The tests in this section are not identified and it is therefore too vague as to which tests should be carried out. It is our recommendation that the following testing regime should be carried out: ● Full bloods, including vit B12 & folate levels ● Cortisol levels, including the short synacthen test ● Full thyroid screening, including antibody test if the results show a 'low normal' ● Full virology including bacterial infection testing, Lyme testing, mould testing and heavy metal testing ● Coeliac test ● MRI and CT scans to investigate or rule out EDS and hypermobility Testing for orthostatic intolerance, POTS (see section 1.11.24) and MCAS	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out which include some of the ones you suggest. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
Parents of Children with ME/CFS Support Group	Guideline	010	1-2	Add: "seeking advice from an appropriate specialist **such as a healthcare professional trained in the new guideline**..."	Thank you for your comment. Appropriate specialist here refers to expertise in supporting the interpretation of signs and symptoms where there is uncertainty and a possible alternative diagnosis. Throughout the guideline where a specialist refers to a ME/CFS specialist this has been made clearer by including ME/CFS before specialist.
Parents of Children with ME/CFS Support Group	Guideline	010	9	It is vital that medical professionals are clear about the impact of suspected ME/CFS on the ability of children and young people to attend full time education, especially those with moderate, severe or very severe ME/CFS. The wording in the draft requires tightening to be clear and specific so as to leave no doubt as to the options available. England has a very	Thank you for your comment. The committee agree early communication with schools and colleges is very important. This recommendation refers to children and young people with suspected ME/CFS and the assumption should not be final diagnosis is ME/CFS. This recommendation is to raise awareness in the short term and

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				punitive attendance system which punishes parents of children with low attendance, and many schools have a very poor understanding of the debilitating and disabling nature of ME/CFS. . Add: "write to the child or young person's place of education or training **with the suspected diagnosis and** to advise about flexible adjustments or adaptations. **This may include, where applicable, stating that the child or young person is unfit to attend school, and signposting local services such as hospital schools or out of school tuition to provide appropriate education for a young person with medical needs via online schooling or a home tutor. Ensure that the Department for Education guidelines are referenced."** We would be happy to assist in the production of a flowchart which highlights best practice in managing health and education needs whilst children have a suspected diagnosis of ME/CFS.	allows for further communication when the diagnosis is confirmed. Further advice is addressed in the recommendations in section 1.9 supporting people with ME/CFS in work ,education and training. Also see the committee discussion in Evidence review A:Information for people with ME/CFS. NICE routinely produce baseline assessment and resource impact tools. To encourage the development of other practical support tools, we run an endorsement scheme aimed at encouraging our partners to develop these in alignment with NICE recommendations. Eligible tools are assessed and if successful, will be endorsed by NICE and featured on the NICE website alongside the relevant guideline.'
Parents of Children with ME/CFS Support Group	Guideline	011	11	This point is going to be challenging to implement. There are very few "paediatric specialist teams experienced in ME/CFS" in England. There are even fewer (and indeed there may not be any) who have experience of treating ME/CFS as a biomedical illness rather than a biopsychosocial one. We anticipate a cost implementation in retraining and rebranding paediatric services for ME/CFS so that they follow the new guideline rather than the previous, low-quality	Thank you for your comment. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I-Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development

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				recommendations from paediatric research which focused on harmful approaches such as CBT & GET. A more cost-effective, alternative option would be to mothball the current paediatric specialist centres and to manage paediatric ME/CFS locally by well-trained GPs and paediatricians. If there is a need for specialist centres, e.g. to coordinate training, then these should be set up from scratch, in hospitals which have not previously been specialist tertiary centres, so that children and their families can trust the services being offered.	of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.
Parents of Children with ME/CFS Support Group	Guideline	011	12	Add: "refer them directly to a paediatric specialist team experienced in ME/CFS to develop a management plan, **which should be a co-produced care plan, involving input from the child and parents.**"	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Parents of Children with ME/CFS Support Group	Guideline	011	13	1. This section assumes that there will be a trained and experienced specialist ME/CFS team to carry out this section. What specialisms will this team have? Until now, the support has predominantly been from physiotherapy, occupational therapy, nurses and psychologists. As the guideline acknowledges that ME/CFS is a complex multi-system illness, it is important that the specialist services have input from cardiology, neurology, endocrinology, gastrology and immunology, and that this is explicitly stated in the guideline. It would be good if this were coordinated by a trained ME/CFS physician/ paediatrician.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS

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				Proponents and defenders of the PACE trial and the use of CBT/GET as a treatment for ME/CFS, especially those who have a biopsychosocial understanding of the nature of ME/CFS need to leave ME/CFS services immediately so that ME/CFS patients can have trust in these services.	specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.
Parents of Children with ME/CFS Support Group	Guideline	012	4	1. Please make it clear that an assessment of the impact of the symptoms on psychosocial well-being **does not mean that a child or young person needs to be referred to CAMHS.** Please also move this to the bottom of the list, to show that is the least important of all the items in the assessment, and make it clear that as assessment should only be carried out to recognise that being ill with a complex, life-changing illness can be challenging and difficult to come to terms with.	Thank you for your comment. The committee note that the assessment describes the routine assessments in a holistic assessment. Any referrals would be based on the outcome of an assessment not the because the assessment has been done. The parts of the assessment are not in any order of priority.
Parents of Children with ME/CFS Support Group	Guideline	012	10	Please add text to describe what a good management plan would look like. This could be a vitally important document to help children and young people receive appropriate educational support and financial support via DLA/PIP. However, it is clear from parents' experiences of the Education and Health Care Plan system that a written document may not	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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				be of high quality or quantified and specific enough to be of use. There is a real danger that stretched NHS services could issue generic management plans with text copied and pasted from a central bank of options to create poor-quality plans, and/or that they are so positive and optimistic that they paint a misleading picture about the disabling nature of ME/CFS symptoms. . We suggest the following text: **"Ensure that the management plan is personalised and specific to the patients' individual circumstances and that it clearly states the disabling nature of their symptoms, and the limitations that occur on a daily basis in work, education, training and at home."** 2.	The plan is developed in collaboration with the person with ME/CFS and explores their aims *and the management of their health and well-being within the context of their whole life and family situation. It should be proportionate, flexible and coordinated and adaptable to a person's health condition, situation and care and support needs.*
Parents of Children with ME/CFS Support Group	Guideline	015	1	As a group of parents of children with ME/CFS, we challenge the statement that the "outlook in children and young people is usually better than in adults". Although there is some research to suggest that this is the case, we do not feel that this is conclusive enough to make such a statement. It is not yet known whether there is any correlation between the severity or aetiology of the child's ME/CFS and the likelihood of recovery, for example. Also, it is the experience of many parents in our group that they have refused to take part in paediatric research due to it being grounded in an epistemology of 'chronic fatigue' caused by biopsychosocial factors rather than specific research into ME/CFS as a biomedical illness. Finally, there is also a lack of large-scale, longitudinal data from childhood to	Thank you for your comment. This recommendation was based on the qualitative reviews exploring the experiences of people with ME/CFS and the committee's experience. See evidence review A for the committee discussion on further information about the long-term outlook for people with ME/CFS. Research recommendations can only be made for interventions where the evidence has been searched for within the guideline The scope for this guideline did not include the aetiology of ME/CFS research and recommendations on this topic cannot be included.

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				adulthood to support this statement. We call upon NICE to flag this area as one requiring further research.	
Parents of Children with ME/CFS Support Group	Guideline	016	5	The whole of this section is a huge concern. Although it may be intended to ensure patient safety, it is shocking to see that this section has been added when it does not appear to be present for other illnesses.It is of paramount importance that it is clear to medical professionals that families of children with ME/CFS do not need investigating for safeguarding concerns. Our preference is to remove this section completely. However, we also recognise that it was added with good intent, in order to prevent unnecessary safeguarding issues from being raised. Therefore if this section must stay in, it is imperative that the section begins with a new bullet point. At the top of this section, add a new bullet point which states: **"There is no requirement or need to routinely assess ME/CFS patients nor their families for safeguarding issues."**	Thank you for your comment and information. After considering the stakeholder comments this section has been reordered and the now second recommendation has been edited to,' *If* a person with confirmed or suspected ME/CFS needs to be assessed'. The committee discussion in Evidence review B includes in detail why the recommendations on safeguarding have been included in the guideline.
Parents of Children with ME/CFS Support Group	Guideline	016	17	Add: "Safeguarding assessments ….. should **only** be carried out or overseen …."	Thank you for your comment. This recommendation has been edited to, 'If a person with confirmed or suspected ME/CFS needs a safeguarding assessment directly involve a health and social care professionals who have training and experience in ME/CFS. The committee hopes this adds some clarity for readers.
Parents of Children with ME/CFS Support Group	Guideline	017	19	In addition to the harm caused by the previous guideline for CFS/ME to patients, there was also significant harm caused to parents of children with ME/CFS. This needs addressing in the new guideline:	Thank you for your comment. This recommendation includes parents or carers and focuses on how advocating on their child's behalf may be misinterpreted as a sign of abuse. For this reason your suggestion has not been added.

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				Add:. **Recognising that the following are not a sign to suspect FII in a parent of a child or a young person with ME/CFS:** ● **asking questions about their child's care** ● **seeking additional diagnoses as well as ME/CFS in order to obtain a full picture of their child's illness** ● **advocating on behalf of their child** ● **learning more about ME/CFS to gain knowledge and insight of their child's illness** **supporting a child to manage their energy by withdrawing them from extra-curricular activities, carefully managing their social interactions and encouraging them to rest**	
Parents of Children with ME/CFS Support Group	Guideline	019	20	For people with severe or very severe ME, it is vital that they have a single room to minimise pain caused by sensory stimuli Change to **"provide a single room".**	Thank you for your comment. There committee noted there could be times when a single room is not appropriate or not available and this should not be a barrier or a cause of delay in people with ME/CFS receiving hospital care. For this reason your suggestion has not been added.
Parents of Children with ME/CFS Support Group	Guideline	020	28	Add **"**wheelchair **or electric wheelchair"**	Thank you for your comment. These are examples in the recommendation and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Parents of Children with ME/CFS Support Group	Guideline	020	29	Add "improve their quality of life **indoors and outdoors"**	Thank you for your comment. These are examples in the recommendation and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.

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Parents of Children with ME/CFS Support Group	Guideline	020	30	Add: **"Include these in the person's management plan.The use of mobility aids, when needed, can help conserve energy in order to carry out other tasks/activities and therefore help the person stay within their energy envelope.**	Thank you for your comment. These recommendation are about aids and adaptions, further information on energy management is included in the managing ME/CFS section of the guideline.
Parents of Children with ME/CFS Support Group	Guideline	021	15	We have considerable experience that schools do not currently follow the Department for Education's guidance, and instead follow the local authority's or academy trust's own policies which may be far from supportive. While it's good to see the DfE's guidance being highlighted, any training and education packages for ME/CFS must highlight that this guidance is the most important document to follow and supersedes any local or regional policies.	Thank you for your comment and information.
Parents of Children with ME/CFS Support Group	Guideline	021	22	We recommend that thorough and detailed information about education options is included here. Parents often have to spend a great deal of time researching these options for their children, as schools and colleges are not experienced and trained in supporting children who are ill with ME/CFS. Add a new bullet point: **"provide information about ME/CFS to explain that cognitive and social energy can have just as much impact on symptoms as physical energy."** Add a new bullet point: **"ensure that any minimum attendance requirements, e.g. for college courses, are waived. If young people can only access an educational setting for 1 - 2 hours per week, that should be supported."**	Thank you for your comment. When writing recommendations there is a judgment to be made about how much information is included in a recommendation. Too much information in a recommendation results in a guideline becoming unwieldy and unusable. Evidence review A includes more detail on education and includes the points you make.

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				Add a new bullet point: **"ensure that all non-attendance is classified as authorised and that non-attendance is not used as a measure for concern or reported as an issue"** Add a new bullet point: **"State clearly in writing if the child or young person is unfit to attend school and recognise that there may be times when children and young people with severe or very severe ME/CFS require a complete rest from formal education. In these cases, a small, limited amount of informal education, e.g. animal therapy may be more appropriate."** Add a new bullet point: "**Support requirements for course work, tests, mock examinations and formal examinations with flexible options such as 25% or 50% extra time, one exam per day, taking exams at home under secure conditions, providing rest breaks, allowing late starts, providing a separate room."**	
Parents of Children with ME/CFS Support Group	Guideline	022	3	Rewrite this bullet point to say "discuss a **flexible** approach to training and education - this could include **a flexible timetable, note taking when at school and when off ill, revision notes provided, the use of a lift, having school bag carried, a transport assistant, extensions to homework / assignments,** online schooling and using assistive equipment **including using assistive technology, e.g. a laptop, speech to text software, an AR robot in the classroom, and being able to use a mobility aid to get around school to conserve energy for learning.**	Thank you for your comment. When writing recommendations there is a judgment to be made about how much information is included in a recommendation. Too much information in a recommendation results in a guideline becoming unwieldy and unusable. Evidence review A includes more detail on education and includes the points you make.

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Parents of Children with ME/CFS Support Group	Guideline	022	4	It is absolutely vital that the phrase **"home schooling"** is removed from this section of the guideline. This phrase could put undue pressure on parents to remove their child from the school roll and home educate them. Moreover, it may give schools a loophole to illegally off roll ill children from their school register.The use of this phrase could lead to children and young people with ME/CFS being denied an education and we request in the strongest possible terms that it be removed.	Thank you for your comment. After considering the stakeholder comments, home schooling has been edited to education at home..
Parents of Children with ME/CFS Support Group	Guideline	022	5	Due to the fluctuating nature of ME/CFS, it is important that any plans for education do not remain set in stone with the requirements to be adhered to. Add a new bullet point: **"arrangements should be reviewed regularly and at a minimum, every half a term"**	Thank you for your comment. The review section of the guidelines includes at least six monthly review of their care and support plan for children and young people with ME/CFS taking into account the severity and complexity of symptoms. Any education plans should be discussed as part of the care and support plan.
Parents of Children with ME/CFS Support Group	Guideline	022	12	Add: **"and that parents, children and young people should take the lead on deciding what is an appropriate balance."** Without the addition of this clause, health care professionals may try and force children and young people in activities which are inappropriate in order to try and provide what they perceive as an appropriate balance	Thank you for your comment. When writing recommendations there is a judgment to be made about how much information is included in a recommendation. Too much information in a recommendation results in a guideline becoming unwieldy and unusable. Evidence review A includes more detail on education and the balance of activities.
Parents of Children with ME/CFS Support Group	Guideline	023	6	Add: "clinical consultation from a specialist **local** team appropriately trained in ME/CFS, as well as other specialists, as needed*	Thank you for your comment. A definition of a ME/CFS specialist term has been added to the terms used in this guideline and includes reference to local and regional services.

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Parents of Children with ME/CFS Support Group	Guideline	023	16	Our recommendation for the transfer into adults' services as follows: - The paediatrician and GP hold a joint handover meeting to agree a transition plan - This transition should include a review of the management plan and full blood tests. - The GP can then refer to adult services, such as a suitably trained physician equivalent to a paediatrician and further specialists as required We feel that this would provide an excellent training opportunity so that GPs can better understand how patients with ME/CFS can be supported via primary care. It is a huge exertion for patients with ME/CFS to travel long distances and it should be remembered that local support via GPs and local hospitals is a more appropriate model than large tertiary care centres. We feel that the video and telephone appointments offered by services during the Covid-19 pandemic should be continued to be offered to ME/CFS patients where appropriate and effective, although with the caveat that the treatment offered by such appointments is in line with the new guideline and does not follow the previous CBT/GET model.	Thank you for your comment. The guideline recommends a personalised approach thought out the guideline and there is a recommendation in the Multidisciplinary care section of the guideline that links to the NICE guideline on transition from children's to adults' services for young people using health or social care services. *Access to services* The committee agree that flexibility in accessing to services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult. Although home visits are used as an example of supporting people with ME/CFS to access care, the committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
Parents of Children with ME/CFS Support Group	Guideline	23	16	We think this section is going to be challenging to implement based on the lived experiences of parents within our group. Children have often been discharged from paediatric services because they have been deemed to be too ill to be treated or parents have had to remove their child from paediatric services because the treatment offered was for 'chronic fatigue' rather than ME/CFS and was therefore causing harm. Please be aware that the outcome of this is a generation of young adults	Thank you for your comment and information. The committee agree it is important that people with ME/CFS have suitable and appropriate care that is collaborative and personalised. The importance of choice and collaborative person centered care is directly reinforced in the guideline sections approach to delivering care, assessment and care planning and in the management of symptoms and at start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in

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				who have ME/CFS and who are without any access to suitable care, and this situation needs including in any training programmes to ensure that these young adults can be identified and offered suitable and appropriate care in adults' services. We have also observed barriers to young people moving into adults' services as the adults' services only seem to be set up to diagnose, not for transfer. As such, young people have often been asked to undertake inappropriate actions (e.g. a course of CBT) before they can access adults' services.	making choices about their care and shared decision making. Throughout the guideline there is reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support plan and supervision for the management of some symptoms. In addition, the committee have made recommendations in the training for health and social care section of the guideline that all staff delivering care to people with ME/CFS should have training that is in line with this guideline. The committee hope this will ensure that situations you describe are avoided with the implementation of this guideline.
Parents of Children with ME/CFS Support Group	Guideline	025	4	Please add text to describe what a good management plan would look like. This could be a vitally important document to help children and young people receive appropriate education and financial support via DLA/PIP. However, it is clear from parents' experiences of the Education and Health Care Plans that a written document may not be of high quality or quantified and specific enough to be of use. There is a real danger that stretched NHS services could issue generic management plans with text copied and pasted from a central bank of options. We suggest the following text: **"Ensure that the management plan is personalised and specific to the patients' individual circumstances and that it clearly states the disabling nature of their symptoms, and the limitations that occur on a daily basis in work, education, training and at home."**	Thank you for your comment. This is an assessment for the energy management plan, a holistic assessment for the care and support plan is set out in section 1.5. This describes in detail what the care and support plan should look like. To note management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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Parents of Children with ME/CFS Support Group	Guideline	025	4	It is our experience that it is very important to work in small, bitesize chunks with children and young people in planning. Add: "**build up the management plan over several appointments, and give time for the patient to think about their suggestions for the plan between one appointment and the next**"	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and it take time to digest information. These issues are addressed in the Access to care section of the guideline. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation
Parents of Children with ME/CFS Support Group	Guideline	027	13	The guideline on osteoporosis is for adults. What advice is there for children with osteoporosis caused by ME/CFS? Please see www.theros.org.uk which has paediatric information and please ensure that some relevant paediatric information is also signposted in this section.	Thank you for your comment and this information. NICE guidelines link to other NICE guidance and there is not a guideline on children with osteoporosis. To note the reference to the NICE guideline on Osteoporosis has been removed noting this was about assessing the risk of fragility fracture.
Parents of Children with ME/CFS Support Group	Guideline	028	22	It would be useful to provide statistics on the outcomes of physical activity programmes from high-quality research in order to support an informed decision, for example, research by the Workwell Foundation or Physios For ME. Excluded from these statistics should be the outcomes of research rated low quality or very low quality by the NICE committee, such as the PACE trial, and the paediatric FITNET trial.	Thank you for your comment. This point was to illustrate that the impact of a physical activity or exercise programme can vary.
Parents of Children with ME/CFS Support Group	Guideline	029	17	Although this section is entitled "Rest and sleep" there is no advice on sleep. Our experience is that very strict sleep hygiene programmes can cause a flare in ME/CFS symptoms in children and young people, and in some cases cause a	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS.

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				significant relapse and that these should therefore not be recommended for children and young people with ME/CFS.	There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Parents of Children with ME/CFS Support Group	Guideline	030	2	Add new bullet point: **"the use of melatonin may help to improve sleep"**	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Parents of Children with ME/CFS Support Group	Guideline	030	14	Only links to information on headaches and neuropathic pain are included. Suggestions for other pain should be included here as not all ME/CFS pain is covered by these two categories. There may be myalgic pain, fibromyalgia-type pain, or pain caused by co-existing conditions eg Hypermobility Spectrum Disorder or h- EDS, for example. It is important to include suggestions for helping with this kind of pain, as otherwise pain relief needed might be denied to those with ME/CFS.	Thank you for your comments. Although pain relief was included in the protocol for pharmacological interventions no evidence was identified and the committee agreed they were unable to make any recommendations for specific medications. The committee linked to NICE guidance that was relevant to people with ME/CFS, the committee acknowledged that this does not address all the type of pain that people with ME/CFS may experience. The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS.

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					Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate.
Parents of Children with ME/CFS Support Group	Guideline	031	4	Add: **"Check for quality of stomach acid, gut dysbiosis, leaky gut, malabsorption issues, food intolerances and nutritional deficiencies"**	Thank you for your comment. This recommendation refers to general strategies to minimise nausea and not investigation of nausea. The following recommendation has examples of when people should be referred for a dietetic assessment.
Parents of Children with ME/CFS Support Group	Guideline	031	6	Whilst we agree that medicines cannot cure ME/CFS, it seems that this sentence would deter health care professionals from prescribing any medicines at all. We suggest adding the following: Add: **"Explain that medicines may can be helpful to treat and manage symptoms of ME/CFS"**	Thank you for your comment. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.' The committee note the following subsection in the guideline is 'medicines for symptom management' and provides advice for prescribers. The discussion section of Evidence review F: Pharmacological management recognises some people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and this should be discussed on an individual basis.
Parents of Children with ME/CFS Support Group	Guideline	034	1	Remove **"cognitive behavioural therapy"** from the title. Other psychological support such as counselling may also be helpful.	Thank you for your comment After considering the range stakeholder comments about the title not being representative of this section the committee edited the title of this section to remove psychological support recognising this only referred to CBT.

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					After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).
Parents of Children with ME/CFS Support Group	Guideline	034	5	Add: **"Advise patients of the cognitive and emotional energy involved as well as the physical energy, and that this can exacerbate symptoms."**	Thank you for your comment. The committee agree that it is important for the risks and benefits to be explained and recommendation 1.12.29 includes this. This is one of the reasons it is important that CBT is only delivered to people with ME/CFS by healthcare professionals with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. They will be aware of the risks that you highlight.
Parents of Children with ME/CFS Support Group	Guideline	035	8	Add: "developing a **CBT** self-management plan **(not to be confused with the co-produced ME/CFS management plan)***"*	Thank you for your comment. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness and if chosen by the person with ME/CFS delivered as part of the care and support plan and energy management plan. The CBT therapist would work with the other healthcare professionals that specialise in ME/CFS. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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					This will avoid the confusion with the management plan here.
Parents of Children with ME/CFS Support Group	Guideline	035	14	We are concerned that CBT is to be considered for children and young people, as in practice, this usually necessitates a referral to CAMHS. It is our experience that the CAMHS service does not have the training or experience required to provide psychological support to children and young people with chronic illnesses. It would be beneficial to clarify that any course of CBT for a child or young person **must be delivered by a healthcare professional who is trained and experienced in ME/CFS.**	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. In this section it is clear that CBT should be only delivered by a healthcare professional with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. This applies to children and young people.
Parents of Children with ME/CFS Support Group	Guideline	036	1	Section 1.12 does not currently include the most common coexisting conditions in children and young people with ME/CFS. It is vital that the following conditions are highlighted in the guideline with reference to children and young people: ● EDS ● Hypermobility ● MCAS ● Lyme This is in addition to sections 1.11.24 to 1.11.26 which cover orthostatic intolerance, which is also a commonly seen coexisting condition in children and young people.	Thank you for your comment. This section links to related NICE guidance on co-existing conditions. Evidence review D- Diagnosis includes comprehensive lists of differential and co-existing conditions that are commonly associated with ME/CFS.
Parents of Children with ME/CFS Support Group	Guideline	043	2	Add: **The term 'payback' is often used by people with ME/CFS to describe a flare in symptoms caused by post-exertion symptom exacerbation or other cause.**	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.

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Parents of Children with ME/CFS Support Group	Guideline	043	8	Add: **Due to the variation in symptoms and their severity, the categories of ME/CFS severity can only be an approximation and there may be people who go across the boundaries. These categories are to be used as a guide.**	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
Parents of Children with ME/CFS Support Group	Guideline	043	18	The definition of moderate ME/CFS requires some adjustments to accurately describe children and young people. Add: "often resting **or sleeping** in the afternoon for 1 - 2 hours" Add: **"They may attend school for a few hours a week, or receive education by flexible means such as online schooling or a hospital tutor visiting the home"**	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
Parents of Children with ME/CFS Support Group	Guideline	044	20	Add: "Symptoms **can** typically …" as some symptoms can appear immediately	Thank you for your comment. ' can' has been added.
Parents of Children with ME/CFS Support Group	Guideline	045	4	Add: "wheelchair **or electric wheelchair"**	Thank you for your comment. These are examples of mobility needs in the definition and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added. To note to provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations.

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Parents of Children with ME/CFS Support Group	Guideline	071	2	Training and education for health care professionals is a huge area of concern, especially for paediatric services which have until now operated under a large, tertiary service model influenced by a biopsychosocial ethos. Please advise what the committee recommendation of a training programme is, along with a detailed plan of how this training is going to be implemented in all settings. What training will, for example, be provided for GPs? It is undoubtedly going to be a huge undertaking to provide a national training programme, with associated cost implications, but such a training programme is imperative in order to successfully support the new guideline. It is also important that any training plans include school nursing services. These are often the first service to be consulted by a school when a child is ill and it is crucial that school nurses are trained in the current guideline too. School nurses are often asked to attend meetings to discuss how to manage a child's illness and they need to be able to accurately recommend best practice actions to support children with ME/CFS. Can NICE develop a certificate to be displayed in healthcare settings once health care professionals have undertaken training and education on the new guideline, and can this only be made available for courses which have been audited and approved as gold-standard to ensure that there is no content based on low quality biopsychosocial research?	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. The committee discussed the level of detail that should be included in training programmes and agreed on a general description to avoid a prescriptive interpretation of the content allowing the recommendations to remain relevant as research in the area develops. *Certificate* It is not within the remit of NICE to develop certificates for training and to quality assure training. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme

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				We would be happy as a group to provide support in developing training for paediatric ME/CFS services, GPs and school nursing services.	
Royal College of General Practitioners	Evidence review	058	1	The committee discussed that "it was important to raise awareness of the clinical conditions that may produce similar symptoms." · Endocrine, nutritional and metabolic disorders: including thyroid disorders, primary and secondary adrenocortical insufficiency, Haemochromatosis, chronic kidney disease, vitamin deficiencies Genitourinary system disorders: chronic bladder infection, chronic vulvar pain Auto-immune and inflammatory disorders: including primary Raynaud's, systemic 6 lupus erythematosus, Sjogren's syndrome, vasculitis, inflammatory bowel disease, 7 coeliac disease, primary biliary cirrhosis, sarcoidosis, kidney disease; endometriosis Infections and infection- related disorders: including HIV, chronic viral hepatitis, tuberculosis, Lyme disease, other chronic infections, including those rare in the UK. Also, recurrent infection associated with immune deficiency disorders Neurological disorders: including multiple sclerosis and myasthenia gravis Cardiorespiratory disorders: including cardiac failure, chronic obstructive pulmonary disease, respiratory failure, chronic endocarditis Haematological disorders: anaemias, lymphoma, chronic leukaemia, myeloma Malignant disease: particularly those cancers which are often not easy to detect such as ovarian carcinoma Sleep-wake disorders: including obstructive sleep apnoea and narcolepsy	Thank you for your comment. The committee have revised this list and added mental health conditions: anxiety, depression or mood disorders.

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				Other chronic pain and multisystem disorders: including fibromyalgia and hypermobility spectrum disorder. Iatrogenic conditions: particularly side effects of medications used for chronic pain. For example, neuropathic pain medications have high NNT and can produce fatigue. Although this list seems exhaustive, there is no mention of mental health conditions, for which a large literature exists confirming these are most commonly part of the differential diagnosis of ME/CFS.	
Royal College of General Practitioners	Evidence Review A	005	20	The PICO includes "people who are suspected of having ME/CFS". Table 5 shows that some of the samples may not have included people with ME/CFS, for example - Bayliss 2016 (unclear), Devendorf 2018 ("patients who self-identify as having ME/CFS"), Hannon 2012 ("severity mixed or unclear"), or simply "self-identifying" or no information at all. So, the evidence base for the recommendations contained in the main guidelines is based on interviews with patients with no confirmation of the diagnosis, indeed at least one of the studies is people "self-identifying". This lack of clarity in the inclusion criteria, when assessing the quality of these studies, is inconsistent with the panel`s decision to downgrade the evidence from trials on CBT and/or GET in other parts of the review.	Thank you for your comment. See the study tables in Appendix D record the applicability of the population. . The decision about the inclusion criteria for the intervention reviews was based on the importance of understanding the impact of treatments on people with ME/CFS. This review aims to explore the views of people with ME/CFS or suspected of having ME/CFS as such the relevance of the population has been evaluated differently. In reference to the studies you have highlighted. Devendorf 2018. Moderate concerns over applicability due to participants being a subset of a previous quantitative study who were self-identified as ME/CFS (not diagnosed according to accepted criteria) with suicidal ideations but not depression. Bayliss 2016. There are no concerns over applicability because the diagnosis of ME/CFS was confirmed by GPs.

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					Hannon 2012.To note the statement about severity being 'mixed/unclear' was added to indicate the strata, as specified in the protocol. *ME/CFS population evaluation in the evidence* When considering the stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed the requirement of PEM was particularly important in the studies evaluating interventions. The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. Whereas in the evidence reviews exploring the experience of people about services and information and support needs the presence of PEM is less likely to have an impact on the findings. For this reason, the relevance of the evidence has been as assessed by considering how the diagnosis was established. For example, in Devendorf 2018 concerns about applicability are recorded due to self-identification as ME/CFS (Appendix D). Relevance is then considered in the body of evidence taking the individual studies into account (Appendix E). *The experience of interventions qualitative review and measurement of applicability and relevance* After considering the stakeholder comments the committee agreed to revisit the qualitative evidence for the experience of interventions further scrutinising the information on PEM reported in the trials and the application of relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the

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					analysis and the impact on the results and interpretation of the evidence.) In summary the same requirement for PEM has been applied to the experience of interventions in line with the clinical and cost effectiveness review of interventions.
Royal College of General Practitioners	Evidence Review D		1.2.5,1,	We think that the committee were in a position to express a view that PEM was essential to a diagnosis of ME/CFS. However, it could have been acknowledged that this was just a view without a strong evidence basis. Therefore, there should have been greater caution before instructing the evidence team to automatically downgrade all bar one of the CBT/GET trials (and incidentally most of the other trials as well) for indirectness. This meant that every trial automatically dropped a grade – with many coming into the very poor range. This is likely to have had a major impact on the committee`s reasoning and decision making, invariably pushing against recommending CBT and GET. The committee were aware of this risk: "The committee noted that the majority of the studies conducted in this area have recruited participants using criteria that do not include post exertional malaise/post-exertional symptom exacerbation as key inclusion criterion" (Section 1.2.5.1 Evidence Review D). In our opinion, this is a potentially important methodological limitation of the review.	Thank you for your comment and information PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS but as noted in the committee discussion the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not know if the people recruited to trials experience PEM as the information is not reported. Where this is the case, the trial population could include people that do not have ME/CFS and this makes it difficult for the committee to be confident of the benefits and risks of the interventions on people with ME/CFS. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was correctly considered taking this into account. See the methods chapter for more information on GRADE and CERQual and indirectness. After considering the stakeholder comments the committee agreed to revisit the quantitative and qualitative evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population $\geq$95% with PEM would be considered direct. (See evidence reviews G and H (appendix G)

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					for the approach taken, the analysis and the impact on the results and interpretation of the evidence.).
Royal College of General Practitioners	Evidence Review D	047	5	We also note the problems in all the diagnostic criteria that the evidence team reviewed. If there were gold standard criteria these should have been clear. PEM itself is neither very sensitive nor specific for a diagnosis of ME/CFS, as we can see from the table of evidence (Table 5) in that review. In addition, PEM is found in other disorders, and is not exclusive to ME/CFS.	Thank you for your comment. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The four symptoms (debilitating fatigue, PEM, unrefreshing sleep, and cognitive difficulties) were agreed by the committee as the best basis for identifying people with ME/CFS and as essential to a diagnosis of ME/CFS. The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail).
Royal College of General Practitioners	Evidence review G	005	9	Decisions on the effectiveness of interventions primarily depend on the level of evidence. The theoretical underpinning can be important but is not enough on its own to make such decisions.	Thank you for your comment, as with all NICE guidelines, recommendations were developed using a range of evidence and other sources of evidence. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The committee took great care to ensure that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what

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					recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Royal College of General Practitioners	Evidence review G	005	13	The introduction states: "People with ME/CFS have reported worsening of symptoms with GET and no benefit from CBT". It would be more helpful if it stated the percentages of people that do/do not benefit from these interventions rather than give such a generic statement.	Thank you for your comment. The wording has been changed to 'some people' to reflect that this does not apply to all people with ME/CFS.
Royal College of General Practitioners	evidence Review G	007	28	The Guideline Panel exclude Larun 2017. This is a Cochrane review, that, if evaluated independently, scores high on AMSTAR as a reliable systematic review. The reasons for excluding it need further review: The first stated reason is that "they did not include all critical outcomes specified in the review protocol". Any given Cochrane review will prespecify outcomes but will also include outcomes in their reporting that they hadn't thought of, but which would be informative. The Guideline Committee could have explored whether the relevant data on any missing outcome could be extracted. The second reason is that the Cochrane Review included study populations where not all the participants had CFS/ME. However, the review included a subgroup analysis of trials with 90% or more of the participants with CFS. In addition, the review also carried out a subgroup analysis by diagnostic criteria.	Thank you for your comment. Larun 2017/2019 was not excluded solely because mortality was not an included outcome. With regards to 'Reason 2', this applies to the Price 2008 Cochrane review on CBT, not the Larun 2017/2019 review. Although the Larun review stated that studies with >90% CFS populations would be included, all participants in the included studies were diagnosed with ME/CFS and all were included in our review. Detailed exclusion reasons have been clarified below and in the report (Evidence review G excluded studies section, and Appendix J excluded study list in Evidence review H). Also note that all included studies within these Cochrane reviews were cross-checked for eligibility for inclusion in this review. Larun 2017/2019: This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows: The approach to meta-analysis was different to our approach. All

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					exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity levels, return to school/work, exercise performance measures, and mortality. However, all studies included in this Cochrane review were included in our review. Also note that Cochrane has acknowledged issues with this review in terms of the methods used and the population definition and they plan to conduct a full update of this Cochrane review. Price 2008: This Cochrane review looked at CBT versus usual care or other interventions in adults with 'CFS'. The main reasons for exclusion are as follows: Studies with mixed populations where at least 90% of participants had a primary diagnosis of CFS were included. The committee agreed it was important that all participants in included reviews were diagnosed with ME/CFS. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, pain, sleep quality, activity levels, exercise performance, and mortality. It is also worth noting that Cochrane has stated that this review is no longer current and should not be used for clinical decision making.
Royal College of General Practitioners	evidence Review G	065	Table 4	Grade here may be incorrect. For SF36 mental component, the confidence cross one, and there are only 117 people in the study. This needs to be downgraded by 2 for imprecision, making this "very low quality". See Grade Handbook.	Thank you for your comment. Imprecision is determined based on clinical decision thresholds (minimally important difference (MID)) determined *a priori* by the

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					committee, not statistical significance. Full details on the process for determining imprecision and MIDs can be found in the methods chapter of the guideline. Studies with a small sample size are more likely to have imprecision in the effect estimates, but this is not always the case. The MIDs for each outcome are reported in Appendix K of Evidence review H. In this case, the MID for SF36 mental component was 5.2. The confidence interval for this outcome was -4.93 to +2.13. As this does not cross either MID (-5.2 or +5.2) there is no imprecision, resulting in an overall quality rating of moderate.
Royal College of General Practitioners	evidence Review G	065	Table 4	Grade here is incorrect. For SF36 physical component, the confidence cross one, and there are only 117 people in the study. This needs to be downgraded by 2 for imprecision, making this "very low quality". To have "moderate quality evidence" on a study with only 117 people gives spurious precision related to small study effects. See Grade Handbook.	Thank you for your comment. Imprecision is determined based on clinical decision thresholds (minimally important difference (MID)) determined *a priori* by the committee, not statistical significance. Studies with a small sample size are more likely to have imprecision in the effect estimates, but this is not always the case. Full details on the process for determining imprecision and MIDs can be found in the methods chapter of the guideline. The MIDs for each outcome are reported in Appendix K of Evidence review H. In this case, the MID for SF36 physical component was 3.5. The confidence interval for this outcome was -2.49 to +3.49. As this does not cross either MID (-3.5 or +3.5) there is no imprecision, resulting in an overall quality rating of moderate.
Royal College of General Practitioners	evidence Review G	065	Table 4	Grade here may be incorrect. For fatigue severity the confidence cross one, and there are only 118 people in the study. This needs to be downgraded by 2 for imprecision, making this "very low quality".	Thank you for your comment. Imprecision is determined based on clinical decision thresholds (minimally important difference (MID)) determined *a priori* by the committee, not statistical significance. Studies with a small sample size are more likely to have imprecision in the effect

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				In addition, this GRADING is inconsistent with the two previous outcomes. One could argue that 0.7 is too small an effect to be important. So "for Fatigue Severity Scale, there may be little or no difference with self-management compared to usual care" would be a fairer assessment. See Grade Handbook and Grade Policy described in Santesso et al, J Clin Epi 2020.	estimates, but this is not always the case. Full details on the process for determining imprecision and MIDs can be found in the methods chapter of the guideline. The MIDs for each outcome are reported in Appendix K of Evidence review H. In this case, the MID for fatigue severity was 2.45. The confidence interval for this outcome was -3.15 to +1.75. As this crosses one MID (-2.45 but not +2.45) this is considered serious imprecision (downgraded by one increment), resulting in an overall quality rating of low. Clinical significance (benefit or harm) is also determined using the MID, but this is considered separately to imprecision and the overall GRADE quality rating. As you have noted the mean difference for this outcome was -0.7, which is smaller than the MID, therefore this is considered to be no clinically important difference. The committee's discussion of the evidence can be found in section 3 of Evidence review G, and more information on how clinical significance is determined can be found in the methods chapter.
Royal College of General Practitioners	evidence Review G	066	Table 5	Grade here may be incorrect. Downgraded by 2 for indirectness on the basis of a) Oxford criteria used, and PEM not a "compulsory feature" may need a review. It appears in several of the GRADE tables. The inclusion criteria of the review are "adults, children and young people diagnosed as having ME/CFS". The inclusion criteria is not "adults, children and young people diagnosed as having ME/CFS by the presence of post exertional malaise". Indirectness refers to how well the population in the studies align with those defined in the PICO. So, the PICO defined in	Thank you for your comment. The PICO characteristics set out the population to be included in the review. As you recognised, we did not specify that study participants must have PEM in order to be included in the review, therefore trials were included if they met the inclusion criteria regardless of whether or not participants had PEM or whether or not this was reported. The committee consider PEM to be an essential feature for a diagnosis of ME/CFS. The committee considered that previous criteria, such as the Oxford Criteria and 1994 CDC criteria identify a heterogeneous population, which may or may not include people with ME/CFS (See Evidence review D –

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				this chapter and the PICO of the patients in the studies is aligned and probably should not be downgraded on indirectness.	diagnosis). This causes difficulty in interpreting the evidence from trials that do not use a criteria that has PEM as an essential feature (and therefore a 100% ME/CFS population) or where the percentage of people with PEM are not reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported, and numbers of people with PEM are rarely reported. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendix G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
Royal College of General Practitioners	evidence Review G	321	15	We note how the committee in 3.3. Evidence Review G promote self-management, using the moderate confidence conclusions from the qualitative literature, rather than the findings from the trials. The trials clearly show no benefit for self-management over usual care, and that both CBT and GET clearly do better. The reviewers indicate that they are prepared to use low quality evidence when there is a lot of it pointing in the same direction – towards self-management. However, the same argument is not used for other treatment approaches and the rationale for this needs to be reviewed.	Thank you for your comment. As with all NICE guidelines, recommendations were developed using a range of evidence and other sources of evidence, including that from, published peer review quantitative and qualitative evidence; a call for evidence for unpublished evidence (studies identified meeting the protocol have been included in Evidence review G), expert testimonies (see Appendix 3), and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature (Appendix 1: Children and young people; Appendix 2: People with severe ME/CFS) were also used to provide additional information to the committee (see

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					ME/CFS methods chapter). As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The quality of the evidence is important but it is only part of the multiple factors considered in decision making. The committee took great care to ensure that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. Although the quantitative evidence identified was limited and no evidence was identified on people's experiences of self-management interventions in the qualitative review of experiences of interventions, evidence identified for other interventions that encouraged self-management techniques showed that people with ME/CFS appeared to value and benefit from this type of support. After considering the evidence identified for self-management, as well as the lack of information and support people with ME/CFS report in managing their symptoms emerging from Evidence review A and their clinical experience, the committee agreed the evidence was unclear but recognised the benefits of self-management strategies for people

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					with ME/CFS and the importance of having access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits (see Evidence review G for the committee discussion on self-management strategies) The committee recognise people may benefit from different self-management strategies and that these should be discussed and agreed with the person with ME/CFS to support them in developing a care and support plan that is tailored to their individual needs as reflected in the recommendations. Please note that after reviewing the evidence available, together with their clinical experience, the committee agreed that CBT is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation to offer CBT was made to ensure this will be available for everyone and regardless of self-management. Considering the worsening of symptoms reported in the qualitative evidence as well as their experience of the effects when people exceed their energy limits, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional.
Royal College of General Practitioners	evidence Review G	335	3	It is suggested here that the low rates of harm of GET that comes through the GET trials might be because they were rarely included as an outcome and reported. In fact, the two biggest and most recent trials clearly did respond to concerns about safety by having what has to be considered exemplary methods of reporting adverse events.	Thank you for your comment. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendations, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and

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					harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee has noted there are difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials and that it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. As with all NICE guidance the committee have been able to utilise their clinical experience along with all sources of information available, including evidence from qualitative studies and expert testimonies. Considering the worsening of symptoms reported in the qualitative evidence, as well as their experience of the effects of when people exceed their energy limits, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been acknowledged in the recommendations made to ensure this type of support is available. The committee agree that the way interventions are delivered is crucial and have also included specific recommendations about the content of programmes involving physical activity or exercise as well as for whom such programs should be considered. In developing recommendations on physical activity and exercise, the content, approach and delivery of physical activity management, the committee considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their own experiences of these types of interventions

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Royal College of General Practitioners	Evidence review G	335	47	The committee raised concerns regarding the theory of deconditioning that underpins GET, which they considered cannot be applied to people with ME/CFS. This is raised throughout the guideline. The committee considered how might bed sores, contractures and DVTs be prevented (Recommendations 1.11.13) and refers the reader to the relevant guidelines, which do include exercise and early mobilisation. The committee appears to believe that advising on the potential benefits of exercise therapy somehow undermines the reality of the condition. However, this is not based on any strong evidence.	Thank you for your comment. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendations, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). As with all NICE guidance the committee have been able to utilise their clinical experience along with all sources of information available, including evidence from qualitative studies and expert testimonies. Considering the worsening of symptoms reported in the qualitative evidence, as well as their experience of the effects of when people exceed their energy limits, and concerns regarding the theory of deconditioning that underpins GET, which they considered cannot be applied to people with ME/CFS, the committee concluded that programs involving fixed incremental increases in exercise or that are based on deconditioning as a cause of ME/CFS are not appropriate. However, they acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been acknowledged in the recommendations made to ensure this type of support is available. The committee agree that the way interventions are delivered is crucial and have also included specific recommendations about the content of programmes involving physical activity or exercise as well as for whom such programs should be considered. In developing recommendations on physical activity and exercise, the content, approach and delivery of physical activity

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					management, the committee considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their own experiences of these types of interventions.
Royal College of General Practitioners	evidence Review G	344	22 onwards	We note that the committee agreed that the interventions comparing GET to usual care showed a benefit of GET for general symptom scales, fatigue, activity levels and exercise performance (VE peak). We are however puzzled as to why they said there was no benefit to GET at 134 weeks. Looking at the descriptions of the trial in Evidence Review H, it seems that the trial ended at 52 weeks, when there was a clinically important benefit on the primary outcomes of the trial – fatigue and physical functioning. But at that point the randomisation was broken, and we can see that considerable numbers of people then opted for either CBT or GET in the usual care group. Using the longest available data, as the committee were doing, to continue to evaluate the trial by its initial random allocation, seems inappropriate and misleading once that was lost. A more plausible explanation might be that gains of GET were maintained, but the other groups caught up because of the fact that more of them were opting for the other two treatments.	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends on what each committee considers useful for decision making for the particular condition or topic examined. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. The study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. For outcomes where long-term follow-up was available (e.g. 134 weeks), this data was

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					preferentially extracted in line with the review protocol, as this was the longest time point that data was available. For the remaining outcomes, 52 weeks was the longest time point that data was available, and this data was extracted. Available 24-week outcome data was not extracted as this time-point was not the longest time-point available. The review has been edited so that it is transparent to which time point outcomes reported correspond to.
Royal College of General Practitioners	evidence Review G	344	30 onwards	We agree that adverse events tend to occur when GET isn't done properly. We note the evidence that assuming that the clinical trials are done properly, with protocols, assessments, individualised care, reviews etc., the committee accepts that adverse events are in fact no more common than in self-management (3.3. Committee discussion, Evidence Review G). Could NICE recommend raising standards of healthcare professionals, and agreeing and monitoring standards via a professional body, rather than not recommending the intervention? That way a person's right to refuse GET is respected, as it is now, since it is impossible to force people into a programme, but the equally important right of those to give informed consent, and receive a treatment which when properly supervised and audited is as safe as self-management, and may result in better outcomes, is also respected.	Thank you for your comment. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendations, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). As with all NICE guidance the committee have been able to utilise their clinical experience along with all sources of information available, including evidence from qualitative studies and expert testimonies. Considering the worsening of symptoms reported in the qualitative evidence, as well as their experience of the effects of when people exceed their energy limits, and concerns regarding the theory of deconditioning that underpins GET, which they considered cannot be applied to people with ME/CFS, the committee concluded that programs involving fixed incremental increases in exercise or that are based on deconditioning as a cause of ME/CFS are not appropriate. However, they acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been acknowledged in the

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					recommendations made to ensure this type of support is available. The committee agree that the way interventions are delivered is crucial and have also included specific recommendations about the content of programmes involving physical activity or exercise as well as for whom such programs should be considered. In developing recommendations on physical activity and exercise, the content, approach and delivery of physical activity management, the committee considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their own experiences of these types of interventions. *Training* The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. To note the training recommendations have been edited.
Royal College of General Practitioners	Evidence review H	093		On a fairly cursory reading of the evidence in the guideline evidence documents, there is in fact indications that this might not be true. The GETSET trial (Clark et al, 2017) stands out as the only CBT/GET trial that has not been downgraded for possible indirectness – because it did use criteria that mandated PEM. Yet, it seems it to have given similar results to all the other trials that have been judged to have population indirectness –	Thank you for your comment. The committee agree that PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM, they just don't know if the information is not reported. To address this the committee agreed that evidence without this

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				the exact opposite of what the committee said would be the case. Again, if heterogeneity did occur, then it would have been possible to check for this, and as far as we can see, two trials did look at this and found that there was no heterogeneity according to different criteria that mandated/did not mandate PEM. It is likely that triallists would possess data on the frequency of PEM, since they would have had to record that if they were using either of the case definitions that the committee regards unsound. We would be most surprised if it were not the case that the vast majority of trial participants experienced this.	information would be 'indirect' acknowledging this uncertainty. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the studies included in the quantitative and the qualitative evidence review, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. To adequately account for concerns over PEM across studies we looked for information regarding PEM across the included, excluded studies and publications associated with the included studies. Available analyses of heterogeneity were also examined within this process but where there was a lack of

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					published data with this information, the committee could not be sure about the indirectness of the population. After the PEM information was gathered, a subgroup analysis was performed where data was available separately for studies where ≥ 95% of participants had PEM andthose where < 95% of participants had PEM, or this was not reported. As you mention, the GETSET trial was the only study for this comparison in which more than 95% of study participants were considered to have PEM (all met the NICE 2007 criteria). Where outcomes from this trial were pooled with trials where less than 95% of participants had PEM (PACE trial) or an unclear percentage of participants had PEM (Moss-Morris 2005), a subgroup analysis was performed to explore the results from these trials separately. Through the PEM reanalysis the committee aimed to ensure concerns limiting the applicability of the population in the studies have been addressed and considered in decision making.
Royal College of General Practitioners	Evidence review H, Appendix D page 518 onwards,			We agree that it is important to be certain that the evidence used in NICE guidelines is about patients with CFS/ME. The committee does not appear to have ascertained consistently whether patients included in patient surveys or in qualitative interviews did indeed have CFS/ME. Most of the studies reported had no measure of PEM, for example.	Thank you for your comment. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the studies included in the quantitative and the qualitative evidence review, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not

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					be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. To adequately account for concerns over PEM across studies we looked for information regarding PEM across the included, excluded studies and publications associated with the included studies; but where there was a lack of published data with this information, the committee could not be sure about the relevance of the population. Through the PEM reanalysis the committee aimed to ensure concerns limiting the relevance of the population in the studies have been addressed and considered consistently in decision making.
Royal College of General Practitioners	Evidence Review H, appendix D	518		We note the contrasts between the way in which the committee approach the qualitative evidence and the way in which they deal with the clinical trials. Because of the indirectness in the Methods, Evidence Review G and H, they downgraded any trial that used either CDC or Oxford criteria. But when it came to the qualitative literature, no such determination existed. For example, at least 40 different studies were considered under the heading of exploring "experiences of people who have had interventions for ME/CFS" – some of these studies used recognised criteria, (such as CDC and Oxford), but most did not. The committee excluded the Cochrane Reviews completely because they felt that there was evidence of indirectness in the trials included – but they did not apply the same rigour in their assessment of the qualitative literature, and in some areas they seemed to be accepting evidence that they would have rejected were it from	Thank you for your comment. No evidence meeting the inclusion criteria of the review protocol has been excluded. Cochrane reviews were also assessed for inclusion against the review protocol. Reasons for not including Cochrane reviews identified have been specified in Evidence review G. Also note that all included studies within these Cochrane reviews were cross-checked for eligibility for inclusion in this review. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the studies included in the quantitative and the qualitative evidence review, the committee agreed to revisit the evidence for the intervention reviews, further

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				trials – as in the discussion on self-management in Review G, 3.3.	scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. To adequately account for concerns over PEM across studies we looked for information regarding PEM across the included, excluded studies and publications associated with the included studies; but where there was a lack of published data with this information, the committee could not be sure about the relevance of the population. Through the PEM reanalysis the committee aimed to ensure concerns limiting the relevance of the population in the studies have been addressed and considered in decision making.
Royal College of General Practitioners	Guideline	General	General statement	The Royal College of General Practitioners (RCGP) welcomes the opportunity to input into this NICE consultation aiming to update the guidance on ME/CFS. The College recognises that ME/CFS is a chronic and often highly disabling and distressing illness for many patients. The cause of the illness is unknown and there is relatively limited conclusive evidence on the effects of interventions, which presents challenges when drafting a clinical guideline. The general principles of person-centredness, a holistic approach to care and shared decision	Thank you for your comment and information.

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				making are equally important in the management of patients with ME/CFS as in other long-term conditions. The RCGP consults its clinical adviser network on all NICE consultations. This is the largest response we have ever received on a guidance with almost unanimous concerns of potential bias within the draft guidance. As GPs, we are committed to offering personalised and holistic care to our patients, including those with ME/CFS, which is specific to their individual needs. There is wide variation in patients' symptoms, experience and severity of ME/CFS with many receiving the majority of their care from GP, primary and community services and successfully managing this illness. Although there are opportunities for improvements and for ensuring that all patients receive high quality care, tailored to their needs, there is a risk that this guideline reads as if most patients with ME/CFS currently have a poor experience of health care services and poor outcomes. The guideline seems to recommend a significant shift of care towards highly specialist services, with the role of the GP and primary care relatively unclear. This approach goes against a more holistic, person-centred and placed-based care delivery which utilises local resources and communities and focuses on the patient and their environment rather than the disease. The rationale for such a shift is not clear and does not seem to be backed by evidence. The composition of the panel may have been influential here and requires some clarification. Some members on the committee seem to have no interests declared but appear to be patients with severe symptoms of ME/CFS or expert witnesses. We note that the guideline group	

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				included only one GP, who is an academic with a specialist interest on the subject. Given the reality of the location of most management, primary care experience and knowledge, and the potential impact of the recommendations on health care resources, input from non-specialist GPs might have been helpful. The patient experience seems to come from the severe end of the spectrum. There does not seem to be a recognition that the ME/CFS (like most long term conditions) has a spectrum and other patient experiences exist. Together with the lack of grassroots GP experience which has expert generalist knowledge, the overall concern is that this guideline may be hard to implement, does not acknowledge that positive patient outcomes are possible, and risks making the patient the passive recipient of highly specialised medical care. The highly contentious nature of this area could be acknowledged with researchers leaving the field due to personal attacks. This does not help progress in this important topic and may partly explain the absence of good quality evidence for many of the proposed interventions. It could be acknowledged that working in this field is difficult for this reason and that extra support for researchers may be required. There appears to be pressure put on healthcare professionals to speedily diagnose ME/CFS. No consideration seems to have been given to the potential harm of this. There is no reference to what is considered a normal pattern of recovery from illnesses. For example, research and other guidance indicate that it takes up to 6 months to recover from pneumonia (see https://www.nhs.uk/conditions/pneumonia/treatment/). The speed of diagnosis in conjunction with the statement that there is no cure and no treatment for the illness, may lead to a	

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				pathway of management which could be perceived as disempowering for patients and their families. The guidance gives conflicting advice around issues such as exercise and CBT and in several areas is counter intuitive. For example, saying that patients should be discouraged from doing any exercise, unless it is part of a structured programme, even if they are doing well independently, appears to support a view that physical activity is dangerous. In addition, this recommendation can have significant resource implications. The suggestions that patients should reduce their exercise, (even if the level they are working at is not causing problems for them) and should not be enrolled in gradual (pacing) exercise programmes are also counter intuitive. Given the known potential for deconditioning and weight gain, the risks of advocating rest need to be clearly articulated. In addition, the lack of evidence on the potential benefits of prolonged rest could be made explicit. There is also a significant absence of consideration of mental health needs (including access to psychiatry and psychology services) within the guideline other than a hyperlink to the NICE depression guidance. There appears to be a prejudge against including mental illness in any diagnostic pathway. However, fatigue is a common symptom of many mental health conditions, as are somatic symptoms. In addition, suicide can be a major cause of death in these patients. It is therefore risky to discourage healthcare practitioners from sensitively exploring these issues within the differential diagnosis and when reviewing the patient. It can be potentially stigmatising to regard the possibility of mental health conditions in this way. Interestingly, the guidance links to the NICE Depression and Pain guidance, both of which suggest	

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				psychological interventions as first line treatments, despite the strong emphasis against these interventions for those with ME/CFS in this guidance. In its current form, the RCGP cannot support this guidance for use by its members. We request that our comments are considered by the panel and are incorporated in its review. We would like to see a bigger emphasis within the guideline: • on a holistic approach to management which includes patients` physical, mental and social care needs following similar principles that apply to other long-term conditions; • on patient safety and the need to avoid potentially harmful and poorly evidenced practice and advice; • on a realistic appreciation of the pressures on existing primary, community and secondary health care resources; and, • a better reflection of the role of the GP, primary and community care teams and specialists in the management of the condition, recognising the spectrum of symptoms and severity.	
Royal College of General Practitioners	Guideline	General	Lightening process. general	We note that the committee has decided to make a recommendation against the use of the Lightning Process as a psychological/behavioural intervention. There has been a recent systematic review of the Lightning Process, published in August 2020. It found a variance in the quality of studies from good to fair and in reported patient outcomes. It concluded, however, that all studies evidenced a level of benefit from the intervention, commonly for the majority of participants.	Thank you for your comment. In the systematic review you mention, Reme and Crawley have been included in the evidence review (see evidence review G and H). The other studies, none are relevant (details below) -Bringsil 2013 --> quantitative survey (excluded from review G due to study design) -Crawley 2013--> randomised feasibility study (excluded from review G for not having relevant outcomes) -Finch 2010--> quantitative survey (not excluded from review G; does not meet protocol due to study design)

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				https://www.sciencedirect.com/science/article/abs/pii/S1550830720302330 Other relevant evidence can be found at: https://adc.bmj.com/content/103/2/155 https://lightningprocess.com/research/ Based on the review, it is unclear whether NICE has sufficiently considered this evidence.	-Finch 2013 --> quantitative non-RCT (not excluded from review G; does not meet protocol) -Finch 2014 --> proof of concept (not excluded from review G; not relevant design) -F0nneb0 et al., 2012 --> case report (not excluded from review G; not relevant design) -Hagelsteen 2015--> paper not english (not excluded from review G but probably not an RCT plus not in english) -Kristoffersen 2016 --> incorrect population: not ME/CFS (not excluded from review G; does not meet protocol) -Landmark 2016 --> not in english (excluded from review G; also not RCT) -ME Association--> quantitative survey (excluded from review G due to study design) -Sussex & Kent society 2010 --> quantitative survey (not excluded from G; does not meet protocol) -Sandaunet & Salamonsen 2012 --> not in English (not excluded from G; does not meet protocol, not in english).
Royal College of General Practitioners	Guideline		9	The box will need updating to state that the long-term management of COVID-19 has been published. Can the committee be more direct and comment on the differences in management between the two conditions? In addition, in the absence of a clear diagnostic test, can the committee comment on how the differential diagnosis between the two conditions can be made? •	Thank you for your comment. This text has been updated. While there is debate about the overlap between ME/CFS and the long-term effects of COVID-19 the development of this guideline started before the COVID-19 pandemic and the committee have only reviewed the evidence relevant to the scope. The long-term effects of COVID-19 is an area of research that is rapidly growing and it is inappropriate for this committee to comment or consider making recommendations that apply to both populations.
Royal College of General Practitioners	Guideline	004	16	Can the committee consider adding that those treating and researching this condition may have also experienced prejudice? This will ensure the guidance acknowledges the difficulties clinicians and researchers also face in this field	Thank you for your comment. This section of the guideline is directed at health and social care professionals and raises awareness about ME/CFS and the prejudice and disbelief people with ME/CFS have encountered.

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				which will need to be addressed in order to ensure that more clinical evidence is generated on this important issue.	The training section of the guideline highlights the importance of supporting health and social care professionals to provide care for people with ME/CFS.
Royal College of General Practitioners	Guideline	005	9	The unexplained medical nature of ME/CFS is of paramount importance. Whilst early and accurate diagnosis is needed, can the committee consider adding that this needs balancing against overdiagnosis and sometimes unhelpful labelling of patients, who may improve and recover. Can the committee consider stating "timely diagnosis" rather than "early diagnosis"? Other causes for the disease will need to be ruled out before a true diagnosis can be made and by its nature this disease is a "chronic disease".	Thank you for your comment. After considering the stakeholder comments the committee have replaced 'early' with 'timely' and hopes this adds clarity. Throughout the guideline the committee have recommended the importance of carrying out investigations to identify other conditions or exclude other diagnoses. The committee have now included examples of investigations that might be carried out.
Royal College of General Practitioners	Guideline	005	9	The use of the term 'accurate diagnosis' needs to be challenged here. The nature of ME/CFS is unclear with unknown pathology as per recommendation 1.1.1. Accurate diagnoses in this area are difficult and usually made after exclusion of other pathology, rather than as a proactive diagnosis which may lead to overdiagnosis. Whether the diagnosis is suspected or definite, should not alter the investigation or symptomatic treatment of patients. Can the committee consider changing this statement to: "Recognise that people with ME/CFS need: Symptomatic care whilst awaiting a timely diagnosis; Regular monitoring and review, particularly when their symptoms are worsening or changing"	Thank you for your comment. After considering the stakeholder comments the committee have replaced 'early' with 'timely' and hopes this adds clarity. The section on advice for people with suspected ME/CFS address the other suggestions you have made and for this reason they have not been added.
Royal College of General Practitioners	Guideline	005	15	Please add "if the person has the capacity to make an informed choice". This recommendation intimates that carers can make the choice to decline or withdraw treatment in cases	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the

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				where patients do not have capacity, but it would only be a person with the legal appointment to do so.	NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.).
Royal College of General Practitioners	Guideline	005	20	It is important to take a child centred approach. Can the committee add that possible parental collusion in diagnosis, treatment and management needs to be considered as a safeguarding issue? As with any condition affecting children, it might be necessary to have an independent voice (appointed via the courts or social services) if the voice of the child might be difficult to hear (too young, overridden by parents, no capacity etc). In addition, giving some information on the prevalence of ME/CFS in children will be helpful.	Thank you for your comment. Safeguarding is addressed in detail in the safeguarding section of the guideline and includes the recommendation that, 'recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. Follow the NICE guidelines on child maltreatment and child abuse and neglect.'. After considering stakeholder comments this recommendation has been edited to include, ' with or without their parents of carers as appropriate' to provide further clarity.
Royal College of General Practitioners	Guideline	006	7	Whilst the definition of severe and very severe CFS is contained in the rationale, it would be useful for clinicians to have this definition at the beginning of the guidance and the rationale/available evidence for how each of these different stages are diagnosed.	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations.

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Royal College of General Practitioners	Guideline	006	7	Missing from this list is depression and anxiety which can be primary or secondary to the physical symptoms and can make the patient's symptoms worse. The rec includes emotional wellbeing but does not detail psychological/mental health disorders or their impact, which health care professionals need to be aware of at an early stage to ensure a full holistic assessment is made. Identification of mental health consequences at an early stage may save lives.	Thank you for your comment. Taking into account the range of stakeholder comments about the location in the guideline of this section the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. In response to your comment this now means that the criteria for suspecting and diagnosing ME/CFS precedes this recommendation providing clarity about the symptoms that are related to a diagnosis of ME/CFS. The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist with ME/CFS and these should be investigated and managed in accordance with best practice. Also to note that after taking into consideration the stakeholder comments the committee have revised the list of differential diagnosis in Evidence review D and added, mental health conditions: anxiety, depression or mood disorders.
Royal College of General Practitioners	Guideline	007	1	Many of the symptoms described in this list would highlight a need for a mental health review to rule out depression. It is essential that the patient is fully assessed and evaluated and that clinicians are not deterred from thinking about mental health causes for these symptoms, as this would put patients at significant risk.	Thank you for your comment. Taking into account the range of stakeholder comments about the location in the guideline of this section the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. In response to your comment this now means that the criteria for suspecting and diagnosing ME/CFS and the assessment and care planning section precedes this recommendation providing clarity about the symptoms that are related to a diagnosis of ME/CFS and the importance of excluding and identifying other diagnoses.

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					The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist with ME/CFS and these should be investigated and managed in accordance with best practice. Also to note that after taking into consideration the stakeholder comments the committee have revised the list of differential diagnosis in Evidence review D and added, mental health conditions: anxiety, depression or mood disorders.
Royal College of General Practitioners	Guideline	007	17	Continuity of care is essential for everyone with complex needs. Can the committee expand on what they mean by "personal care and support"? Would it be better to highlight continuity of care and person-centred care here, rather than just "personal care and support", or does this refer only to social care services? Clarity is required to ensure clinicians understand what is being asked of them.	Thank you for your comment. Personal care and support refers to any care involving direct interaction with the person with ME/CFS this could include health or social care services. The committee agree this is good clinical practice and should happen routinely. This recommendation has been included based on Appendix 2 and the committee's experience that health and social care professionals who do not know the person with ME/CFS can underestimate the impact interactions can have on the person with severe or very severe ME/CFS.
Royal College of General Practitioners	Guideline	008	4	It is important to state the ME/CFS is made as an exclusion diagnosis and only once other conditions have been ruled out. This has been omitted from this guidance but is essential to include to ensure consistency of understanding amongst patients and clinicians.	Thank you for your comment. The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have added examples of investigations to be done when suspecting ME/CFS and have added that ME/CFS should be suspected if the 'symptoms are not explained by another condition.'
Royal College of General Practitioners	Guideline	008	5	Can the committee change the statement to include "appropriate".	Thank you for your comment.

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				- "Appropriate clinical history" (there is no such thing as a comprehensive clinical history). - "Appropriate physical and mental health examination guided by symptoms". This is essential to ensure a mental state examination is carried out for those presenting with phycological and psychiatric sequelae, to ensure underlying depression or other mental health conditions are not missed. It is very important that healthcare professionals are supported in carrying out this examination and that patients understand the clinical need to do this. A "psychological wellbeing" assessment may mean different things to different people and may encompass things such as life accomplishment and satisfaction. We must ensure this guidance is specific enough to be understood by healthcare professionals and patients. - "Appropriate baseline investigations to rule out alternative causes for symptoms". There is a long list of differential diagnoses that can mimic ME/CFS that is not included. Can the committee consider adding a list of investigations that need to be carried out to rule out other disorders? For example, FBC, coeliac and thyroid function tests for fatigue, B12 and folate for paraesthesia etc.	After considering stakeholder comments about the assessment the recommendation was edited to,' If ME/CFS is suspected, carry out: - a medical assessment (including relevant symptoms and history, comorbidities, overall physical and mental health) - a physical examination - an assessment of the impact of symptoms on psychological and social wellbeing assessment - baseline investigations to exclude other diagnoses, (for example (but and not limited to)….' The committee have now included examples of investigations that might be carried out and include those you mention. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. The committee emphasise the importance of using clinical judgment when deciding on additional investigations and note this is relevant to all areas of the assessment.
Royal College of General Practitioners	Guideline	008	10	The importance of an early diagnosis is clear to improve rehabilitation and treatment pathways however understanding the normal pattern of recovery from an acute illness (e.g. viral illness) is important when considering a diagnosis of ME/CFS. The RCGP has significant concerns regarding overdiagnosis of this condition in people who are simply taking longer to recover than usual after an acute illness. For example,	Thank you for your comment. The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the qualitative evidence and their experience the committee agreed it is important that people

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				glandular fever can take months to fully recover and labelling this group of patients (even with a provisional diagnosis) at 4 weeks (in a child) and 6 weeks (in an adult) could be too soon. There is no evidence provided that we can see that indicates why this shortened time to diagnosis was chosen or why there is a difference in the children and adult timelines. At 4-6 weeks after infection, differentia diagnosis would begin to be investigated and ruled out. There are concerns that making a diagnosis before such investigations are completed may increase the overdiagnosis of the condition.	with this combination of symptoms are given advice that may prevent them getting worse as early as possible. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted. The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. • Further investigation/differential diagnoses. The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have added examples of investigations to be done when suspecting ME/CFS and have added that ME/CFS should be suspected if the 'symptoms are not explained by another condition.'
Royal College of General Practitioners	Guideline	008	17	Giving a patient a provisional diagnosis of a chronic condition when it is only suspected, could be damaging to their mental health. It is important that this diagnosis is not made until the clinician is *certain* of the diagnosis, rather than risk overmedicalisation, overdiagnoses or wrong diagnoses being made. We request that this rec is reconsidered.	Thank you for your comment. After considering the stakeholder comments on early diagnostic labels the committee have amended the wording to remove the recommendation on making a provisional diagnosis of ME/CFS. Diagnosis is now introduced at 3 months.

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Royal College of General Practitioners	Guideline	009	21	This rec will lead to overdiagnosis and potential misdiagnosis. Telling someone at 4 or 6 weeks that they might have ME/CFS before investigating for thyroid disorder, anaemia and cancer amongst other things could be harmful. It does not feel as though the voice of clinicians who understand the primary care pathway for patients with ongoing symptoms that need to be investigated have been sufficiently heard in the writing of these recommendations.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses and to tailor management appropriately. Taking into consideration the stakeholder comments the committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. In addition the committee have added that ME/CFS should be suspected if the, 'symptoms are not explained by another condition.' However after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted for the following reasons: ○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis

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Royal College of General Practitioners	Guideline	010	1	Can the committee explain what an "appropriate specialist" is in this rec and how the "advice" would be given? There are no provisions for this type of advice at the current time. Are NICE recommending a service is commissioned to give GPs advice on ME/CFS from specialists? If so, can the guideline group be explicit on this to ensure that the necessary services are commissioned. If not, can this rec be changed accordingly please? Although the majority of cases will present within general practice, secondary care specialists may also have patients with relevant symptoms. Therefore, this recommendation could refer to "health care professionals" rather than "primary healthcare professionals". There is an emphasis throughout on specialist teams managing this chronic condition when in reality the majority of patients will be cared for within primary care teams. Is there any robust evidence on the effectiveness of relevant interventions delivered solely in specialist centres versus shared care with primary care teams or versus interventions delivered primarily by primary care teams?	Thank you for your comment. Appropriate specialist here refers to expertise in supporting the interpretation of signs and symptoms where there is uncertainty and a possible alternative diagnosis. Throughout the guideline where a specialist refers to a ME/CFS specialist this has been made clearer by including ME/CFS before specialist.
Royal College of General Practitioners	Guideline	010	5	Can the committee explain why a child (which we assume is up to the age of 18) cannot be investigated in primary care, in the usual way? In view of the variability in terms of clinical presentation, this rec will add burden to an already overstretched paediatric service and delay the investigations that would normally occur in primary care, such as routine blood tests. Can the committee consider stating "once a diagnosis is made". Again, an emphasis on specialist care rather than generalists is being made within the guidance when the majority of patients will be cared for in primary care.	Thank you for your comment. The committee added referral at the 4 week point to a paediatrician in the first instance for further assessment and investigation and then to a ME/CFS specialist for confirmation of a ME/CFS diagnosis to ensure children and young people will have a timely accurate diagnosis of ME/CFS. See Evidence review D- for the evidence and committee discussion. The committee acknowledged that non-specialists may not feel confident in diagnosing ME/CFS and recommended that people

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					with suspected ME/CFS are referred to a ME/CFS specialist service for confirmation of the diagnosis (Evidence review B). In addition, the referral to community paediatricians for further investigations before ME/CFS specialist teams is the experience of committee members of working with children and young people.
Royal College of General Practitioners	Guideline	010	15	Can the committee further clarify the definition of an "energy envelope"? This is a vague term and not one fully recognised within the health care community. This rec is also restrictive as does not necessarily take into account the individual needs of patients. Can the committee consider changing this to state: "Give personalised advice about managing their symptoms, that over time they may get better and advise them to listen to their own body, gradually increase their exercise, improving their tolerance as they go along, not to assume that they can exert themselves in the early stages of the disorder, but to gradually increase and pace themselves over time as their symptoms allow".	Thank you for your comment. After considering the stakeholder comments the committee agreed that this concept and energy envelope* might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits. There is a definition of energy limits in the terms used in the guideline. *Re energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits.

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					This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies).
Royal College of General Practitioners	Guideline	010	21	Healthy balanced diet. Can weight management be added to this? The guidance is recommending patients rest significantly and so their calorific needs will significantly reduce. Please consider: "Maintain a healthy balanced diet, paying attention to the calorific intake as with reduced exercise and increased resting, weight increases are possible, which will further impact on health and recovery."	Thank you for your comment. This recommendation refers to people with suspected ME/CFS and for short duration during a potential period of acute illness and this has not been added to this recommendation. However the committee have added weight gain as a reasons for referral for a dietetic assessment in the management of symptoms section of the guideline recognising that inactivity in some people with ME/CFS can result in weight gain.
Royal College of General Practitioners	Guideline	011	5	This part of the guidance is very confusing. A provisional diagnosis is recommended at 4 or 6 weeks yet a full diagnosis not until 3 months. There does not appear to be any evidence to support these timings. Can the committee add "Diagnose ….. persisted for 3 months and only once other diagnoses have been ruled out and once certain of the diagnosis". In patients presenting with multiplicity of symptoms, often medically unexplained, where no obvious cause is apparent, the diagnosis must be one of exclusion – including exclusion of depression and other psychological disorders – and care must	Thank you for your comment. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your point and added some clarity for readers. In summary the edits to the point you make are: • 'Provisional' diagnosis has been deleted. As you note the symptoms should be investigated for other causes and the committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months.

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				be taken not to over-diagnose or misdiagnose patients with this condition, which could lead to further trauma, stress or worry.	• It is clear in the diagnosis section that diagnosis is dependent on the criteria persisting for 3 months and other conditions have been excluded.
Royal College of General Practitioners	Guideline	011	9	This rec suggests a child (up to 18) will be seen initially by a paediatrician and then by an ME /CFS specialist. This is potentially over medicalising a condition that will mainly be managed in the community. For some children (especially those over 8), a GP may undertake the initial investigations as with adults and so the paediatric referral may not be required. Mandating such a referral may simply add to waiting times for tests and investigations that could be completed elsewhere. Referrals should be based on need and so the rec should reflect this rather than stating it is essential for all children of all ages.	Thank you for your comment. The committee added referral at the 4 week point to a paediatrician in the first instance for further assessment and investigation and then to a ME/CFS specialist for confirmation of a ME/CFS diagnosis to ensure children and young people will have a timely accurate diagnosis of ME/CFS. See Evidence review D- for the evidence and committee discussion. The committee acknowledged that non-specialists may not feel confident in diagnosing ME/CFS and recommended that people with suspected ME/CFS are referred to a ME/CFS specialist service for confirmation of the diagnosis (Evidence review B). In addition, the referral to community paediatricians for further investigations before ME/CFS specialist teams is the experience of committee members of working with children and young people. See Evidence review D- for the evidence and committee discussion.
Royal College of General Practitioners	Guideline	011	15	Can the committee change this to "appropriate history". The type of history depends upon the presenting complaint.	Thank you for your comment. After considering the range of stakeholder comments this has been edited to, 'medical assessment'. The committee agree the specific content would depend on the judgment of the clinician carrying out the assessment.

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Royal College of General Practitioners	Guideline	011	18	Can the committee be explicit and state physical, mental health and social history please if this is what is suggested?	Thank you for your comment. Physical and mental health is included in the medical assessment*. After considering the range of stakeholder comments the third bullet point this has been edited to,' the impact of symptoms on psychological, emotional and social wellbeing'. Medical assessment has replaced full history.
Royal College of General Practitioners	Guideline	012	3	Physical functioning should include activities of daily living assessment, which would include access to shopping and cooking as per line 9, so this can be removed from there.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Royal College of General Practitioners	Guideline	012	5	This statement appears to encourage the use of vitamin and mineral supplements and there is no evidence to support this. Can NICE be clearer? If the guideline supports their use please show the evidence, and if not, clearly state "There is no evidence to support the use of vitamins, minerals or alternative diets for CFS."	Thank you for your comment. This is part of the assessment and does not encourage the use of vitamins and mineral supplements. The dietary management and strategies includes a recommendation that there is not enough evidence to support routinely taking vitamin and mineral supplements.
Royal College of General Practitioners	Guideline	012	7	A dietary assessment can only fully be undertaken by a dietician. Is the committee suggesting every patient should be referred for dietetic review? The recs have already recommended a "balanced diet be continued" and so the addition of a dietary history here seems excessive. Clinicians other than dieticians can only recommend healthy and balanced diet plans and are not experts on restrictive or alternative diets. If every patient needs a specialist dietary assessment, services will need to be commissioned specifically for this. Are NICE recommending these alternative diets or not recommending them? Can the NICE guideline group make this clear within the rec please?	Thank you for your comment. The committee disagree, the assessment is carried out by a member of a specialist ME/CFS team and they are aware of the need and to assess the dietary needs of people with ME/CFS and have the skills to do this. The dietary management and strategies sections of the guideline (including that for people with severe and very severe ME/CFS) has clear indications when people should be referred to a dietician with a special interest in ME/CFS for their expertise. This is a recommendation about assessment and the refers to an assessment of the use of restrictive and alternative diets, it is not a recommendation about the use of such diets. In the dietary management and strategies section there is a recommendation

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				e.g. Do not recommend restrictive or alternative diets Recommend a well-balanced health diet taking into consideration the calorific needs based on reduced activity and increased rest to prevent weight gain and obesity.	to refer to someone has a restrictive diet to a dietician with a special interest in ME/CFS for their expertise for an additional assessment.
Royal College of General Practitioners	Guideline	012	10	The addition of psychological and psychiatric needs must be added to ensure a full holistic management plan. It is essential to ensure a full holistic approach to this condition as the guidance itself advises.	Thank you for your comment. The medical assessment* includes mental health in the examples. *full history has been edited to medical assessment.
Royal College of General Practitioners	Guideline	013	8	The mental health needs must be added to this stem to ensure this is taken into account, as it is with every chronic disease.	Thank you for comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.). In line with this the bullet points have been deleted as this is reflected in the aims of a care and support plan. The personalised care and support plan is based on the person's needs and includes the areas listed. The plan is developed in collaboration with the person with ME/CFS and explores their aims *and the management of their health and well-being within the context of their whole life and family situation. It should be proportionate, flexible and coordinated and adaptable to a person's health condition, situation and care and support needs.*
Royal College of General Practitioners	Guideline	013	12	It may not be appropriate or feasible to offer home visits for all patients with severe CFS. This, as with all home visits, will need to be assessed on a patient-by-patient basis, using shared decision making to determine what is the best consultation approach depending on need. Consider changing to:	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home

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				Offer alternative appointment times and appointments using remote consulting (such as telephone/video) where appropriate, to undertake a holistic assessment, accommodating for the fluctuating nature of the illness which may mean patients may not be able to attend the practice for face-to-face appointments and may need to change appointments for times when they are more able to attend. Use shared decision making with the patient (and carer where appropriate) to determine if a home visit would be appropriate for those with severe or very severe CFS.	visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. To note after considering the stakeholder comments the committee agreed to bring the recommendations on people with severe and very severe ME/CFS together in one section to ensure their particular needs were not hidden within the guideline. In the context of home visits, this recommendation on offering home visits is now followed by the recommendation on providing flexible access. The committee agreed it is important that people are offered home visits for the assessment and development of the care and support plan but other methods may be more appropriate depending on the person's symptoms.
Royal College of General Practitioners	Guideline	014	15	It is important that the information given to patients is balanced and at the right time of their diagnosis journey. Giving this before the patient has a confirmed diagnosis could be detrimental to their health and wellbeing. When giving balanced information, it is also important to explain that patients can lead fulfilling and independent lives and some people do recover from this condition, which will also give patients hope. Currently, the information list seems overly pessimistic and does not appear to reflect any possible positive outcome to their condition.	Thank you for your comment. This section is for people with ME/CFS, after they have received a diagnosis. After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS.
Royal College of General Practitioners	Guideline	014	25	Some people can live well with this condition and lead fulfilling lives and this needs to be balanced within this statement.	Thank you for your comment. After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to

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					adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS.
Royal College of General Practitioners	Guideline	015	11	This could include both social care and social prescribing.	Thank you for your comment. This section directly addresses how to access social care for formal support and how some people may find this difficult as a result of previous experiences. As social prescribing is a less formal form of support it is not as relevant to this section.
Royal College of General Practitioners	Guideline	015	18	Health care professionals would use shared decision making when making social care and other referrals, guided by a need assessment and taking into account service and resource availability.	Thank you for your comment and information.
Royal College of General Practitioners	Guideline	016	5	Safeguarding is essential but does not need to be undertaken by specialists. This can be impractical. Safeguarding of children and adults with all conditions is the responsibility of *all* health care professionals and moving this to a specialist service can cause delays and harm. Can the committee add a statement that safeguarding considerations must be taken into account when reviewing adults and children who present with complex and medically unexplained symptoms? Any child or adult presenting with unexplained symptoms is usually considered for a safeguarding assessment as part of the process of ruling out alternative causes for the symptoms and presentation. It is essential to empower healthcare professionals to undertake appropriate safeguarding investigations whenever necessary. We understand that in ME/CFS there is a risk of symptoms being misunderstood from a safeguarding perspective, but we need to ensure all children and adults are safe and there is a risk that safeguarding issues may be dismissed, or that healthcare professionals may be	Thank you for your comment. The committee agreed that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. With regard to safeguarding the importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The NICE guidelines on child maltreatment and child abuse and neglect should be followed..

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				discouraged from undertaking full evaluations if this rec remains as it is currently written. The RCPCH has a relevant guide which is currently being updated https://www.rcpch.ac.uk/resources/fabricated-or-induced-illness-fii-carers-practical-guide-paediatricians.	This is clear that if a professional has concerns they should be addressed in the same way as with any child or young person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
Royal College of General Practitioners	Guideline	017	8	This statement currently does not empower a clinician to perform a full safeguarding assessment, which is essential if a child or adult presents with concerning features and patterns of illness. Can the stem be strengthened please? Consider: "It is recognised that certain patterns of illness are seen as safeguarding risks and a full safeguarding assessment must be undertaken if a child or adult is deemed at risk. It is acknowledged that there can be overlap of clinical presentations with cases of abuse or neglect, and this possibility must be assessed in the appropriate way to ensure patient safety."	Thank you for your comment. These recommendations are to raise awareness about the difficulties that some children and young people and their families have experienced when safeguarding concerns have been raised. The importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. The committee disagree these recommendations do not empower clinicians to perform a full safeguarding assessment. Recommendation 1.7.5 is 'that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability.' The NICE guidelines on child maltreatment and child abuse and neglect are cross referred to. This is clear that if a professional has concerns they should be addressed in the same way as with any person Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended

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					that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk. For this reason your suggestion has not been added.
Royal College of General Practitioners	Guideline	019	4	The provision of single rooms *should be based on clinical need* taking into account the need for accessibility of the nursing staff to review and monitor patients. If a patient with ME/CFS is severely affected and needs more intensive care than others, it may be more appropriate to place them in an area where there is increased nursing support, and this may not be in a single room. In addition, there are other conditions where a single hospital room may be preferable including autistic spectrum disorders, learning disability, palliative care etc. It may be more appropriate to say: "if clinically appropriate and depending on availability" rather than "if possible".	Thank you for your comment. The committee agree that these considerations are applicable to all people accessing health services and is an example of best practice (see Patient experience in adult NHS services: improving the experience of care for people using adult NHS services). This is a guideline on people with ME/CFS and highlighted here as consideration for people with ME/CFS. The committee note that while clinicians are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement the guidance does not override the responsibility of healthcare professionals and others to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.
Royal College of General Practitioners	Guideline	019	17	Admitting patients with ME/CFS straight to a ward should only occur if clinically appropriate. It may be appropriate from a clinical perspective for a patient to be admitted to A&E where lifesaving care is required. In addition, any pathways assisting decisions on direct admissions to wards will need to take into account other conditions (e.g., LDs, autistic spectrum disorders, the elderly, infirm, frail and those with palliative care needs) and the general principle of not increasing health inequalities.	Thank you for your comment. The committee note that while clinicians are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement the guidance does not override the responsibility of healthcare professionals and others to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.
Royal College of General Practitioners	Guideline	019	19	Please see comment above under 19.4	Thank you for your comment. The committee agree that these considerations are applicable to all people accessing health services and is an example of best practice (see Patient experience in adult NHS services: improving the experience of care for people using adult NHS

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					services). This is a guideline on people with ME/CFS and highlighted here as consideration for people with severe or very severe ME/CFS. The committee note that while clinicians are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement the guidance does not override the responsibility of healthcare professionals and others to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.
Royal College of General Practitioners	Guideline	020	2	It needs to be clear whether this is a social services assessment or a healthcare assessment.	Thank you for your comment. This refers to the social care needs assessment in recommendation 1.6.9.
Royal College of General Practitioners	Guideline	020	28	Blue badges are now under the remit of local councils and will be issued after a need assessment. They are not recommended by healthcare professionals themselves. We suggest this rec is removed unless the guidance will be directed at councils who provide blue badges in which case some clarification will be required.	Thank you for your comment. These recommendations refer to the social care needs assessment and the aids and adaptions identified as part of that assessment. This has been made clearer in the recommendations.
Royal College of General Practitioners	Guideline	020	20 and 23	It is not clear whether the terms "prompt" and "without delay" suggest that ME/CFS patients need to be prioritised above patients with other conditions (such as those for example with learning disabilities or with palliative care needs). If this is not the case, perhaps acknowledging the need for service prioritisation depending on the level of need and demand may be appropriate.	Thank you for your comment. These recommendations refer to the social care needs assessment and the aids and adaptions identified as part of that assessment. This has been made clearer in the recommendations.
Royal College of General Practitioners	Guideline	021	1	Who is this rec aimed at? Social care, GPs, secondary care? The way this rec is written may generate confusion and can add significant workload to primary and secondary care services, which should be undertaken elsewhere. For example:	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social

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				- Parents and schools can refer children to the school nursing teams who can then undertake assessments and liaise with the school on the child's behalf. Can this be clarified please? - The responsibility of the school is also not clear in these recs. The school can refer to the school nurse and child and adolescent mental health services and can undertake educational psychology assessments if needed. This is not the remit of the GP. Can this be clarified please? - The responsibility of employers is not clear here. Employers have a responsibility to provide occupational health services that will liaise on behalf of the patient at work. Can this be clarified please? Can NICE ensure the correct professionals are engaged when updating this guidance to ensure the appropriate professionals are clear of their responsibilities within in it?	care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS and not who should be delivering all the aspects of care (Evidence review I _Multidisciplinary care (Benefits and Harms section). The multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse. NICE has looked to consult with a wide range of stakeholder groups including professional bodies, and a wide range of stakeholders have commented on the draft guideline.
Royal College of General Practitioners	Guideline	022	13	Mental health (including psychiatric and psychological) conditions need to be added to this list for a full holistic view of this disease. It is essential for all clinicians to consider these to prevent missed diagnoses or harm.	Thank you for your comment. The recommendation has been edited to include,' physical, psychological, emotional and social' to reflect that people's mental health wellbeing should be considered.
Royal College of General Practitioners	Guideline	023	5	This recommendation seems to suggest that no patient with ME/CFS can ever be discharged back to primary care. This can have potentially serious implications for specialist services, waiting times and in terms of over medicalisation. The vast majority of CFS patients are managed within primary care, like most patients with chronic conditions.	Thank you for your comment. The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no one single model of care. Some of the committee members described experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support.

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Royal College of General Practitioners	Guideline	024	6-24	This section may be perceived as negative as it suggests a poor prognosis. A distinction may need to be made on whether the evidence suggests that no intervention can result in positive outcomes versus the absence of evidence on the effectiveness of certain curative interventions.	Thank you for your comment. This section focuses on energy management and does include that it is not curative but this does not imply a poor prognosis. To note after considering the range of stakeholder comments on this bullet point in recommendation 1.6.4 it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS.
Royal College of General Practitioners	Guideline	024	6	Some clarity is required on the evidence for "energy management". We understand there is some good evidence-base for pragmatic rehabilitation[1] and graded activity[2] and that pacing is not evidence-based.[2] It is unclear why the committee uses the symptom of "post-exertional symptom exacerbation, including debilitating fatigue" as a reason for not providing GET, when a trial of GET, published in The Lancet,[1] showed that it significantly reduced this symptom more than staying within one's energy envelope. 1. Wearden A, Dowrick C, Chew-Graham C, Bentall R, Morriss R, Peters S, Riste L, Richardson G, Lovell K, Dunn G. A randomised controlled trial of a nurse-led home-based self-help treatment for patients in primary care with chronic fatigue syndrome – the FINE Trial. BMJ 2010 340: c1777. 2. White PD, Goldsmith KA, Johnson AL, et al., PACE trial management group. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies).

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				specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. *Lancet*2011;377:823-36. doi:10.1016/S0140-6736(11)60096-2 pmid:21334061 The evidence base for any recommendations and the level of evidence will need to be explicit to assist informed decision making and fair allocation of resources.	Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS. GET The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G.' The committee recommended that physical activity or exercise programmes that use are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. The committee recognised that although graded exercise therapy is not recommended it was important that people with ME/CFS

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					have access to a ME/CFS specialist team to provide support with physical activity and exercise programmes as outlined in this guideline where appropriate
Royal College of General Practitioners	Guideline	024	14	The term "energy envelope" is used here, which is not defined or necessarily easily understood by healthcare professionals. Can this be clarified please? The term may medicalise normal experience of daily activity.	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* There is a link to a definition. The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
Royal College of General Practitioners	Guideline	025	4	Please add mental health (psychiatric and psychological) impacts.	Thank you for your comment. This is an assessment for the energy management plan, a holistic assessment for the care and support plan is set out in section 1.5. and includes a medical assessment of physical and mental health.
Royal College of General Practitioners	Guideline	025	5	By "energy management plan", does NICE mean implement a gradual exercise plan?	*Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits.

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					This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). This is not a gradual exercise plan.
Royal College of General Practitioners	Guideline	025	16	"Energy envelope" is used again here and this requires some further clarification.	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* There is a link to the definition. The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
Royal College of General Practitioners	Guideline	025	18	We are concerned about the first action to REDUCE exercise. Would this be the case if the exercise level the patient is at, is beneficial to them or does not cause them problems? What evidence is there for the benefit of a reduction in exercise levels for all?	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to, agree a sustainable level of activity as the first step, which may mean reducing activity.'
Royal College of General Practitioners	Guideline	026	1	This rec is welcomed and perhaps can be moved forward at an earlier stage of the management section. However, physiotherapists provide exercise advice and rehabilitation and do not "manage energy". Can the committee please use the correct terminology for these services so that the intervention referred to is clear?	Thank you for your comment. This section refers to referral for physical activity and exercise programmes.

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Royal College of General Practitioners	Guideline	027	3	Clinicians are asked to assess bed sores, DVTs and contractures in people with severe ME/CFS, but prevention must be highlighted rather than accepting that these will occur. Encouraging movement and mobility is essential to prevent the complications listed here. Can the committee consider adding a section on "preventing complications of immobility"?	Thank you for your comment. In the physical functioning and mobility section of the guideline the committee recommend that strategies to maintain and prevent the deterioration of physical functioning and mobility should be included in the care and support plans for people with ME/CFS. Areas for consideration include cardiovascular health and bone health. The committee note that this recommendation refers to people with severe or severe ME/CFS with very limited mobility.
Royal College of General Practitioners	Guideline	027	20	The use of the symptom of "post-exertional symptom exacerbation, including debilitating fatigue" is used as a reason for not providing GET. However, a trial of GET showed that it significantly reduced this symptom more than staying within one's energy envelope. Could this be clarified please?	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors

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					including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Evidence review G describes the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) Based on the evidence mentioned above and their own experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount

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					of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS.
Royal College of General Practitioners	Guideline	027	21	We are concerned that this rec may disempower patients to take control of their own recovery and illness. If the patient would like to participate in unstructured exercise that is not part of a supervised programme – is there any evidence that this would be harmful?	Thank you for your comment. The committee agree there is little dispute amongst clinicians working with people with ME/CFS that they should not undertake exercise that is not part of a programme overseen by a ME/CFS specialist team, such as telling them to go to the gym or exercise more. It is commonly agreed that people with ME/CFS experience post exertional malaise (PEM) after activity. PEM is a worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated. It is in this context, and recognising the evidence from people with ME/CFS indicating that misunderstanding of the impact of PEM

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					and inappropriate advice on how to incorporate physical activity (and exercise) into their lives has resulted for some in a deterioration of their condition, that this guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS.
Royal College of General Practitioners	Guideline	027	24	The stem says 'Do not offer …' which can be interpreted as advising health care professionals to avoid any exercise recommendations. However, further down the same recommendation it sets out when and how graded exercise programmes should be considered. This can be very confusing. Under 1.11.19 and 1.11.20 the guideline acknowledges that some people do benefit from exercise programmes. This rec could deter healthcare professionals from even discussing graded exercise, and any patients who use the guideline might be quick to reject such advice.	Thank you for your comment. The recommendation describes the types of physical activity or exercise programmes that should not be offered to people with ME/CFS. It does not advise healthcare professionals to avoid any exercise recommendations. After considering the stakeholder comments, the committee have added exercise into the following recommendations on considering a programme to clarify where these apply to exercise. The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and

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				The evidence of harm appears to come from qualitative evidence. It would be helpful to report the level of evidence in such recommendations as they can have important implications and may confuse any relevant public health messages on the benefits of physical activity.	application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy 'based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence * and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important people referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.

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					*See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). NICE do not include the level of evidence in the recommendations.
Royal College of General Practitioners	Guideline	028	12	This rec is in direct opposition to rec 1.11.16. Can the committee consider removing rec 1.11.16 as it seems to be unsafe and may put patients at harm?	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The

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					committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
Royal College of General Practitioners	Guideline	028	18	The overreliance on specialists, including specialist physiotherapists, for the management of patients may introduce unintended delays to accessing care.	Thank you for your comment. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services , to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed.
Royal College of General Practitioners	Guideline	029	2 and 10	The term "energy envelope" will need further clarification.	After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
Royal College of General Practitioners	Guideline	033	3	The overreliance on specialists, including specialist dieticians, throughout this document for the management of patients may introduce unintended delays to accessing care.	Thank you for your comment. The committee agree there is a lack of dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The committee also agreed this was true for all health and social care professionals specialising . To note the recommendation has been reworded as a 'dietician who has a special interest in ME/CFS'. This is because the

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					committee recognised that currently dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are dieticians that provide expertise to ME/CFS services. Special interest describes this group of professionals better. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. The re-wording might reduce the risk of increased waiting time but some areas might need to invest in training to implement this recommendation.
Royal College of General Practitioners	Guideline	034	1	A treatment is defined as "the use of drugs, exercises, etc. to improve the condition of an ill or injured person, or to cure a disease". CBT is used to help a patient adjust to their illness and improve their quality of life, and therefore it could be considered as a treatment/therapy: Cognitive behavioural therapy (CBT) - NHS (www.nhs.uk). Could this part of the guideline be reviewed please?	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.
Royal College of General Practitioners	Guideline	034	1	Properly supervised and expertly managed programmes of either graded exercise therapy (GET) or cognitive behavioural therapy (CBT) do not claim miracle cures or dramatic improvements, but the evidence shows that these approaches can offer symptom improvement. In the absence of other safe and effective interventions for the management of the condition, the role of GET and CBT may need to be acknowledged. By not recommending these interventions, services may be decommissioned, reducing the help available to ME/CFS patients, some of whom do benefit.	Thank you for your comment. After reviewing the evidence available, together with their clinical experience, the committee agree that although CBT is not curative for ME/CFS, it is a useful intervention to help people manage their condition and reduce the distress associated with having a chronic illness that it should be available to all people with ME/CFS. Recommendations made in the present guideline aim to ensure this will be the case. In regards to GET, after the worsening of symptoms reported in the qualitative evidence, the committee concluded that programs

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				Other relevant evidence includes the following: a. Chew-Graham, Cahill G, Dowrick C, Wearden A, Peters S. Use of multiple sources of evidence about CFS/ME in primary care consultations. Annals of Family Medicine. 2008; 6: 340-348. b. Chew-Graham C, Dowrick C, Wearden A, Richardson V, Peters S. Making the diagnosis of CFS/ME in primary care: a qualitative study. BMC Family Practice. 2010, 11:16. c. Pilkington K, Ridge D, Igwesi-Ngobi CN, Chew-Graham CA, Little P, Babatunde O, Corp N, MacDermott C, Cheshire A. A relational analysis of an invisible illness: A meta-ethnography of people with chronic fatigue syndrome/myalgic encephalomyelitis and their support needs (CFS/ME). Social Science and Medicine. Sept 2020 https://doi.org/10.1016/j.socscimed.2020.113369	involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. Please note that for the present guideline, a wealth of evidence meeting our protocols has been reviewed, including reference 'a' you have kindly provided, and an earlier publication of reference 'b' (included in Evidence review C). Pilkington did not meet the inclusion criteria in the review protocols for the guideline.
Royal College of General Practitioners	Guideline	034	1	CBT is actively discouraged in this guidance, yet in other overlapping NICE guidance appropriate for ME/CFS patients (chronic pain and mood disorders) it is proactively recommended. For example, psychological therapy for chronic primary pain: "Consider acceptance and commitment therapy (ACT) or cognitive– behavioural therapy (CBT) for pain for people aged 16 years and over with chronic primary pain. Do not offer biofeedback to people aged 16 years and over to manage chronic primary pain."	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence

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				"Only offer cognitive behavioural therapy (CBT) to people with ME/CFS who would like to use it to support them in managing their symptoms of ME/CFS and to reduce the psychological distress associated with having a chronic illness. Do not offer CBT as a treatment or cure for ME/CFS." Of note, there are also some inconsistencies with respect to exercise which is not recommended within this guidance but is within the separate chronic pain guidance. NICE chronic pain guidance states: "Offer a supervised group exercise programme (for example, cardiovascular, mind–body, strength, or a combination of approaches) to people aged 16 years and over to manage chronic primary pain. Take people's specific needs, preferences and abilities into account." "Encourage people with chronic primary pain to carry on with their exercise for longer-term general health benefits (also see NICE guidelines on physical activity and behaviour change: individual approaches)." •	reviews G and H for the evidence and the committee discussion on these recommendations). *Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The Chronic Pain Guideline recommended that CBT be offered for people with Chronic primary pain, but did not look at the evidence for CBT in people with ME/CFS. In Chronic primary pain, the Chronic Pain Guideline Committee noted that although most of the evidence showed that CBT for pain improved quality of life for people with chronic primary pain. A consistent benefit was not demonstrated in other outcomes.
Royal College of General Practitioners	Guideline	034	21	This definition of CBT is not a true reflection of the intervention patients will receive. Can the committee consider removing this rec and only having rec 1.11.46 which is more accurate?	Thank you for your comment, Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage

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					their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out the principles of CBT in reference to people with ME/CFS and how it should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Royal College of General Practitioners	Guideline	039	1	The suggestion of an annual review in primary care may introduce duplication and may negatively impact workload. Can this be rephrased to state "If a person has not been seen, consider offering an annual review in primary care". The need for an annual review will depend on the patient`s circumstances including the involvement of secondary care, whether the patient is already under regular review within primary care and on the severity of the condition.	Thank you for your comment. The committee noted in the committee discussion in Evidence review J that people with ME/CFS report little or no follow up care, monitoring or scheduled reviews. This is reflected in Evidence review C: Access to care and the reports on children and young people with ME/CFS (Appendix 1: Children and Young people), and people with severe ME/CFS (Appendix 2: People with severe ME/CFS). The committee emphasised that inadequate or inappropriate follow up and review impacts not only on care related to ME/CFS but screening and assessment for other conditions and preventative care. This has the potential consequence of worsening of symptoms and overall deterioration in health. The committee agree that the need for an annual review will depend on the person's circumstances. Some people may not need an annual review for various reasons, including involvement of secondary care services, or will decline a review but the committee agreed it was important that people with ME/CFS were offered the opportunity to have care related to their ME/CFS reviewed at least once a year in line with other long term conditions.

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Royal College of General Practitioners	Guideline	040	7	This rec means that children diagnosed with ME/CFS will have to stay under the care of a paediatrician in the long term, potentially over medicalising their condition. Further evidence is required on the value and cost-effectiveness of the content, frequency and location of follow ups, considering the implications for service provision and patient outcomes.	Thank you for your comment. The committee agreed that optimal care for children and young people with ME/CFS is provided by health and social care professionals that having training in ME/CFS. In particular a paediatric ME/CFS specialist team should confirm the diagnosis and develop the care and support plan. It follows from this that reviews are carried out or overseen by a paediatrician with expertise in ME/CFS. In evidence review I-Multidisciplinary care, the committee note that in particular children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations, confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres. A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams. Service delivery, including location of clinics, is not within the scope of this guideline. The committee agree that the frequency and content will influence the cost effectiveness of follow-up but decided that there was too much uncertainty to specify these details in the guideline.
Royal College of General Practitioners	Guideline	041	1	It is unusual for a guideline to recommend further mandatory training for healthcare professionals. The rationale, costs and implications of this on workforce and workload need careful consideration and justification.	Thank you for your comment. The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. A strong theme from the evidence was the lack of understanding about ME/CFS and training in health and social care professionals and the committee agreed it was important to make recommendations about training. Your comments will also be

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					considered by NICE where relevant support activity is being planned.
Royal College of General Practitioners	Methods			METHODS, EVIDENCE REVIEW D, EVIDENCE REVIEW G We find the approach taken by the committee to downgrade nearly every trial of CBT and GET, and all of those that were included in the last review, on the grounds of indirectness, is problematic. The reason given is that the committee believes that trials that use the criteria that were the most popular at the time, Oxford and CDC, might be flawed because they did not mandate the symptom of post exertional malaise (PEM). We find this inherently difficult to accept, because although no one is disputing the importance of PEM in CFS, at the same time no one has yet found a single satisfactory definition for this. We think it likely that the trials of the time included the same populations as are seen in clinical practice today and we are not aware of any evidence that this is not the case. We also question whether in other reviews the change in the rating of a symptom, from a recognised part of the diagnostic criteria to one that is mandatory, would have been sufficient to downgrade all previous work on the condition.	Thank you for your comment. The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence. When considering the stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied

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					differently across the evidence reviews, the committee agreed the requirement of PEM was particularly important in the studies evaluating interventions. The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. Whereas in the evidence reviews exploring the experience of people about services and information and support needs the presence of PEM is less likely to have an impact on the findings.
Royal College of General Practitioners	Methods			We are also struck by the fact that the committee did not produce some evidence to back up their hunch – and it is a hunch – as they admit.	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE

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					guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Royal College of General Practitioners	Rationale	065	8	The guidance states that pain is a common symptom in ME/CFS. NICE has released its draft guidance on chronic pain (defined as pain lasting for more than 3 months) which would align with the ME/CFS diagnosis period of 3 months. However, this guidance does not align with the chronic pain draft guidance, which does recommend CBT. Can NICE clarify whether this approach or the chronic pain approach is more appropriate in this group of patients?	Thank you for your comment. The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that when managing any co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account.
Royal College of Physicians (RCP)	Appendix 3	005		NICE expert testimonies There are three expert testimonies. We note that one of the testimonies is from a recognised advocate against trials and evidence in interventions who has served on the Board of Phoenix Rising. Their career and academic standing is based on laboratory research and pharmaceutical interventions, as opposed to guidelines development or pragmatic trial designs for health and social interventions. Our experts believe that the testimony shows a lack of understanding of this area of research. The fluctuating nature of the illness is a problem in RCTs, but if they are sufficiently powered it should not be a problem. Again, these trials cannot be blinded. Respondent bias is recognised	Thank you for your comment. Professor Edwards was invited to provide to the committee his expertise on some of the methodological controversies in undertaking research in his area. His testimony describes and reflects his opinion. The committee acknowledged in his testimony the lack of objective outcome measures of effectiveness for interventions for ME/CFS and the limitations of subjective measures. The committee discussed these methodological issues and recognised they are challenging in conducting complex interventions and are not just related to ME/CFS.

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				in trials, and this is not a reason to dismiss them; and it is possible then to match up those where respondent bias may be a problem, with other measures of functioning or exercise that can be independently assessed. Our experts believe that a lack of understanding on how the theoretical model is simply used to think about the processes that might be in play to explain why the intervention may be effective; in itself, the theory should not be used to dismiss the results of a trial after the trial is completed simply because the reader doesn't agree with it. Our experts believe that the comment about Cochrane and peer review is misplaced; this review was extensively peer reviewed. Our experts believe that the methods are being criticised here as belief disconfirmation bias is being experienced. Our experts believe that to dismiss all the evidence from trials in ME/CFS is idiosyncratic and that the detail of this presentation is largely anecdotal. Our experts believe that the chair of the guidelines panel or the Director of NICE needs to instruct the panel to dismiss this expert witness as it stands against the whole NICE evidence-based process in general for complex interventions.	All of the additional evidence enabled the committee to consider and discuss a wider range of evidence, including that from, published peer review quantitative and qualitative evidence. To note that expert witnesses are not members of the committee and are not involved in the final decisions or influence the wording of recommendations.
Royal College of Physicians (RCP)	Evidence	General	General	We have some major concerns about the way that the evidence has been handled. Specific points are set out in the point-by-point response below, but in general our experts consider that the committee has taken an unreasonably harsh view of the quality of the research evidence that does exist.	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as

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				Instead our experts believe that the committee has relied on unreferenced the qualitative evidence of a small number of individuals /experts who have strong personal views and are members of 'activist' groups. Quite often, they have relied on the anecdotal personal experience of committee members themselves. This seems to underpin a lot of the recommendations – often in direct contravention of the available research evidence. Our experts find this very worrying – particularly given that several members of the committee have already stated explicitly that they do not support or agree with certain treatments or belong to organisations that have made such statements. We believe that this has created an unacceptable bias and there is under-representation from patients who have recovered from ME/CFS	practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee took into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). *Quality ratings of the evidence* All NICE guidelines follow the process for evaluating the quality of evidence as set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. The process for quality rating used in NICE guidance is an internationally agreed process and it is not unusual for evidence to be graded as low or

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					very low quality. This does not mean it cannot be used to make recommendations but affects the strength of recommendations. *Unreasonably harsh view of the quality* This point we think refers to the decision by the committee to downgrade evidence that did not use a diagnostic criteria that includes post exertional malaise (PEM) as essential. PEM is widely acknowledged in ME/CFS specialist practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just do not know how many if the information is not reported. Where this is the case, the trial population could include people that do not have ME/CFS and this makes it difficult for the committee to be confident of the benefits and risks of the interventions on people with ME/CFS. Using GRADE and CERQual the committee agreed that evidence without this information would be 'indirect' (relevance in CERQual) acknowledging this uncertainty about the population. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and CERQual. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative and qualitative evidence and the application of indirectness and relevance. As part of this they agreed that any evidence with a

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					population > 95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) *Underrepresentation from patients who have recovered from ME/CFS* The committee membership had a broad range of professional and personal knowledge about the different experiences of people with ME/CFS and this was discussed and considered at all stages of the decision making. It is true that there is little representation in the literature of people who have recovered from ME/CFS and the committee hope that where this can be published it will be as this can only further inform the care and support of people with ME/CFS.
Royal College of Physicians (RCP)	Evidence	General	General	Our experts believe that evidence from the committee has been relied upon despite there being a great deal of published research. Our experts believe that this has research has been dismissed on several pre-texts Our experts note that the literature reviews rejected over 500 papers. Important evidence that would have provided guidance in many areas is only present in the list of excluded studies – suggesting that the committee either asked the wrong questions or used an extraordinarily narrow set of filters. For example: • The decision not to allow any evidence other than RCTs meant that the service evaluation literature was never consulted. This means that important analyses from the national outcome database, collating outcome data from hundreds of clinic patients (Crawley et al, 2013, https://doi.org/10.1093/qjmed/hct061v and Collin et	Thank you for your comment. We do not agree that the whole evidence evaluation process is flawed and needs to be reviewed and re-done for the reasons set out below. *A review team that is independent of the committee* One of the strengths of NICE guidance is the committee. Evidence reviews for guideline development require the input of a committee to ensure they are relevant to practice. An evidence review without the input of an expert committee can be lacking in the detail that fully explores the complexities of the implementation of evidence in clinical practice. *Pre stated views or an interest in a particular outcome* The NICE Policy on declaring and managing interests for NICE advisory committees sets out the processes for :

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				al, 2017 https://doi.org/10.1186/s12913-017-2437-3) have been ignored • Critical outcomes were poorly thought out. For example, they include 'mortality' even though there is no evidence that ME/CFS affects mortality (other than possibly through suicide rates). Important studies (including the Cochrane review by Larun 2017) were excluded based on not including critical outcomes such as mortality • Trials were downgraded in quality simply because they did not use the latest 2015 Institute of Medicine (IoM) criteria for diagnosis of ME/CFS – even though they used the criteria that were current at the time, which differed from the 2015 criteria by whether one single symptom, post exertional malaise, is either included or mandated.. No evidence is provided to support or refute the Committee's assertion that this called into question the findings of the trials, which made up over 90% of those before the Committee. • Some of these decisions were made by the committee rather than the review team Our experts believe that the whole evidence evaluation process is flawed and needs to be reviewed and re-done by a review team that is independent of the committee and comprises people with experience in methodology and evidence evaluation as opposed to individuals who have pre-stated view or an interest in a particular outcome.	• what interests need to be declared and when • how declared interests should be recorded • when a declared interest could represent a conflict of interest and the action that should be taken to manage this. As with any other guideline this Policy has been applied to this guideline. The Interests Register for the committee is published on the NICE website (https://www.nice.org.uk/guidance/indevelopment/gid-ng10091/documents) . The register has been updated throughout the development of the guideline and includes the decisions and actions made on the interests declared. *Excluded evidence* All NICE guidelines follow the process for evidence synthesis as set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. Accordingly no study has been excluded that met the review protocols. If the studies did not have any of the outcomes listed in the protocol then they would have been excluded. With reference to Larun 2017: This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this

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					guideline. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity levels, return to school/work, exercise performance measures, and mortality. However, all studies included in this Cochrane review were included in our review. Also we note that Cochrane has acknowledged issues with this review in terms of the methods used and the population definition and they plan to conduct a full update of this Cochrane review. *Study design* The most appropriate design for the review was included in the protocols. See chapter 4 Developing review questions and planning the evidence review in Developing NICE guidelines: the manual. *Downgrading of evidence* It is not correct that trials were downgraded in quality simply because they did not use the latest 2015 Institute of Medicine (IoM) criteria for diagnosis of ME/CFS. PEM is widely acknowledged in ME/CFS specialist practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just do not know how many if the information is not reported. Where this is the case, the trial population could include people that do not have ME/CFS and this makes it difficult for the committee to be confident of the benefits and risks of the interventions on people with ME/CFS.

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					Using GRADE and CERQual the committee agreed that evidence without this information would be 'indirect' (relevance in CERQual) acknowledging this uncertainty about the population. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and CERQual. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative and qualitative evidence and the application of indirectness and relevance. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) *Some of these decisions were made by the committee rather than the review team* The review protocol is developed by the review team and the guideline committee. The review protocols were drafted by the reviewing team and then refined and agreed with the committee members. It is then reviewed and approved by NICE staff with responsibility for quality assurance. The input of the committee is critical in ensuring that the protocol will identify the evidence that is relevant to answer the question informing clinical practice. The decisions about PEM where made by the committee (see above) and then applied by the review team to the evidence. As is usual practice in a guideline where there was a lack of clarity in the

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					evidence in a study, here over the population, the committee were consulted.
Royal College of Physicians (RCP)	Evidence Review	General	General	Evidence evaluation Our experts note a major problem with the NICE methodology is that it is designed for single discrete interventions (eg drugs) in well-defined and homogenous target populations. It does not work well for complex interventions in complex and heterogenous conditions. The approach to evaluating evidence necessitates breaking down such interventions into their individual component parts so that each can be examined in separate PICO questions. As noted above, integrated rehabilitation takes a holistic individually tailored approach. For patients with CFS/ME, in clinical practice such programmes typically combine a range of physical, cognitive and psychological approaches depending on patients' needs, preferences and priorities. These may include elements of CBT, GET, pacing, etc in varied proportions, incorporated where possible into everyday activities. Unfortunately, current NICE methods would discount any RCTs of this fully integrated approach based on risk of bias, inconsistency, imprecision, and subjective outcomes. To overcome this, RCTs break down rehabilitation into separate component parts so that patients are allocated to one or more isolated interventions (eg CBT or GET, or adaptive pacing) irrespective of their actual needs or preferences. Our experts believe thar this fragmented piecemeal approach bears little relation to real life clinical practice and runs the risk of producing guidance that is not only illogical and unhelpful, but which may have unintended consequences that are potentially harmful.	Thank you for your comment. *NICE methodology and complex interventions* Developing NICE guidelines: the manual. Chapter 4 *Developing review questions and planning the evidence review* addresses the topic about approaches to take when considering the design of studies to be included in a systematic review. In summary the effectiveness of an intervention is usually best answered by a RCT because a well-conducted RCT is most likely to give an unbiased estimate of effects. Where such evidence is not available (for example, where interventions it can be difficult or unethical to assign populations to control and intervention groups). In such cases, a non-randomised controlled trial might be a more appropriate way of assessing association or possible cause and effect. The Medical Research Council (MRC) has produced guidance on evaluating complex interventions (Craig et al. 2008) and using natural experiments to evaluate health interventions delivered at population level (Craig et al. 2011). When developing the protocols for the intervention reviews, a RCT was agreed to be the most appropriate study design to evaluate clinical effectiveness. In recognition that the views of people with ME/CFS who had experienced the interventions was important a qualitative review was done with an accompanying call for evidence to identify any unpublished evidence. The committee agree that in clinical practice a holistic personalised approach to care may

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				There is now reasonably strong evidence that individual physical psychological and cognitive interventions benefit at least some patients. The critical questions are now what approaches work best for which types of patient, and how we identify their individual needs and make sure that they get the type(s) of rehabilitation and support that they need. In long term conditions, large scale longitudinal cohort analyses of systematically collected data gathered in real life clinical practice provide the best way to answer these questions which can never be answered by short term piecemeal RCTs. Our experts believe that if NICE wish to provide meaningful guidance in the arena of complex and long term conditions, it should consider using alternative appraisal systems (of which there are several) that are independent of trial design, providing a better fit for this kind of evidence. In this respect the RCP has for many years been producing pragmatic evidence-based guidelines for complex conditions, and our experts recommend that NICE should take this opportunity to reconsider its approach for future guidelines in these more complex areas of clinical practice.	typically combine a range of physical, cognitive and psychological approaches depending on patients' needs, preferences and priorities. These may include elements of different intervention varied proportions, incorporated where possible into everyday activities. Current NICE methods do not discount any RCTs of this approach. In ME/CFS the protocol for non-pharmacological interventions includes combinations of treatments (including combinations with pharmacological treatments). Unfortunately, very few RCTs combining any treatments were identified. The committee agree that the critical questions in all areas of clinical practice are what works for individual patients and how this is identified and implemented. The committee hope this research will be conducted and published as this can only further inform the care and support of people with ME/CFS.
Royal College of Physicians (RCP)	Evidence review A	005	20	The PICO includes people who are 'suspected of having ME/CFS' Table 5 shows that some of the samples may not have included people with ME/CFS Bayliss 2016 (unclear), Devendorf 2018 ("patients who self-identify as having ME/CFS"), Hannon 2012 ("severity mixed or unclear"), and the list could go on. The evidence base for the recommendations contained in the main guidelines here is based on interviews with people where we have no confirmation of the diagnosis, indeed at least one	Thank you for your comment. All the studies have been critically appraised and the quality of the evidence assessed. For each study applicability is recorded in the individual study tables in (Appendix D). Relevance is then considered in the body of evidence taking the individual studies into account (Appendix E). For Devendorf, Moderate concerns are recorded for applicability due to participants being a subset of a previous quantitative study who were self-identified as ME/CFS (not diagnosed

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				of the studies is people 'self-identifying'. The review authors do not critically appraise these studies or assess their quality. Devendorf 2018 contributes to seven of the themes in table 3. Our experts believe that this lack of rigor in the inclusion criteria, in assessing the quality of the studies, and in particular being clear whether the patients actually had ME/CFS, represents a double standard with the exclusion of studies from the RCT analysis where the Guidelines Panel propose studies that don't report on PEM should be downgraded	according to accepted criteria) with suicidal ideations but not depression (Appendix D). In the theme Information about ME/CFS (Appendix E. table 5). Relevance is assessed as having minor concerns. The explanation in the footnote is, 'minor concerns over relevance due to participants in one study being self-identified as having ME/CFS rather than having been diagnosed according to accepted criteria (Devendorf 2018) and participants of one study consisting of people previously recruited in a RCT (Chew-graham 2008) but no further concerns in any other contributing study.'. *ME/CFS population evaluation in the evidence* When considering the stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed the requirement of PEM was particularly important in the studies evaluating interventions. The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. Whereas in the evidence reviews exploring the experience of people about services and information and support needs the presence of PEM is less likely to have an impact on the findings. For this reason, the relevance of the evidence has been as assessed by considering how the diagnosis was established. *The experience of interventions qualitative review and measurement of applicability and relevance* After considering the stakeholder comments the committee agreed to revisit the qualitative evidence for the experience of interventions further scrutinising the information on PEM reported in the trials and the application of relevance in the evidence. As part of this they agreed that any evidence with a population ≥

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					95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) In summary the same requirement for PEM has been applied to the experience of interventions in line with the clinical and cost effectiveness review of interventions.
Royal College of Physicians (RCP)	Evidence Review G	General	General	In relation to the above our experts have some major concerns about how the evidence has been handled – these are detailed further down in our response, but for now we will proceed with comments on the guideline itself.	Thank you for your comment.
Royal College of Physicians (RCP)	Evidence review G	General	General	Our experts have major concerns about how the evidence has been handled – these are detailed further down in our response	Thank you for your comment.
Royal College of Physicians (RCP)	Evidence review G		Table 80	Our experts believe that this table is quite telling, as it is generally positive about the effects of graded exercise therapy. Our experts note that this is in complete contrast to the narrative promoted by the 'activist voice' that GET 'caused them to be ill for ever' and induces setbacks that they never recover from. What is unclear is why the findings from the research contrast so markedly with the rhetoric against GET contained in the guideline. This is explored in more detail below.	Thank you for your comment. There was evidence of both positive and negative experiences with GET including reports of reductions in fatigue and tiredness, improved sleep but also experiences of no difference with treatment, uncertainty, or lack of impact, often related to school and cognitive activities emerging for children and young people. Positive experiences have been acknowledged in the committee's discussion and interpretation of the evidence (Evidence review G). The committee also noted there was no clear picture of benefit from the quantitative evidence, and the evidence was inconsistent. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the

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					trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Considering the worsening of symptoms reported in the qualitative evidence as well as their experience of the effects when people exceed their energy limits, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been reflected in the recommendations and based on clinical experience the committee concluded the same considerations were also applicable to children and young people.
Royal College of Physicians (RCP)	Evidence review G	009 - 061	Table 2	In Table 2, the review proceeds to summarise the studies included in the evidence review. Out of 56 included studies representing a very substantial body of research conducted over the last 25 years, all but 5 were downgraded due to 'Serious population indirectness – 1994 CDC criteria used; PEM is not a compulsory feature.' Our experts believe that this is unreasonable as it results in the dismissal of a substantial number of trials – many of them very significant in terms of both size and strength of outcome.	Thank you for your comment. No evidence meeting the inclusion criteria of the review protocol has been dismissed. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to

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					be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
Royal College of Physicians (RCP)	Evidence review G	072 -119	Tables 9-26	Similar findings were seen for CBT in relation to other interventions	Thank you for your comment. There was evidence of both positive and negative experiences of CBT and other interventions emerging from the qualitative findings. Both types of experiences have been acknowledged in the committee's discussion and interpretation of the evidence (Evidence review G). As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the

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					trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The evidence was therefore not the only information that the committee has considered, and it is important for all the information that underlined the committee's decision making to be reflected in the guidance. The discussion of how the evidence informed the recommendations is detailed briefly in the rationale in the guideline, where the committee's consideration of people's positive and negative experiences have also been acknowledged and in more detail in the discussion of the evidence sections in Evidence review G.
Royal College of Physicians (RCP)	Evidence review G	072 - 119	Table 8	This table presents the clinical evidence summary for CBT vs usual care across a variety of parameters including quality of life, general symptoms, fatigability, physical function cognitive function, psychological status and pain, activity levels and exercise performance. Despite fairly consistently better outcomes in the intervention group virtually all evidence was downgraded to 'very low' on the basis of 'risk of bias' (lack of double blinding), 'indirectness' (not the latest criteria) and 'imprecision' (wide confidence intervals due to the expected heterogeneity.	Thank you for your comment. As with all NICE guidelines the committee used its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee considered many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Whether or not there is a clinically important benefit or harm for a particular outcome is considered separately to the GRADE quality rating for the outcome, however these are both factors the committee consider as part of their decision making. As you point out, most studies were downgraded for risk of bias due to the lack of blinding, however some studies had other sources of

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					bias, for example for example selection bias if study participants differed at baseline or attrition bias if there was a significant amount of missing data. This is detailed for each outcome and each study in the data extraction tables in Appendix D of Evidence Review H. Imprecision was determined based on clinical decision thresholds (minimally important difference (MID)) determined *a priori* by the committee. Imprecision is not a measure of heterogeneity, but rather an assessment of the width of the confidence intervals around an effect estimate in relation to the MID. Imprecision is often a reflection of studies with small sample sizes or low number of events, which results in wide confidence intervals resulting in uncertainty around the effect. No heterogeneity was detected for any of the outcome measured in this comparison that were pooled.
Royal College of Physicians (RCP)	Evidence review G	137 -155	Tables 38-43	These present similar findings for GET in relation to other interventions Our experts note that some of the evidence is downgraded inconsistency (ie lack of standardisation of the intervention), despite the guidelines insistence that GET should not be offered in standardised programmes.	Thank you for your comment. We are unsure if this is the correct reference none of these tables include downgrading for inconsistency.
Royal College of Physicians (RCP)	Evidence review G	137 -155	Table 37	This table presents the clinical evidence summary for CBT vs usual care across a variety of parameters including quality of life, general symptoms, fatigability, physical function psychological status and pain, activity levels and exercise performance.	Thank you for your comment. Table 37 refers to graded exercise therapy versus standard care in adults, severity mixed or unclear.

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				Virtually all evidence was downgraded to 'very low' based on 'risk of bias' (lack of double blinding), 'indirectness' (not the latest criteria) and 'imprecision' (wide confidence intervals due to the expected heterogeneity)	As with all NICE guidelines the committee used its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee considered many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Whether or not there is a clinically important benefit or harm for a particular outcome is considered separately to the GRADE quality rating for the outcome, however these are both factors the committee consider as part of their decision making. As you point out, most studies were downgraded for risk of bias due to the lack of blinding, however some studies had other sources of bias, for example for example selection bias if study participants differed at baseline or attrition bias if there was a significant amount of missing data. This is detailed for each outcome and each study in the data extraction tables in Appendix D of Evidence Review H. Imprecision was determined based on clinical decision thresholds (minimally important difference (MID)) determined *a priori* by the committee. Imprecision is not a measure of heterogeneity, but rather an assessment of the width of the confidence intervals around an effect estimate in relation to the MID. Imprecision is often a reflection of studies with small sample sizes or low number of events, which results in wide confidence intervals resulting in uncertainty around the effect. No

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					heterogeneity was detected for any of the outcome measured in this comparison that were pooled.
Royal College of Physicians (RCP)	Evidence review G	139 - 140	Table 37	Two trials had already provided systematic measurements of six safety outcomes (non-serious adverse events, serious adverse events, serious adverse reactions to treatment, deterioration in global health, deterioration in physical function, withdrawal from treatment), finding no excess harms associated with GET, in comparison with control interventions (White et al, 2011, https://doi.org/10.1016/S0140-6736(11)60096-2; Clark et al, 2017, https://doi.org/10.1016/S0140-6736(16)32589-2). There was one exception - SAEs were more common in GET participants in one trial in comparison to specialist medical care participants, but independent scrutineers did not attribute these SAEs to GET (White et al, 2011). Furthermore, there was no significant difference in numbers reporting SAEs after GET compared to adaptive pacing therapy (White et al, 2011). These two trials recruited 852 patients, 267 of whom received GET or guided self-help based on GET. The safety data for these trial applied the standard protocols required by the European Union Clinical Trials Directive for medicinal products (https://ec.europa.eu/health/human-use/clinical-trials/directive_en).	Thank you for your comment. The committee agree there needs to be better reporting and long-term data collection of harms in RCTs. The difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials is not disputed (for example see https://bmjopen.bmj.com/content/9/2/e024537). Notwithstanding this, it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. Ideally this takes both a quantitative and qualitative approach and includes the experiences and opinions of all people who have had the intervention, patient experience is invaluable. As with all NICE guidelines the committee uses its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee considered many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Royal College of Physicians (RCP)	Evidence review G	139 - 140	Table 37	Our experts question what a strength of a trial should be. That using the best methods available, these two trials showed that there were very few serious adverse events and reactions. But the review makes these small numbers a weakness,	Thank you for your comment. The committee agree there needs to be better reporting and long-term data collection of harms in RCTs. The difficulties with

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				downgrading that evidence to 'very poor', when the obvious explanation is that there were few SAEs and SARs, despite looking for them with stringent methodology. Meanwhile the non-serious adverse events, which of course are always going to be more frequent, get a higher quality rating, simply because they are commoner. This is clearly not what the GRADE system was designed to do – and the committee should have pointed this out, rather than listing it as a weakness.	the collection, analysis and reporting of adverse events in randomised controlled trials is not disputed (for example see https://bmjopen.bmj.com/content/9/2/e024537). Notwithstanding this, it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. Ideally this takes both a quantitative and qualitative approach and includes the experiences and opinions of all people who have had the intervention, patient experience is invaluable. As with all NICE guidelines the committee uses its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee considered many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Royal College of Physicians (RCP)	Evidence review G	005	4-17	The review question purports to answer the following open questions 1. What is the clinical and cost effectiveness of non-pharmacological interventions for people with ME/CFS? 2. What are the experiences of people who have had interventions for ME/CFS? But then the introduction starts with the statement *'There is no known cure for ME/CFS'* and proceeds with **Previous guidance has recommended the use of Cognitive Behavioural Therapy (CBT) and Graded Exercise Therapy (GET) but these have been controversial. The use of CBT**	Thank you for your comment. Guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. In addition to this, as with all NICE guidelines, recommendations were developed using a range of evidence and other sources of evidence. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the

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				and GET has been strongly criticised by people with ME/CFS on the grounds that their use is based on a flawed model of causation involving abnormal beliefs and behaviours, and deconditioning. People with ME/CFS have reported worsening of symptoms with GET and no benefit from CBT. Although research on pacing is sparse, this method of activity management is preferred by many people with ME/CFS. Interventions such as counselling, meditation and yoga are sometimes used to improve mobility and/or general wellbeing. Evidence here is also lacking Our experts note that this might be reasonable if there was a balancing statement such as mentioning that some patients have reported benefit or that the previous 2007 guidelines recommended GET and CBT as the interventions for which there is the clearest research evidence of benefit. Either of these might have provided credible evidence that the Committee was starting from a neutral position, but our experts believe that the absence of such a balancing statement gives the appearance of bias from the very start. Indeed, this potentially raises questions about the integrity of NICE guidelines processes. There should be methodologists producing summaries of the evidence, this should NOT be the Guideline Panel of Topic Specialists and consumers (people with ME, rather than those that have recovered). This lack of separation between viewpoints and an independent assessment of the evidence is a feature throughout this Nice Guideline. This is perhaps best demonstrated by the inexplicable decision, taken by the committee not the review team, to downgrade trials that did not mandate post-exertional malaise. This should have been left to the review team to examine to	literature. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However, while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. The variability of positive and negative experiences with CBT and GET have been captured by the evidence and have been discussed in the main body of the current report (see the committee's interpretation and discussion of the evidence, Evidence review G). Please note that after reviewing the evidence available, together with their clinical experience, the committee agree that although CBT is not curative for ME/CFS, it is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation has been made to offer CBT to ensure this will be the case. In regards to GET, considering the worsening of symptoms reported in the qualitative evidence as well as their experience of

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				see if data support such a move and enhance that with a sensitivity analysis to see if that affected outcomes.	the effects when people exceed their energy limits, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been reflected in the current recommendations, in the rationales in the guideline and in more detail in the discussion of the evidence in Evidence review G. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence by addressing it in the quality assessment and the assessment of confidence in the quantitative and the qualitative evidence respectively through addressing concerns
Royal College of Physicians (RCP)	Evidence review G	006		Our experts believe that the PICO characteristics are inappropriately phrased which is unusual in an updated guideline where the previous evidence base is well known. For example, the interventions do not actually include GET, which is a medically defined, structured programme of rehabilitation, and different from the broad topic of 'exercise interventions'. Nor is there reference to CBT, which again is a specific intervention, and not the same as behavioural nor psychological support. The critical outcomes – (which are the outcomes the guideline panel would use in making decisions about whether to recommend or not an intervention also odd. The first listed is 'mortality' which is not an outcome relevant to the interventions in this condition. Our experts cannot understand this choice, given that best evidence shows that there is no premature mortality in patients with CFS/ME (except for death by suicide.	Thank you for comment. This table of PICO characteristics are a summary of the full review protocol. The full review protocol goes into more detail, with specific examples given including CBT and GET. Keep in mind that these lists are intended as examples only, and studies eligible for inclusion were not restricted to those with listed interventions. The full protocol can be found in Evidence review H, Appendix A The committee disagree with your view that mortality is not an important outcome just because it is not an expected outcome. If deaths (for example suicide) had occurred unexpectedly in any studies this would be important for the committee to consider as part of their decision making.

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				See: Carr et al, 2019, https://doi.org/10.1017/S0033291719001065 Roberts et al, 2016, http://dx.doi.org/10.1016/S0140-6736(15)01223-4).) Our experts question whether the panel really believe that sleep interventions, complementary therapies or occupational advice will, in randomised controlled trials, impact on mortality. In addition, elsewhere the panel argue that 'post-exertional malaise' is an important symptom in this condition, yet they do not list this as outcome. Our experts note that this is unusual, as recovery from ME/CFS would be indicated by resolution of this symptom. On the converse, the panel argue that PEM is made worse by exercise, and therefore it must be mandatory that they include this as an outcome to evaluate this hypothesis. Had they done so, they would have found one large trial that did examine this as an outcome (White et al, 2011, cited above).	
Royal College of Physicians (RCP)	Evidence review G	007		The Guideline Panel exclude the Cochrane Review by Larun 2017 (revised 2019), which, if evaluated independently, scores high on AMSTAR as a reliable systematic review. The reasons stated for exclusion are against any evidence-based practice. **Reason 1. because they did not include all critical outcomes specified in the review protocol.** Our experts believe this is spurious, because any Cochrane review will prespecify outcomes but will also include outcomes in their reporting that they had not thought of, but which would be informative. Mortality was perhaps the main outcome specified by the guideline panel, which was not included but is irrelevant to the intervention. Our experts believe that the Cochrane review should not be excluded on the basis that it did not include 'mortality' as a critical outcome, as this is not relevant to the condition or the interventions, and not measured in any of the trials.	Thank you for your comment. Larun 2017/2019 was not excluded solely because mortality was not an included outcome. With regards to 'Reason 2', this applies to the Price 2008 Cochrane review on CBT, not the Larun 2017/2019 review. Although the Larun review stated that studies with >90% CFS populations would be included, all participants in the included studies were diagnosed with ME/CFS and all were included in our review. Detailed exclusion reasons have been clarified below and in the report (Evidence review G excluded studies section, and Appendix J excluded study list in Evidence review H). Also note that all included studies within these Cochrane reviews were cross-checked for eligibility for inclusion in this review. Larun 2017/2019: This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows:

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				Reason 2. The review included study populations where not all the participants had CFS/ME. This is incorrect. The review includes trials with a few other participants who did not have a diagnosis of CFS/ME, but these trials had to include 90% or more of the participants with CFS were included in a subgroup analysis, so the panel would be able to examine these data. In addition, the review also carries out a subgroup analysis by diagnostic criteria. The panel should consider this. Given that the guideline panel describe the difficulty in diagnosing ME/CFS, then this review is highly relevant to this Guideline Panel's decision making. Again, the refusal of the panel to consider this review is spurious and may reflect its biases. The document states '***see the excluded studies list in the appendices'*** but these are not provided. Therefore, the reason for exclusion is not clear, and our experts note that we must assume is the explanation given above.	The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity levels, return to school/work, exercise performance measures, and mortality. However, all studies included in this Cochrane review were included in our review. Also note that Cochrane has acknowledged issues with this review in terms of the methods used and the population definition and they plan to conduct a full update of this Cochrane review. Price 2008: This Cochrane review looked at CBT versus usual care or other interventions in adults with 'CFS'. The main reasons for exclusion are as follows: Studies with mixed populations where at least 90% of participants had a primary diagnosis of CFS were included. The committee agreed it was important that all participants in included reviews were diagnosed with ME/CFS. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, pain, sleep quality, activity levels, exercise performance, and mortality. It is also worth noting that Cochrane has stated that this review is no longer current and should not be used for clinical decision making.
Royal College of Physicians (RCP)	Evidence review G	066	Table 5	Grade here is incorrect. Downgraded by 2 for indirectness based on a) Oxford criteria used, and PEM not a 'compulsory feature' is incorrect. It appears in several of the GRADE tables.	Thank you for your comment. The PICO characteristics set out the population to be included in the review. As you recognised, we did not specify that study participants must have PEM in order to be included in the review, therefore trials were included

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				The inclusion criteria of the review are '*adults, children and young people diagnosed as having ME/CFS'*, not "*adults, children and young people diagnosed as having ME/CFS by the presence of post exertional malaise*". Indirectness refers to how well the population in the studies align with those defined in the PICO. So, the PICO defined in this chapter and the PICO of the patients in the studies is aligned and should not be downgraded on indirectness. **General issue on downgrading on indirectness related to diagnostic criteria** If the panel decide that there is a difference in response between people defined clinical with ME/CFS and people defined clinically with ME/CFS explicitly on the presence of PEM, then our experts believe it is not appropriate to downgrade on indirectness, but to carry out sensitivity analysis for ALL studies To begin with, it is very unusual to have a condition where, within a diagnostic frame, some patients benefit, and some patients get worse. It appears that the panel has raised the question of whether there is a subgroup of patients in the GET trials who are made worse by the intervention, and yet the rest of the patients benefit, so this latter subgroup overwhelms the former. Our experts question whether the panel imagine all these other patients did NOT have ME/CFS. Our experts do not agree with throwing out a treatment based on a more recent addition to the diagnostic criteria. Our experts suggest that the review panel do some sensitivity analysis. If there is new data from	if they met the inclusion criteria regardless of whether or not participants had PEM or whether or not this was reported. The committee consider PEM to be an essential feature for a diagnosis of ME/CFS. The committee considered that previous criteria, such as the Oxford Criteria and 1994 CDC criteria identify a heterogeneous population, which may or may not include people with ME/CFS (See Evidence review D – diagnosis). This causes difficulty in interpreting the evidence from trials that do not use a criteria that has PEM as an essential feature (and therefore a 100% ME/CFS population) or where the percentage of people with PEM are not reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported, and numbers of people with PEM are rarely reported. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendix G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.

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				those trials on prevalence of PEM then a stratified analysis could be done on the main outcome by prevalence in the sample of PEM, which would include a subgroup which did not record this. This analysis would then look to see whether high/low prevalence of PEM in the primary studies influenced the effect estimate. One would expect that if a trial had a high prevalence of PEM ANDshowed benefit then in fact the argument about indirectness should be rejected. If any individual trials had conducted subgroup analysis by PEM presence that would also be helpful. The panel should also have extracted PEM (presence or improvement/worsening as an outcome of all interventions. In interventions where the panel propose that the intervention makes ME/CFS worse, reporting of this as an outcome is vital. Our experts believe that the panel should have drawn on methodological advice in appropriate analyses to examine the evidence for downgrading in this instance. Our experts note that this is a major flaw in the methods and that diagnostic criteria should not be retrospectively applied in this way without appropriate analysis.	
Royal College of Physicians (RCP)	Evidence review G Guidance	335 28	3-5 1-9	**The committee noted that no harms [of GET] were identified in the clinical evidence but also noted these were rarely included as an outcome and reported.** **1.11.16 Do not offer people with ME/CFS: [programmes based on GET]**	Thank you for your comment. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and

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				Our experts found it difficult to reconcile these two statements – that there were no harms in the clinical evidence but GET should still be banned as a treatment. Perhaps it was because the committee believed that if harm was rarely included and/or reported, then there was insufficient evidence to be sure that GET was safe. Our experts have examined the evidence to see if there was insufficient evidence of safety.	harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee has noted there are difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials and that it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. Considering the worsening of symptoms reported in the qualitative evidence, as well as their experience of the effects of when people exceed their energy limits, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate. The wording of the recommendations has been changed to reflect this and previous wording about programs based on GET has been removed. The committee also acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been reflected in the recommendations made to ensure this type of support is available. The committee agree that the way interventions are delivered is crucial and have also included specific recommendations about the content of programmes involving physical activity or exercise as well as for whom such programs should be considered. In developing recommendations on physical activity and exercise, the content, approach and delivery of physical activity management, the committee considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their own experiences of these types of interventions

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Royal College of Physicians (RCP)	Evidence review G Guidance	335 28	3-5 1-9	The committee took the view that studies of harm 'were rarely included as an outcome', and that 'safety outcomes are insufficiently reported in them to allow definitive interpretations' although they did come to a definitive conclusion that bans 'any therapy based on physical activity or exercise as a treatment … for ME/CFS'	Thank you for your comment. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee has noted there are difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials and that it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. As with all NICE guidance the committee have been able to utilise their clinical experience along with all sources of information available, including evidence from qualitative studies and expert testimonies. For example, the committee has considering the worsening of symptoms reported in the qualitative evidence, as well as their experience of the effects of when people exceed their energy limits when making recommendations about exercise programs. In developing recommendations on physical activity and exercise, the content, approach and delivery of physical activity management, the committee considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their own experiences of these types of interventions.

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Royal College of Physicians (RCP)	Evidence review G Guidance	335 28	3-5 1-9	Our experts suggest that there are other indicators of possible harm than just adverse events, which the reviews could have considered. For example, numbers of participants withdrawing from treatment, or numbers of participants dropping out of trial follow up, compared to the control intervention participants, are both frequently used measures. Another outcome often used is clinical global impression (CGI) change scores of overall health, by which participants report whether they consider their health as 'much worse' or 'very much worse'. And looking the data synthesis provided to the Review by the evidence team, many of the trials provided just such data.	Thank you for your comment. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee has noted there are difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials and that it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. As with all NICE guidance the committee have been able to utilise their clinical experience along with all sources of information available, including evidence from qualitative studies and expert testimonies. For example, the committee has considering the worsening of symptoms reported in the qualitative evidence, as well as their experience of the effects of when people exceed their energy limits when making recommendations about exercise programs. In developing recommendations on physical activity and exercise, the content, approach and delivery of physical activity management, the committee considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their own experiences of these types of interventions.

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Royal College of Physicians (RCP)	Evidence review G Guidance	335 28	3-5 1-9	Our experts therefore undertook an analysis using the data from the 10 trials included in the review. All but one trial was therapist delivered GET, the other was guided self-help based on GET (Clark et al, 2017, reference above). This is a summary of the pooled data that our experts found. All but one result from one trial are available in the published papers. Clinical Global impression change scale scores of 6 or 7: GET: 19/307 (6%) Control: 17/301 (6%) OR (CI): 1.10 (0.56, 2.16) Withdrawals from treatment: GET: 38/435 (9%) Control: 37/435 (9%) OR (CI): 1.03 (0.64, 1.65) Drop-outs from trial follow up: GET: 87/679 (13%) Control: 47/600 (8%) OR (CI): 1.73 (1.19, 2.51) Tabulated data have been prepared and are submitted for publication. Unfortunately, we are informed that these cannot be submitted with our response either as an attachment as an appendix, but a simple table (one-side A4) has been prepared and is available from the RCP on request. We urge the evidence review panel to request this, as we believe it may help to provide an accurate picture and will save them some time.	Thank you for your comment. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee has noted there are difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials and that it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. As with all NICE guidance the committee have been able to utilise their clinical experience along with all sources of information available, including evidence from qualitative studies and expert testimonies. For example, the committee has considering the worsening of symptoms reported in the qualitative evidence, as well as their experience of the effects of when people exceed their energy limits when making recommendations about exercise programs. In developing recommendations on physical activity and exercise, the content, approach and delivery of physical activity management, the committee considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their own experiences of these types of interventions.

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Royal College of Physicians (RCP)	Evidence review G Guidance	335 028	3-5 1-9	If GET is delivered as it should be, and is indeed harmful, one would expect more people to report that their health has worsened, or that they had quit the programme during treatment. Our experts note that that was simply not the case in these trials. However, it was the case that 5% more GET participants dropped out of follow-up by the end of the trials. The reason for this is unclear. The highest number of such dropouts occurred in the two trials that used the highest intensity of exercise initially, and in the one trial of anaerobic rather than aerobic exercise. These issues could be studied in future trials, which our experts suggest should be considered as a research recommendation. These newly analysed data provide support for the safety of graded exercise programmes, when prescribed at appropriate levels of exercise intensity. When added to the other more detailed evidence of safety already published (see above), our experts suggest that this provides reassurance to patients and healthcare professionals as to the safety of this treatment. Any medical treatment can cause harm if delivered at either the wrong dose or frequency. Our experts note that a treatment would not be banned on that basis.	Thank you for your comment. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee has noted there are difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials and that it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. Considering the worsening of symptoms reported in the qualitative evidence, as well as their experience of the effects of when people exceed their energy limits, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been acknowledged in the recommendations made to ensure this type of support is available. The committee agree that the way interventions are delivered is crucial and have also included specific recommendations about the content of programmes involving physical activity or exercise as well as for whom such programs should be considered. In developing recommendations on physical activity and exercise, the content, approach and delivery of physical activity management, the committee considered the benefits and harms associated with graded exercise therapy that had been identified

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					in the qualitative evidence and their own experiences of these types of interventions.
Royal College of Physicians (RCP)	General	General	General	The RCP is grateful for the opportunity to respond to the above consultation. In doing so we have shared our response with the Association of British Neurologists (ABN) and the Royal College of Paediatrics and Child Health (RCPCH) and we have been sighted on their respective responses. We have also liaised with our Joint Committee for Rehabilitation Medicine and our Sports and Exercise Medicine Committee and would like to comment as follows.	Thank you for your comments.
Royal College of Physicians (RCP)	Guideline	General	General	There are many aspects of the guideline that are clearly reasonable and should be supported. For example, they emphasise: • Developing a working partnership with the patient and their family (maintained long term if necessary) • Open discussion of the risks and benefits of any course of any action (or inaction) • Tailoring recommendations to the specific needs and abilities of the individual patient. • Involving a multidisciplinary team that is familiar with the condition • Recognising the role for a range of physical, cognitive and psychological treatments / management strategies depending on the patient's individual goals and preferences for treatment • Educating the patient, their family and clinical teams about the condition • Considering plausible alternative or additional diagnoses	Thank you for your comment. In addition the committee have edited the management plan to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.). This further supports the guideline's emphasis upon being centred on the patient's needs and wishes and adopting a holistic approach. The personalised care and support plan supports the person's aims and the management of their health and well-being within the context of their whole life and family situation. The committee composition was agreed during the scoping phase as appropriate for the expertise for the guideline scope. Great care was taken to ensure the committees was formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline.. The committee membership reflects the multidisciplinary approach to treating ME/CFS and includes medically qualified clinicians and allied health professionals who lead and work in specialist ME/CFS services.

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				These are the characteristics of any specialist rehabilitation programme and it would be appropriate for people with moderate - severe chronic fatigue syndrome to be seen within such a rehabilitation service - indeed many are. In addition to providing restorative rehabilitation, specialist rehabilitation services also provide life-long support for patients with severe complex disabilities. Our experts note that the committee does not appear to be aware of such services – possibly because there is no representative from the specialty of Rehabilitation Medicine (RM) on the committee. Consultants in RM specialise in the management and support of patients with complex disabling conditions, of which ME/CFS is a prime example. We recommend that in future NICE guidelines that address such areas should always have representation from the field of RM. (It is otherwise tantamount to writing guidance for a cardiac condition without representation from a cardiologist, or a neurological condition without a neurologist).	
Royal College of Physicians (RCP)	Guideline	General	General	Integrated rehabilitation takes a holistic, individually planned approach with the patient and the rehabilitation team working through collaborative partnership as outlined above. For ME/CFS, such programmes combine a range of physical, cognitive and psychological treatment approaches depending on the priorities and treatment preferences of the individual. Rehabilitation prescriptions are one way to help ensure that patients can access the services they need. • These are person centred, patient-held records of their individual needs for rehabilitation and support and the plans to provide for them. • They are supported by centralised data collection to track how well those needs are met over time.	Thank you for your comment. *Rehabilitation prescription* A rehabilitation prescription has been used to capture met and unmet needs for rehabilitation following, for example, major trauma or severe illness requiring intensive care. It may be used to document the needs of patients with severe illness/ injury and identify how they will be addressed (British Society of Rehabilitation Medicine 2014. Rehabilitation for patients in the acute care pathway following severe disabling illness or injury: BSRM core standards for specialist rehabilitation. https://www.bsrm.org.uk/downloads/specialist-rehabilitation-prescription-for-acute-care-28-11- 2014-ja--(ap1-redrawn).pdf). The management plan (now renamed the 'personalised care and

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				They are not just about restorative rehabilitation aimed at improving function – they can equally be used to monitor ongoing needs for care and support in patients with long term disabilities, including those with severe ME/CFS. Proof of principle already exists within the major trauma pathways https://www.kcl.ac.uk/cicelysaunders/about/rehabilitation/nhs-audit-report-v9-rgb.pdf and is now being extended into other areas, including long-term care https://www.bsrm.org.uk/downloads/covid-19bsrmissue2-11-5-2020-forweb11-5-20.pdf. Our experts strongly recommend that use of a personalised rehabilitation should be recommended in the context of ME/CFS	support plan'*) is similarly based on the person's needs and includes the areas listed. The plan is developed in collaboration with the person with ME/CFS. The personalised care and support plan supports the person's aims and the management of their health and well-being within the context of their whole life and family situation. Like the RP we would hope that the care and support plan would be available to the health and social care professionals involved in the person's care. *To note management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Royal College of Physicians (RCP)	Guideline	General	General	A significant problem with these guidelines as written is that the recommendations conflict with NICE guidelines in areas that have some overlap with ME/CFS. For example: • The recommendations are in marked conflict with the draft chronic pain guideline – this is problematic as there is a very considerable overlap in clinical presentations – indeed ME/CFS and fibromyalgia (widespread chronic pain) are overlapping syndromes, confirmed by over 20 papers ex Rusu C, Gee ME, Lagacé C, Parlor M. Chronic fatigue syndrome and fibromyalgia in Canada: prevalence and associations with six health status indicators. Health Promot. 2015;35(1):3–11 with PEM been very prevalent in both conditions. There are also dozens of combined ME/CFS/fibromyalgia support groups	Thank you for your comment, *Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. As such the difference between the guidelines is not a problem. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that any when managing any co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account.

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

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				across the UK. The pain guidelines recommend offering both exercise and CBT. • The recommendations are also in marked conflict with the draft guidelines for Post-COVID-19 Syndrome ('Long COVID'), of which the RCP had sight last week. As noted in point 16, many of patients with Long COVID would meet the criteria for suspecting / diagnosing ME/CFS, as set out in sections 1.2 and 1.4. However, the Long COVID guidelines correctly recommend early referral for rehabilitation and take a more positive outlook forwards improvement with the correct approaches to treatment and intervention.	*COVID- 19* At this time the ME/CFS guideline and the COVID-19 rapid guideline: managing the long-term effects of COVID-19 address different populations. The key difference being the presence of post exertional malaise in people with ME/CFS. The COVID-19 rapid guideline: managing the long-term effects of COVID-19 includes a broader set of common symptoms and does not include post exertional malaise as a key symptom for diagnosis. While there is debate about the overlap between ME/CFS and the long-term effects of COVID-19 the development of this guideline started before the COVID-19 pandemic and the committee have only reviewed the evidence relevant to the scope. RE rehabilitation
Royal College of Physicians (RCP)	Guideline	General	General	Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a very important condition that is often misunderstood by clinicians. We welcome the fact that NICE has produced guidance in this area. We welcome the fact that it includes specific guidance for children and young people. We also welcome separate guidance for the more mildly affected patients from those with severe/very severe ME/CFS. The latter is a small, but very important, group and we do not know whether they are a continuum with the milder cases.	Thank you for your comment.
Royal College of Physicians (RCP)	Guideline	General	General	We acknowledge that patients with ME/CFS have often felt disbelieved by health and social care professions and that this has led to a feeling of mistrust, which is appropriately highlighted in the guidelines.	Thank you for your comment.

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				It is clearly vital that patients with ME/CFS are managed with sensitivity and that their symptoms are believed, so that a healthy working partnership can be built between them and their treating teams.	
Royal College of Physicians (RCP)	Guideline	General	General	We fully support the emphasis on a personalised approach to treatment and management in accordance with the patient's individual needs, priorities and preferences.	Thank you for your comment.
Royal College of Physicians (RCP)	Guideline	General	General	However, while some of the recommendations are very helpful, we find the guidance as a whole to be unbalanced. It reinforces that this is an illness that they cannot recover from, which is incorrect – especially given the new duration criterion of just 3 months to diagnosis. Many people do recover from CFS after this time. This is particularly important in the current climate as many people with 'Long COVID' would have symptoms that fit the diagnostic criteria – as would others, eg with post-ICU syndrome or other post viral fatigue. Many patients experiencing symptoms of Long COVID would be extremely frightened to read the guidance as currently written.	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.) In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS.

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					After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted. The committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. *Reduction in timeline* After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. People with ME/CFS do experience delays in diagnosis and the committee recognised that referral to a specialist team for confirmation of diagnosis can take months, taking this into account it is important that this process is started at 3 months and people are given appropriate advice until they are seen by a ME/CFS specialist team
Royal College of Physicians (RCP)	Guideline	General	General	We fully support the principle of early access to appropriate holistic assessment and rehabilitation from an early stage. However, guidelines take an overly fatalistic approach, emphasising the sick role and need for patients to adapt their life to living with ME/CFS. They mention the requirement for specialist care and support, but at no point do they mention the	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have

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				need for holistic specialist multidisciplinary rehabilitation (see also points 9 and 10 below). We consider this to be a serious omission – especially with this shortened timescale for diagnosis. In view of this, we believe that applying the label of ME/CFS (even if only 'suspected') at just a few weeks after onset could be highly damaging and we do not support this.	as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.) In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. In addition the committee have edited the management plan to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.). This further supports the guideline's emphasis upon being centred on the patient's needs and wishes and adopting a holistic approach. The personalised care and support plan supports the person's aims and the management of their health and well-being within the context of their whole life and family situation. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has

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					addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted. The committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. *Reduction in timeline* After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. People with ME/CFS do experience delays in diagnosis and the committee recognised that referral to a specialist team for confirmation of diagnosis can take months, taking this into account it is important that this process is started at 3 months and people are given appropriate advice until they are seen by a ME/CFS specialist team
Royal College of Physicians (RCP)	Guideline	General	General	We acknowledge that exercise (in the form of graded exercise programmes), has become highly contentious in ME/CFS circles. This may be partly because patients have often been offered inappropriate forms of exercise or other interventions that are not tailored to their individual needs. We agree that unsupervised, unstructured exercise and programmes based on fixed incremental increases are not appropriate. But it is essential not to reject exercise completely.	Thank you from your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This

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				Once again, the guideline is unbalanced in that it repeatedly emphasises the harms of activity and exercise, without addressing its benefits, nor the very significant harms of inactivity. This was an important opportunity to clarify the types of approach to physical psychological and cognitive rehabilitation that are helpful in this context, as well as those that are not. Unfortunately, it has been missed.	when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people

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					with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed it was important that people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Royal College of Physicians (RCP)	Guideline	011 - 013	Section 1.5	**Section 1.5 Assessment and care planning…Recommendations1.5.1-1.5.5** Our experts note that this whole section reinforces the sick role and reinforces that this is an illness that they cannot recover from, which is incorrect. Some people do recover from ME/CFS	Thank you for the comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.) In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden

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					within the guideline nor mistaken to reflect the experience of all people with ME/CFS.
Royal College of Physicians (RCP)	Guideline	010 - 011 51	 5-9	**Section 1.3 Advice for people with suspected ME/CFS** The guidelines advise to not use more energy than they perceive that they have and stay within their energy envelope and not push through activity. They should also rest as they need to. Our experts believe the guidelines mention rest a disproportionate number of times with bias towards positive reporting of the benefits of rest with insufficient evidence. In comparison, the references towards activity and exercise are reported with a negative emphasis despite good evidence to the contrary (see later section). The rationale for this advice states that, **the qualitative evidence and the committee's experience suggested that managing symptoms early may prevent them getting worse and the person's health deteriorating. To reflect this, the committee made a recommendation to give people advice on symptom management drawn from their own knowledge and experience.** Our experts believe that because the committee is overly dominated with people who have long term ME/CFS, there is an assumption behind this advice that patients will indeed prove to have long term debilitating ME-CFS. Our experts believe that to simply advise patients to stay within their 'energy envelope' means therapeutic nihilism, since there is no evidence for its efficacy The guidelines fail to recognise that very many people will still feel fatigued in the first few weeks after a severe illness or a	Thank you for your comments. The beginning of the discussion section in Evidence review E states ,'the committee discussed this evidence with the findings from the reviews on Information for people with ME/CFS and their families and carers (report A), Information and Support for health and social care professionals (report B), access to care (report C), Diagnosis (D) non pharmacological management (report G) and the report on Children and Young people (Appendix 1). The committee took this evidence into account as well as their own experience and expertise. This has been clarified in the discussion section. The committee composition was agreed during the scoping phase as appropriate for the expertise for the guideline scope. Great care was taken to ensure the committees was formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This included members with different experiences of ME/CFS. *Energy envelope* After considering the stakeholder comments the committee agreed that this concept might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms.

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				viral infection, but the large majority of those will improve and many will recover completely. Our experts agree with the principle of providing early appropriate advice, but do not agree with the content of this advice as written. It is essentially telling people just to rest and not do too much, but nothing else until 3 months when their diagnosis can be confirmed. This is not appropriate at just 6 weeks. At this stage, as well as appropriate advice on pacing and rest periods, people should be given more positive advice on sensible, appropriately paced rehabilitation and on how to access suitable sources of support.	*Advice to rest* The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and this would not cause harm to anyone. The committee agreed that people should be given personalised advice about managing their symptoms and recommend this in the advice for people with suspected ME/CFS section of the guideline. * To note that after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit Energy envelope to use energy limits.
Royal College of Physicians (RCP)	Guideline	022 - 023	P22 line13to p23 line4	**Recommendations 1.10 on Multidisciplinary care "Provide care for people with ME/CFS using a coordinated multidisciplinary approach..."** Our experts support the multi-disciplinary approach but consider that this should have input from a consultant in rehabilitation medicine (RM). As noted above, RM consultants are experts not only in restorative rehabilitation but also in complex disability management – providing life-long care and support when required. This is a key area where the speciality can help – both in managing problems and prevention of deterioration	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS and this includes access to rehabilitation services (Evidence review I _Multidisciplinary care).

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				There are specialist rehabilitation services all around the country many of which do provide rehabilitation and long-term support for patients with ME/CFS. We suspect that the reason this has not figured in the guideline is because of NICE's general lack of awareness of the role of specialist rehabilitation and the fact that these services exist.	
Royal College of Physicians (RCP)	Guideline	039 - 040	1-25	**Recommendations 1.14.1-5 Offer adults with ME/CFS a review of their care and management plan in primary care at least once a year (see recommendation 1.14.3 for what to review)** Our experts agree with the need for regular review. However, this should include a review of the rehabilitation needs recorded through a rehabilitation prescription (RP), how well these have been met at the time of review, and the ongoing plans for providing for them. In common with any long-term condition, Patients with ME/CFS will have both short term and longer-term requirements. The RP is not just about sort term time-limited rehabilitation interventions but about longer-term management strategies. A second important feature of the RP is that the key elements should be recorded in a centralised database which can help to monitor that patients get their annual review, and whether there were needs arising from these that require action. As yet there is nothing in these guidelines that suggests keeping a systematic registry of patients to ensure that their ongoing needs are met.	Thank you for your comment. *Rehabilitation prescription* A rehabilitation prescription has been used to capture met and unmet needs for rehabilitation following, for example, major trauma or severe illness requiring intensive care. It may be used to document the needs of patients with severe illness/ injury and identify how they will be addressed (British Society of Rehabilitation Medicine 2014. Rehabilitation for patients in the acute care pathway following severe disabling illness or injury: BSRM core standards for specialist rehabilitation. https://www.bsrm.org.uk/downloads/specialist-rehabilitation-prescription-for-acute-care-28-11- 2014-ja--(ap1-redrawn).pdf). The management plan (now renamed the 'personalised care and support plan'*) is similarly based on the person's needs and includes the areas listed. The plan is developed in collaboration with the person with ME/CFS. The personalised care and support plan supports the person's aims and the management of their health and well-being within the context of their whole life and family situation. Like the RP we would hope that the care and support plan would be available to the health and social care professionals involved in the person's care.

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					*To note management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Royal College of Physicians (RCP)	Guideline	011 - 012	p11, line 15 to p12, line 9	**Recommendation 1.5.1: After confirming a diagnosis of ME/CFS, carry out and record a holistic assessment** Our experts agree with the need for holistic assessment, but what is described here does not meet that description. Our experts believe that this should include evaluation of the individual's personal goals for treatment, their understanding of their condition and their attitudes / personal preferences to different types of intervention (eg physical, psychological etc) ie what do they think would help most and what are their priorities for treatment. Our experts question why this should wait for 3 months or until ME/CFS is confirmed and note that this sort of assessment should be happening much earlier.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) This approach supports personalised care and support planning where a plan is developed after an initial holistic assessment. This assessment takes place after referral to a ME/CFS specialist team. In the committee discussion in Evidence review I-multidisciplinary care set out the importance of this detailed and complex assessment in confirming the diagnosis and in developing the personalised care and support plan. Feedback from stakeholders and experience from the committee indicates that GPs do not have enough time to carry out the assessments needed to confirm a diagnosis of ME/CFS or to develop a care and support plan in a single standard appointment.
Royal College of Physicians (RCP)	Guideline	026 - 027	p26 line 17 to line 2 p27	**Recommendation 1.11.11 recommends that physical maintenance should be included in the management plan including thinking about joint mobility, muscle flexibility, muscle strength and endurance, bone health and cardiovascular health** Our experts recommend doing more than just 'thinking about' this and note the importance of action. Our experts question how this will be achieved without some sort of physical activity. Physical maintenance refers to joint flexibility, muscle	Thank you for your comment. This recommendation has been edited to be more directive as is now,' include strategies to maintain and prevent the deterioration of physical functioning and mobility in the care and support plans'. 'Think' refers to what should be included in the plan and will be individual to the person. This is considered as part of the energy management plan and the implementation and impact of these strategies within that.

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				flexibility, postural and positional support, muscle strength and endurance, bone health and cardiovascular health. There is overwhelming evidence that all of these attributes are gained through activity and exercise and that rest and inactivity significantly increase the likelihood of poor outcomes in the listed attributes.	To note after considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.
Royal College of Physicians (RCP)	Guideline	045 - 046	P45 line 21 To P47 line 6	**Recommendations for research mention:** **Diagnostic tests, a core outcome set for trials of treatment and managing symptoms of ME/CFS** **Also self-monitoring strategies to guide energy management, sleep management and dietary strategies** Firstly, one might reasonably question the need for an outcome set for trials of treatment since, on the basis of performance to date, the committee is still likely to dismiss any trials on the basis of risk of bias, inconsistency, indirectness and etc Secondly, the recommendations for research fall short of addressing the key things that we really need to know which are: • Which patients benefit most from which types of treatment intervention not just in terms of recovery but also in terms of ongoing symptom and life experience? • What are the outcomes that matter most to patients and how well are these achieved? • What is the current level of provision of specialist service for patients with MS/CFS in relation to need, and how do we make sure that they get the treatments and support that they require?	Thank you for your comment. *Research recommendations* The committee have made recommendations to address the difficulties and limitations in diagnosing ME/CFS (see Evidence review D for the committee discussion on this). The committee identified the validation of the consensus criteria recommended in the guideline as high priority for research. This committee hope this will enable future research to accurately identify people with ME/CFS and determine the impact of interventions on them. They thought this was particularly important before recommending any research trials on physical activity or exercise interventions. As noted in the rationale for core outcomes set,' There is considerable controversy over the outcome measures used in trials of treatments for ME/CFS and symptom management of ME/CFS. Inconsistency in outcomes used and concerns over the validity of some outcome measures in an ME/CFS population makes it difficult to combine and compare results from different trials, limiting the ability to draw conclusions on the clinical and cost effectiveness of

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				- What are the long-term outcomes for patients who meet the criteria for possible diagnosis at 6 weeks, 3 months, 6 months and 1 year? - What are the requirements for rehabilitation and support at each of these time points? How do they change over time? Our experts believe that these are the key questions. They cannot be answered by RCTs, They require systematically collated longitudinal data collected in the course of real life clinical practice and collated in a central dataset alongside the NHS number so that patients can be tracked from start-to-end down the rehabilitation care pathway.	interventions. The development of a core outcome set will allow the direct comparison of treatments for ME/CFS and symptom management and shape and optimise ME/CFS trial design.' The committee agree that the long term follow up of trials is important and this has been included in the design of the research recommendations included in the guideline. All NICE research recommendations are reviewed by the NIHR to consider for their funding streams. Other research funders also consider NICE research recommendations. It is beyond the remit of the guideline to provide more detailed information on how research in these areas should be conducted. Research recommendations can only be made where the evidence has been searched for within the guideline. Service design was not included in the scope of this guideline as a topic to consider, and therefore the committee were unable to make research recommendations on this topic.
Royal College of Physicians (RCP)	Guideline	028 - 029	P 27 line 20 to p 29, line 16	**Recommendation 1.11.20 If a physical activity programme is agreed with the person with ME/CFS, it should be personalised and should:** Our experts are fully supportive of this recommendation and note that this is a sensible and positive description of what a good physical activity programme should_look like.	Thank you for your comment. Recommendations 1.11.16 to 1.11.19 are important part of the management of physical activity and exercise in people with ME/CFS and have not been removed. See evidence review G-non-pharmacological management for the committee discussion on physical activity and exercise.

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				Our experts strongly advise keeping recommendations 1.11.15 and 1.11.20 but to remove recommendations 1.11.16-1.11.19	
Royal College of Physicians (RCP)	Guideline	001	Title	The 2007 NICE guidelines were entitled CFS/ME. The latest draft reverses the title to ME/CFS, suggesting that this is a definite disease affecting the brain and spinal-cord, while chronic fatigue syndrome is free of assumptions about the cause and nature of this condition. • The NHS UK website for CFS/ME states that most people with CFS get better over time, while the CDC emphasises that there is no cure for ME/CFS although some symptoms can be treated or managed. • No justification is given for the change in title, but it may perhaps account for some of the shift in paradigm between the two sets of guidance. Our experts believe it would be helpful if the rationale for changing the title were to be openly addressed and discussed.	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'*
Royal College of Physicians (RCP)	Guideline	005	15-18	**Recommendation 1.1.5 Explain to people with ME/CFS and their family or carers that they have the right to decline or withdraw from any part of their management plan and it will not affect other aspects of their care. They can begin or return to an intervention if they feel able to resume.** Our experts acknowledge the sentiment behind this but believe it is unrealistic to state that withdrawing from one part of the programme 'will not affect other aspects of their care'. This fosters a piecemeal approach and undermines the requirement for ongoing dialogue and collaboration between the patient and their treating team to discuss and negotiate an agreed	Thank you for your comment. The committee agree that a collaborative relationship between people with ME/CFS and health and social care professionals is critical to good care and this is raised in recommendation 1.1.3. Recommendation 1.1.5 is supported by Evidence review A and Appendices 1 and 2 and the committee's experience. Some people with ME/CFS reported negative reactions from health and social care professionals when they did not want to follow the advice given (see Evidence review A, Appendices 1 and 2). The committee agreed it was important to make a recommendation supporting people's choices and involvement in their care.

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				overall plan based on the individual's needs and priorities. If this is done properly there would be no need to 'withdraw' from individual parts of the programme. But since all aspects of care are inter-connected it is reasonable to expect than not providing one aspect of care will not have knock-on effects on other aspects.	
Royal College of Physicians (RCP)	Guideline	007	22-26	**Recommendation 1.1.11 Risk assess each interaction with a person with severe or very severe ME/CFS in advance to ensure its benefits will outweigh the risks to the person (for example, worsening their symptoms). For people with very severe ME/CFS, think about discussing this with the person's family carer on their behalf.** This is unclear. As written, this implies that family members may be able to make decisions on behalf of the patient. If it is thought that the patient might not have the mental capacity to make decisions for themselves and those decisions need to be made for them on the basis of their best interests, there is a statutory requirement under the Mental Capacity Act 2005 to undertake a capacity assessment as the legal basis for others to make decisions on their behalf. Best interests decision-making should include discussion with family members to gain information the patient's likely wishes, but (unless they have been appointed to do so under the provisions of the MCA 2005 eg through a Lasting Power of Attorney for Health and Welfare or an Advance Decision to Refuse Treatment) they cannot make decisions on the patient's behalf. Our experts believe that this recommendation should be re-written to ensure it is legally accurate.	Thank you for your comment. 'if appropriate' has been added to the recommendation. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

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Royal College of Physicians (RCP)	Guideline	008	10-16	**Recommendation 1.2.3 Suspect ME/CFS if:** **• the person has had all of the persistent symptoms (see box 1) for a minimum of 6 weeks in adults and 4 weeks in children and young people** **• the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels** **• symptoms are new and had a specific onset.** The Guidelines accept that there is currently no diagnostic test for ME/CFS (1.2.1) and outline 4 symptoms that the patient must have had for 6 weeks to suspect the diagnosis. In Evidence Review D, 9 criteria are analysed and the committee concluded that all 9 have serious limitations or very serious limitations. All were published in peer reviewed journals and many had multiple collaborators involved in daily care of CFS/ME patients or those with research experience in the condition. Despite this, the committee decided to a) Agree that the criteria for suspecting ME/CFS should be based on personal experience and dismiss the 9 criteria as at the least having serious limitations b) Agree, despite lack of evidence and again based on personal experience, that criteria for suspecting the diagnosis should also be the diagnostic criteria (Section 1.41) Our experts believe this to be a potentially dangerous recommendation which must be changed. These symptoms are common across very many conditions, including COVID-19. At this early stage many people will recover and will not go on to develop CFS. Given the outlook for ME/CFS as described in the guideline and the negative attitude towards rehabilitation interventions in the guideline as written, our experts believe this would make a	Thank you for your comment. *Decision making in NICE guidelines* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee included members with clinical and personal experience of children and young people with ME/CFS and with different experiences of severity. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature (as mentioned in your comment). As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). *Suspecting and diagnosing ME/CFS* See Evidence review D-diagnosis for the evidence. The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters.

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				very large number or people extremely (and quite unnecessarily) fearful of their future, increasing the likelihood that they will indeed decline through expectation.	See evidence review D. Appendices D and E for how quality was assessed and an explanation of the method used. In summary the AGREE II tool was used and we acknowledge that although this review does not include guidelines the principles of the decision making are similar in developing consensus based diagnostic criteria and it has been used the evaluation of consensus statements. While applying the AGREE II tool and assigning a score is less useful in this context the relevant items in the domains provide a robust set of principles to measure in consensus criteria development. Table 11 in appendix D sets out the AGREE II domains and the relevant items evaluated in this review. *Suspecting ME/CFS* The committee agree these symptoms are seen in other conditions particularly fatigue, but note it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS. The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. They noted that the advice recommended at this stage would not be detrimental to people who are then not diagnosed with ME/CFS. *Misdiagnosis_ ME/CFS* The committee discussed the potential harm of applying the recommendations in this guideline to people that are misdiagnosed with ME/CFS. For example, and as noted in many stakeholder comments, for other conditions physical activity and exercise is recommended as a part of the management of

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					symptoms such as pain. In this guideline it is clear that if people with ME/CFS have these symptoms this management approach is not appropriate. For this reason the committee agreed it was very important to ensure that only people that meet the diagnostic criteria use these guidelines. In addition misdiagnosis may result in people not receiving appropriate treatments. *Clarifications* After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted for the following reasons: ○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis.
Royal College of Physicians (RCP)	Guideline	008	Box 1	Post exertional symptom exacerbation (PESE) or Post exertional malaise (PEM) is a complaint that is difficult to show objectively (Bazelmans et al J Psychosom Med 2005;59:201)	Thank you for your comment and information.

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				It is a complex and variable phenomenon, cannot be captured by a single definition Stussman et al 2020: Frontiers in Neurology 2020; https://doi.org/10.3389/fneur.2020.01025 Assessing PESE is also unreliable – interviews and questionnaires do not give the same results (Jason et al J Prev Interv Community.2015 43(1): The evidence cited in the Diagnostic Review prepared for the Committee suggests it has only modest sensitivity and specificity for the diagnosis of ME/CFS, and is found in many other conditions, and even in some normal subjects. The importance of orthostatic intolerance (OI) is overrated`; The largest study of this association found no more OI in CFS cases than in other cases with fatigue, in (Roerink et al J Int Med 2017;281:179)	
Royal College of Physicians (RCP)	Guideline	009	17-20	**Recommendation 1.2.5 Do not delay making a provisional diagnosis of ME/CFS. As soon as ME/CFS is suspected, based on the criteria in recommendation 1.2.3, give the person advice about symptom management (see the section on managing ME/CFS).** For the same reason as given in our response to recommendation 1.2.3, our experts consider this to be a dangerous recommendation. As noted above there is no valid rationale for bringing the diagnosis forward to 3 months especially if they are then to be given the advice as currently written on managing ME/CFS (see further comments below)	Thank you for your comment. After considering the stakeholder comments on early diagnostic labels the committee have amended the wording to remove the recommendation on making a provisional diagnosis of ME/CFS. Diagnosis is now introduced at 3 months.
Royal College of Physicians (RCP)	Guideline	010		**Recommendation 1.3.2. Explain to people with suspected ME/CFS that their diagnosis can only be confirmed after 3 months of persistent symptoms. Reassure them that they can return for a review if they develop new or worsened**	Thank you for your comment *Reduction in timeline* After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to

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				symptoms, and ensure they know who to contact for advice. Our experts do not agree that it is appropriate to confirm a diagnosis of ME/CFS after just 3 months of symptoms. As noted above, most diagnostic criteria (including the IoM 2015 criteria that this guideline relies upon to discount much of the research evidence as indirect) specify a minimum of 6 months duration of symptoms. In addition, our experts do not agree with the approach that ME/CFS will prove to be their diagnosis or with telling them simply to return if they get worse. Our experts suggest considering a differential diagnosis. This is the time for early proactive management in the form of appropriately monitored rehabilitation and positive support, including the advice (as per the NHS website) that most people's symptoms improve over time.	diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. Based on the evidence and their clinical experience the committee found no reason why the time to diagnosis should be different in adults compared to children and young people noting that 5 of the 7 diagnostic criteria reviewed in Evidence review D do not have separate time referrals. The committee acknowledge that this is further reduced from the 6 months in the IOM criteria The committee agreed that although a 6-month delay to diagnosis is built into the IOM criteria, the criteria could be safely amended by the reduction of this delay period to 3 months. It was agreed that the function of a delay is partly to reduce the number of misdiagnoses through allowing short-lived fatigue to be excluded. In addition to not being disadvantageous, removal of the delay was seen as beneficial, as this might facilitate earlier management and potentially allow improvement in longer term outcomes. As you note people with ME/CFS do experience delays in diagnosis and the committee recognised that referral to a specialist team for confirmation of diagnosis can take months, taking this into account it is important that this process is started at 3 months and people are given appropriate advice until they are seen by a ME/CFS specialist team. (see evidence review -D for the committee discussion).
Royal College of Physicians (RCP)	Guideline	010	15-21	**Recommendation 1.3.1 When ME/CFS is suspected, give people personalised advice about managing their symptoms. Also advise them:** • **not to use more energy than they perceive they have − they should plan their daily activity to stay**	Thank you for your comment. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that

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				within their energy envelope and not push through activity - **to rest as they need to** - **to maintain a healthy balanced diet, with adequate fluid intake.** We agree with giving appropriate advice on pacing etc to prevent 'boom and bust', but at the same time, people should be offered much more positive advice on strategies to aid their recovery including sensible rehabilitation and support.	advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term. The committee agreed it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and this advice would not result in harm to anyone. Taking this into account the committee agreed it is too soon to suggest other management strategies that could be potentially harmful depending on the final diagnosis(es). The committee agreed that people should be given personalised advice about managing their symptoms and recommend this in the advice for people with suspected ME/CFS section of the guideline.
Royal College of Physicians (RCP)	Guideline	011		**Recommendation 1.4.1 Diagnose ME/CFS in a child, young person or adult who has the symptoms in recommendation 1.2.3 that have persisted for 3 months.** Most diagnostic criteria specify a minimum of 6 months duration of symptoms. All were published in peer reviewed journals and many had multiple collaborators involved in daily care of CFS/ME patients or those with research experience in the condition. The rationale for reducing this timescale is given as follows: **The committee agreed that although a 6-month delay before diagnosis is built into the Institute of Medicine criteria, the criteria could be safely amended by reducing this period to 3 months.** - **The committee saw removing this delay as useful because it might enable earlier management and could potentially improve longer-term outcomes.**	Thank you for your comment. *Reduction in timeline* After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. Based on the evidence and their clinical experience the committee found no reason why the time to diagnosis should be different in adults compared to children and young people noting that 5 of the 7 diagnostic criteria reviewed in Evidence review D do not have separate time referrals. People with ME/CFS do experience delays in diagnosis and the committee recognised that referral to a specialist team for confirmation of diagnosis can take months, taking this into account it is important that this process is started at 3 months and people are given appropriate advice until they are seen by a ME/CFS specialist team.

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				• **Reflecting the evidence that non-specialists in ME/CFS are not confident about diagnosing and managing ME/CFS, the committee recommended referring people with ME/CFS to a ME/CFS specialist team at 3 months to confirm their diagnosis develop a management plan.** While our experts agree entirely with the principle of ensuring that patients with the symptoms set out in Box 1 should have early proactive assessment and management from a specialist team, they do not agree with giving them a label that, according to the guidelines, has such a poor chance of improvement or recovery. Moreover, if all the specialist team is going to do is to provide a management plan as set out in recommendation 1.5.2 with no proactive rehabilitation component, it is unlikely to improve their longer-term outcomes. Our experts would strongly recommend retaining the internationally accepted 6-month criterion for diagnosis but using a different term to describe people with these symptoms to ensure that they get timely access to the appropriate management and rehabilitation, but without the label.	*Further investigation/differential diagnoses.* The committee have similar experience of people being referred and having another diagnosis and throughout the section on suspecting ME/CFS the committee have recommended that investigations should be done to exclude other diagnoses and this should continue where ME/CFS is suspected. If in any doubt specialist advice should be sought. The committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'.
Royal College of Physicians (RCP)	Guideline	012	10-30	**Recommendation 1.5.2: Develop a personalised management plan with the person with ME/CFS (and their family members or carers, as appropriate) informed by the holistic assessment.** Our experts agree with the need for a personalised management plan, but note that this is incomplete, and talks only of maintenance. There is no mention of rehabilitation needs or how these will be met. The plan should include their goals for rehabilitation and how these will be met. Our experts strongly recommend the use of a Rehabilitation Prescription as a means to record their needs for rehabilitation,	Thank you for your comment and information. Thank you for your comment. A rehabilitation prescription has been used to capture met and unmet needs for rehabilitation following, for example, major trauma or severe illness requiring intensive care. It may be used to document the needs of patients with severe illness/ injury and identify how they will be addressed (British Society of Rehabilitation Medicine 2014. Rehabilitation for patients in the acute care pathway following severe disabling illness or injury: BSRM core standards for specialist rehabilitation.

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				the immediate plan for how these will be met, and any future /or outstanding needs (including those that cannot be met within the existing service provision. Only through recording and central collation of this information (including unmet need for services) will we realistically be able to expand the much-needed services for rehabilitation and support of people with ME/CFS.	https://www.bsrm.org.uk/downloads/specialist-rehabilitation-prescription-for-acute-care-28-11- 2014-ja--(ap1-redrawn).pdf). The management plan (now renamed the 'personalised care and support plan'*) is similarly based on the person's needs and includes the areas listed. The plan is developed in collaboration with the person with ME/CFS. Far from being incomplete, the personalised care and support plan supports the person's aims and the management of their health and well-being within the context of their whole life and family situation. This is clear from the sections noted in the bullet points, which outline ongoing needs and how they may be addressed. *Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.).
Royal College of Physicians (RCP)	Guideline	014		**Recommendation 1.6.4:** ***Explain that ME/CFS…*** • ***although a small proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS*** • ***can have a major impact on people's lives, including their daily activities, family and social life, and work or education, so they may need to adjust how they live*** • ***may be self-managed with support and advice*** Our experts do not agree with explaining this to people at 3 months. At this stage our experts would recommend a much more positive explanation. Our experts do not agree with the explanation that they can be self-managed with support and advice – at this stage patients should be having a holistic rehabilitation programme -	Thank you for your comment. After considering the range of stakeholder comments on this recommendation it has been edited to, • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS. • varies widely in its impact on people's lives, and can affect their daily activities, family and social life, and work or education (these impacts maybe severe) • can be self-managed with support and advice This is to reflect the experience of all people with ME/CFS.

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				professionally delivered, carefully monitored and centred around their individual needs and abilities.	The previous section on assessment and care and support planning by a specialist team describes the process of the holistic assessment and development of a personalised care and support plan. The personalised care and support plan is based on the person's needs and includes the areas listed. The plan is developed in collaboration with the person with ME/CFS and explores their aims and the management of their health and well-being within the context of their whole life and family situation. It should be proportionate, flexible and coordinated and adaptable to a person's health condition, situation and care and support needs. This is delivered by a ME/CFS specialist team, in addition in the review in primary care section of the guideline, the minimum of an annual review is recommended to review the person's care and support plan. This is the process that underpins,' can be self-managed with support and advice'. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.).
Royal College of Physicians (RCP)	Guideline	015	4-7	**Recommendation 1.6.6: Give people (and their families and carers, as appropriate) information 4 about: self-help groups, support groups and other local and national resources for people with ME/CFS** Our experts agree with the need to give advice about sources of self help and advice, but would not agree with pointing them	Thank you for your comment. This section is for people that are diagnosed with ME/CFS.

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				towards resources specifically for ME/CFS at this early stage – especially of they are then to be given negative information about the chances of improvement. Our experts agree however, that it would be appropriate for patients at a later stage, once it becomes clear that this is the diagnosis.	
Royal College of Physicians (RCP)	Guideline	016	9-11	**Recommendation 1.7.3: If an assessment under the Mental Health Act 1983 or the Mental Capacity Act 2005 is needed, involve health and social care professionals who have training and experience in ME/CFS. This should be done within 24 hours in an emergency.** If decisions need to be made for a patient under the MCA 2005, their mental capacity has, by law, to be considered at the time that each treatment decision is made and acted upon. It will not always be possible to have an ME/CFS expert on site to make or be involved in such evaluations. Our experts believe that what is referred to here is a formal assessment, especially in a more nuanced situation, in which case this should be stated. Otherwise the suggestion that this may not need to be done until 24 hours later may not be in line with the legal requirements of the MCA.	Thank you for your comment. After considering the stakeholder comments the reference to 24 hours has been removed to acknowledge the involvement of health and social care professionals with ME/CFS may be later in the process.
Royal College of Physicians (RCP)	Guideline	017	1-19.	**Recommendation 1.7.6: Recognise that the following are not necessarily a sign of abuse in C&YP with confirmed or suspected ME/CFS [list].** Whilst our experts recognise that the circumstances listed are not necessarily a sign of abuse, there should nevertheless be robust safeguarding processes in place especially if more than one of the scenarios is applicable. Further assurances would be needed to be certain of appropriate safeguarding.	Thank you for your comment. The importance of this section is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families.

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					Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The NICE guidelines on child maltreatment and child abuse and neglect should be followed. This is clear that if a professional has concerns they should be addressed in the same way as with any person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
Royal College of Physicians (RCP)	Guideline	019	9	**Recommendation 1.8.6: The guideline sets out a range of conditions for when people with severe / very severe ME/CFS are admitted to hospital including "stimuli should be kept to a minimum…being cautious about the pressure of touch…minimising strong smells".** While our experts agree that these are things to consider in an ideal situation, many of these are simply not possible given the other constraints within an already over-stretched NHS. There is no strong evidence base for these recommendations, (which again arise out of the committee's view) but instead of using more cautious language for that context (ie 'Think about' or "Be aware of..") the guideline issues a clear instruction to do it. We have concerns at a number of levels: 1. Some of these recommendations may unwittingly reinforce a sickness role.	Thank you for your comment. Discussing and considering how someone can access health services and how challenges to this can be overcome is best practice (see Patient experience in adult NHS services: improving the experience of care for people using adult NHS services). This is a guideline on people with ME/CFS and highlighted here as consideration for people with severe or very ME/CFS. The committee note that while clinicians are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement the guidance does not override the responsibility of healthcare professionals and others to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

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				2. It is also necessary to take into account the needs of other patients, especially in multi-bed bays 3. They may raise unrealistic expectations, for example that a side room would be available, and if they cannot be fulfilled, they may prevent ME/CFS patients seeking the medical care that they require. Our experts strongly recommend that if this section is included it should be phrased in the more cautious language.	
Royal College of Physicians (RCP)	Guideline	020	23-25	**Recommendation 1.8.10 Enable prompt assessment for funding for home adaptation. If the person is not eligible for funding, continue to offer information and support in arranging home adaptations.** Our experts note that it is not clear who this recommendation is aimed at. Our experts question whether it refers to clinicians, social services, or housing. It is not within the power of most clinicians to 'enable' assessment for housing applications. The best that most can do is to assist by providing information to support funding applications. We think it is important to define what is meant by continuing to offer 'information and support'. Clinicians can clearly provide advice about how to about the application process, who to contact etc but we are concerned about potential legal liability if they give specific advice about specific adaptations that patients will then go on to procure through self-funding arrangements.	Thank you for your comment. These recommendations refer to the social care needs assessment and the aids and adaptions identified as part of that assessment. This has been made clearer in the recommendations.
Royal College of Physicians (RCP)	Guideline	024	4-5	**Recommendation 1.11.1 Be aware there is no current treatment or cure (non-pharmacological or pharmacological) for ME/CFS.** The rationale given for this statement is as follows	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any

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				Overall, the evidence for non-pharmacological and pharmacological interventions for ME/CFS was heterogenous and inconclusive, with limited evidence for any one intervention, and this supported the committee's experience. **The committee was aware of claims that have been made about cures for ME/CFS and that there is often a financial cost to people with ME/CFS when they pursue these. To address this, the committee agreed to raise awareness in the recommendations of the current lack of treatment or cure for ME/CFS.** Whilst our experts acknowledge that ME/CFS is a life-long condition for some patients, this is not necessarily the case for patients who present with the symptoms set out in 1.2.3 at 3 months post onset. If the sentiment behind this statement is to prevent people being enticed into paying in appropriately for falsely promised 'cures', this should be made clear in the statement. For example: *"Be aware there is no current cure for ME/CFS, and patients should be wary of being enticed to have to pay for interventions (pharmacological or non-pharmacological) that are offered with the promise of a cure"*	misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. However the committee agree there currently isn't a cure for ME/CFS and it is important that people with ME/CFS are aware of this. As you note the rationale provides further information about avoiding claims that interventions will cure ME/CFS. For this reason, the committee have not further edited the recommendation.
Royal College of Physicians (RCP)	Guideline	027	22-23	**Recommendation 1.11.15 Do not advise people with ME/CFS to undertake unstructured exercise that is not part of a supervised programme, such as telling them to go to the gym or exercise more, because this may worsen their symptoms.** Our experts agree that unstructured unsupervised exercise programmes are inappropriate for patients with ME/CFS.	Thank you for your comment.

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Royal College of Physicians (RCP)	Guideline	028 63	1-11 1-20	**Recommendation 1.11.16 Do not offer people with ME/CFS…** This recommendation offers a list of 'do nots' in relation to physical activity. Our experts note that firstly, this is not helpful in a guideline. A guideline should provide advice to the practitioner to help patients. Secondly, this section seems to be fundamentally biased against even considering exercise as a treatment for ME/CFS. The rationale for this is as follows: **Because of the harms reported in the qualitative evidence, as well as the committee's experience of the effects when people exceed the limits of their energy envelope, the committee recommended that people with ME/CFS should not undertake a physical activity or exercise programme unless it is delivered or overseen by a physiotherapist or occupational therapist who has training and expertise in ME/CFS. The committee reinforced there is no therapy based on physical activity or exercise that is effective as a treatment or cure for ME/CFS.** **The committee considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their own experiences of these types of interventions. They recommended not to offer any programme based on fixed incremental physical activity or exercise, for example graded exercise therapy or structured activity or exercise programmes that are based on deconditioning as the cause of ME/CFS**	Thank you for your comment. After considering the stakeholder comments, the committee have added exercise into the recommendations on considering a physical activity programme to clarify where these apply to exercise. The recommendation describes the types of physical activity or exercise programmes that should not be offered to people with ME/CFS. The previous recommendation in the energy management section includes that people who would like to incorporate a physical activity or exercise programme into managing their ME/CFS (see the section on physical activity and exercise) should be referred to a physiotherapist or occupational therapist working in a ME/CFS specialist team. The following recommendation in the physical activity section reinforce this and includes that if a physical activity or exercise programme is offered, it should be overseen by a physiotherapist in a ME/CFS specialist team. *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the

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				Our experts take strong objection to the above section. With good evidence from randomised controlled trials and robust independent synthesis, for example the Cochrane review, this contradicts the evidence base. It also misrepresents Graded Exercise Therapy (GET) as 'fixed incremental increases…' The Cochrane review seeks adverse effects-which would include exacerbation of symptoms in adverse effects, with no increase demonstrated in the point estimate, although numbers are small. Thus, the demonstration of 'harm' of properly implemented GET is not shown from good quality RCTs. Our experts note that previous NICE guidelines have included the significant benefits gained from GET. Much of this evidence (Evidence review G), despite being graded highly in 2007, was reviewed and graded as poor quality with little rationale. One of the largest studies (PACE trial White et al Lancet 2011) showed clear benefits to both CBT and larger benefits for GET in a host of outcome measures in a parallel group randomised trial. There was considerable criticism from the committee that the study included large numbers of people without Post exertion symptoms and therefore dismissed the benefits of GET. However, subgroup analysis of 427 and 329 of the 641 eligible patients met the International or London criteria respectively that did include post exertion malaise/symptoms and the benefit of GET remained. Moreover, PACE is in fact the only trial to have examined PEM as an outcome. It found that PEM was reduced more by GET and CBT than the comparison treatments of specialist medical care and adaptive pacing therapy (White et al, 2011, table 6). Our experts are concerned that the findings of the above study were only analysed at the 134 week point when the trial	qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. *PEM (disbarred evidence)* No evidence was excluded that met the evidence review protocols.

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				concluded at 52 weeks. Clear benefits to GET were seen at the time point when the trial ended and the 134-week data was following unblinding with a good number of patients taking up the GET and CBT treatments subsequently. Our experts believe that this will minimise benefits seen between initially assigned groups but is further evidence of the chronicity of the benefits of GET and CBT. Our experts note that there is an overwhelming mass of evidence of the benefits of exercise to the major causes of mortality and morbidity including cardiovascular disease, stroke, diabetes, osteoporosis, depression, cancer, cancer survival, rheumatoid arthritis and osteoarthritis. The WHO report and guidance on physical activity in relation to health and chronic conditions strongly advocates the use of regular exercise to minimise the impact of the above and multiple other chronic conditions. Our experts question whether NICE suggest, despite the overwhelming evidence, that CFS/ME is the only chronic condition in which exercise causes harm as the draft guidelines state. More detail of Our experts' concerns relating to the evidence evaluation for this section are specified below. Taken individually, it is possible to see where the committee may have been coming from – for example physical exercise should not be offered as a 'cure' or general panacea. Nor are standardised programmes based on fixed increments appropriate – all rehabilitation interventions should be tailored to the individual's needs. However, this recommendation appears to dismiss all graded exercise therapy (GET), any programme to address deconditioning and any programme based on principles of	It is commonly agreed that people with ME/CFS experience post exertional malaise (PEM) after activity. PEM is widely acknowledged in ME/CFS specialist practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just do not know how many if the information is not reported. Where this is the case, the trial population could include people that do not have ME/CFS and this makes it difficult for the committee to be confident of the benefits and risks of the interventions on people with ME/CFS. Using GRADE and CERQual the committee agreed that evidence without this information would be 'indirect' (relevance in CERQual) acknowledging this uncertainty about the population. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and CERQual. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative and qualitative evidence and the application of indirectness and relevance. As part of this they agreed that any evidence with a population $\geq$95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.)

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				osteopathy, life coaching or neurolinguistic processing (such as the Lightning Process (LP)) Our experts note that the decision on LP is particularly arbitrary as it was supported by data from the only RCT, and used a diagnostic definition that meant that all participants had to have the symptom of PEM So it has been banned solely on the basis of qualitative data, which seemed to be mixed. Our experts note that for such a severe and varied condition, no single intervention will benefit everyone ME/CFS. But there is a large body of evidence from RCTs and Cochrane reviews that GET programmes can provide benefit for a proportion of patients (see below), and there is also evidence from case studies and one RCT that some patients report benefit from LP. GET programmes come in all shapes and sizes (they are by no means all fixed increment regimens). Our experts fully acknowledge that the randomisation process in RCTs and some of the less personalised GET programmes would have meant that proportion of patients were allocated to exercise programmes that were not well suited to their needs and made them feel worse, but this is not to say that all such programmes should be banned Our experts believe that to say in a NICE Guideline that they should not be done, will effectively mean that any further research to explore what approaches work best for which patients (including flexible approaches as recommended in 1.11.20) would not be supported or funded). Our experts find it unacceptable that a body of evidence and any future research should be disbarred by a committee based on anecdotal experience. Furthermore, our experts note the absence of the voices of frontline NHS clinicians and patients who have	The committee discussed the London criteria at length and concluded that on the basis of the written criteria used to assess participants in the PACE trial it could not be established that they experienced post exertional malaise. *Follow up* Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. *Methods* This guideline has updated the 2007 guideline using Developing NICE guidelines: the manual Process and methods [PMG20] Published: 31 October 2014 Last updated: 15 October 2020. The process for quality rating now used in NICE guidance is an internationally agreed process (see the methods chapter for information on GRADE and CERQual). *Deconditioning* To note after considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice

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				benefitted from these approaches over the years. Our experts question how their views been considered.	on maintaining and preventing the deterioration of physical functioning and mobility. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer people with ME/CFS therapies based on the Lightning Process'. The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H) *Underrepresentation of people and professionals who have benefited from GET.* The committee membership had a broad range of professional and personal knowledge about the different experiences of people with ME/CFS and this was discussed and considered at all stages of the decision making. There is little representation in the qualitative literature of people who have benefited from GET and the committee hope that where this can be published it will be as this can only further inform the care and support of people with ME/CFS. *Treatment or cure* After considering the range of stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. Research recommendations

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					The committee have made recommendations to address the difficulties and limitations in diagnosing ME/CFS (see Evidence review D for the committee discussion on this). The committee identified this as high priority for research. This committee hope this will enable future research to accurately identify people with ME/CFS and determine the impact of interventions on them. They thought this was particularly important before recommending any research trials on physical activity or exercise interventions.
Royal College of Physicians (RCP)	Guideline	028	12-15	**Recommendation 1.11.17 Only consider a physical activity programme for people with ME/CFS who are ready to progress their physical activity beyond their current activities of daily living or would like to incorporate physical activity into the management of their ME/CFS.** Our experts believe that the sentiment behind this statement is reasonable – any intervention that involves the active participation of an individual (including doing more physical activity) needs to be done with their agreement and choosing or it will not happen. However, as written this reads it suggests that clinicians should not even consider offering support to patients to help them extend their level of physical and social activities unless they positively ask for it. Some patients need more active support and encouragement to have the confidence to extend their range of activities. (In addition, this could be used as a gate-keeping measure by commissioners who are reluctant to pay for this additional support) Our experts suggest rewording this recommendation.	Thank you for your comment. After considering stakeholder comments this bullet point has been edited to,' feel ready'. This recommendation is preceded by one in the energy management section that is to refer people who feel ready to progress their physical activity or would like to incorporate physical activity or exercise programme into managing their ME/CFS. To refer anyone would necessitate a discussion between the person and the healthcare professional. The guideline recommends a holistic personalised approach to the care and support of people with ME/CFS and any discussion are specific to the individual. It is clear in the guideline that this support should be available to people with ME/CFS.
Royal College of Physicians (RCP)	Guideline	028	16-18	**Recommendation 1.11.18 A physical activity programme, if offered, should only be delivered or overseen by a**	Thank you for your comment.

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				physiotherapist or occupational therapist with training and expertise in ME/CFS. Our experts are concerned about the requirement that any physical activity programme, if offered, should only be delivered/overseen by a physiotherapist/occupational therapist with training and expertise in ME/CFS. This would significantly limit the ability of the NHS to deliver what we feel is a key aspect of the care of many people suffering from ME/CFS. It excludes other trained exercise specialists/professionals who may have significant expertise and experience in delivering such programmes and will also prevent General Practitioners recommending basic advice on the benefits of physical activity and exercise for symptom management. A trial showing that guided self-management based on the principles of GET is effective in relieving the fatigue of CFS suggests that wider application of this treatment is possible (Clark et al, 2017, http://dx.doi.org/10.1016/S0140-6736(16)32589-2) Our experts acknowledge the sentiment behind trying to ensure that patients with ME/CFS are managed by therapists with the appropriate skills and knowledge of the condition. However, there are not currently enough dedicated specialist in ME/CFS to go around. (Especially if, in line with 1.2.3, all the patients with Long COVID were to be included as well.) As written, this recommendation suggests that if there is no-one available with specific expertise in ME/CFS they should not have any physical activity programme at all. Our experts strongly disagree with this.	Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services , to implement some

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					recommendations in the guideline. However, this guideline highlights areas where resources should be focussed.
Royal College of Physicians (RCP)	Guideline	028	19-21	**Recommendation 1.11.19 Tell people about the risks and benefits of a physical activity programme. Explain that some people with ME/CFS have found that physical activity programmes can make their symptoms worsen, for some people it makes no difference and others find them helpful.** As with any intervention, patient should be informed of the likely benefits and harms. However, this should be done in an evidence-based way, rather than based on the anecdotal experience of a group, some of whom have campaign actively against such interventions. According to the largest RCT (the PACE study) at 1 year, 41% of patients who undertook graded exercise reported positive change in their overall health, whereas only 7% reported negative change. The same proportion reported negative change after adaptive pacing therapy. Here and throughout the guideline, emphasis is placed on the potential harms of physical activity in favour of explaining the possible benefits. Our experts do not believe that this is justified by the evidence base. In addition, properly balanced information should also include a discussion of the very considerable harms of prolonged inactivity. It is well recognised across the whole of medicine that prolonged inactivity and immobility leads to deconditioning. This is not to say that deconditioning is the cause of ME/CFS. But it is critical to acknowledge it as a	Thank you for your comment. The discussion of risks and benefits would take place between the physiotherapist or occupational therapist working within a specialist ME/CFS team. *Deconditioning* To note after considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.

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				consequence which requires proactive management in its own right. As noted above, recommendation 1.11.11 relates to many of the consequences of prolonged inactivity which in effect are features of deconditioning of the body. Our experts question what sort of management plan could be implemented to combat these that does not involve some sort of physical activity.	
Royal College of Physicians (RCP)	Guideline	029 64 24 25 42	17-22 1-4 6-24 1-29 4-9	**1.11.23 Advise people with ME/CFS:** **• on the role of rest in ME/CFS** **• that rest periods are part of all management strategies for ME/CFS** **• how to introduce rest periods into their daily routine, including how often and for how long, as appropriate for each person.** **In their experience, understanding the role of rest and how to introduce rest periods was important in successful energy management.** The draft recommendations devote a great deal of space to the role of rest, all based on the theory of 'energy envelopes'. The Committee endorse 'self-management' with 'energy management' otherwise known as pacing, which means staying within an 'energy envelope', avoiding exertion if it induces symptoms. **Energy envelope** **The amount of energy a person has to do all activities without triggering an increase in their symptoms.** **Energy management**	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand

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				A self-management strategy that involves managing a person's activities to stay within their energy envelope. Our experts note with interest that the largest trial, which did test the model of pacing as outlined in the Review, based on the work of Pesek and colleagues (https://doi.org/10.1300/J137v03n01_04), found that it was no more effective than specialist medical care by itself (White et al, 2011, reference above). If anything pacing was associated with further deterioration in physical functioning (Dougall et al, 2014, https://doi.org/10.1016/j.jpsychores.2014.04.002). The summary of the evidence provided to the Committee did include this, but the Committee decided not to use this evidence, rating it as very poor quality. Our experts are unconvinced as to why this was the case (which is detailed elsewhere), and suggest that it was an error to ignore these data.	but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS. *Pacing* To note the committee discussed the use of the term pacing agreed that it means something different to different people with many different versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it.
Royal College of Physicians (RCP)	Guideline	029 64 27	17-22 1-4 3-13	**1.11.23 Advise people with ME/CFS:** **• on the role of rest in ME/CFS** **• that rest periods are part of all management strategies for ME/CFS** **• how to introduce rest periods into their daily routine, including how often and for how long, as appropriate for each person"** **"In their experience, understanding the role of rest and how to introduce rest periods was important in successful energy management."** Our experts note that the dangers of prolonged bedrest have been well described over the years even before the late and great Richard Asher's seminal review of 1947 (Asher, 1947, https://dx.doi.org/10.1136%2Fbmj.2.4536.967https://doi.org/10.1016/S0140-6736(98)10063-6). Allen's and colleagues	Thank you for your comment and information. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep, this would include the risks and benefits, and personalised sleep management advice.

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				systematic review (https://doi.org/10.1016/S0140-6736(98)10063-6) showed that prescribed bed rest is either ineffective or harmful across many medical conditions. A meta-analysis showed a linear loss of aerobic fitness associated with time spent in bed (Ried-Larsen et al, 2017, https://doi.org/10.1152/japplphysiol.00415.2017). Early mobilisation had no effect on mortality and showed only benefits in even the sickest patients seen in hospital (Tipping et al, 2016, https://doi.org/10.1007/s00134-016-4612-0). Our experts suggest that the guidance provides both more emphasis and evidence regarding the harms associated with prolonged rest.	
Royal College of Physicians (RCP)	Guideline	029 38 64	17-22 1-5 2-4	Our experts would also like to draw attention to this year's World Health Organisation report and guidance on physical activity in relation to heath, and specifically chronic conditions (WHO, 2020, https://www.who.int/publications/i/item/9789240015128). The guidance provides an up to date review on the harms associated with sedentary behaviour. We understand that this might have arrived too late for the committee to consider as part of its conclusions, but there is still time for that to be corrected, because it is important work with direct relevance to the deliberations of the Review. Our experts wish to bring this important work to the attention of the guidance committee. The WHO recommends the following, when a chronic condition does not allow following the normal recommendations about physical activity: "When not able to meet the above recommendations, adults with these chronic conditions should aim to engage in physical activity according to their abilities. Adults with these chronic conditions should start by doing small amounts of physical	Thank you for your comment. The committee agreed there is little dispute amongst clinicians working with people with ME/CFS that they should not undertake exercise that is not part of a programme overseen by a ME/CFS specialist team, such as telling them to go to the gym or exercise more. It is commonly agreed that people with ME/CFS experience post exertional malaise (PEM) after activity. PEM is a worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated. It is in this context, and recognising the evidence from people with ME/CFS indicating that misunderstanding of the impact of PEM and inappropriate advice on how to incorporate physical activity (and exercise) into their lives has resulted for some in a deterioration of their condition, that this guideline has recommended that people with ME/CFS should be supported by a

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management

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				activity and gradually increase the frequency, intensity and duration over time. Adults with these chronic conditions may wish to consult with a physical activity specialist or health-care professional for advice on the types and amounts of activity appropriate for their individual needs, abilities, functional limitations/complications, medications, and overall treatment plan. Pre-exercise medical clearance is generally unnecessary for individuals without contraindications prior to beginning light- or moderate-intensity physical activity not exceeding the demands of brisk walking or everyday living." (World Health Organisation, 2020). Regarding sedentary behaviour, the WHO recommends: "Adults and older adults with chronic conditions should limit the amount of time spent being sedentary. Replacing sedentary time with physical activity of any intensity (including light intensity) provides health benefits. (Strong recommendation, low certainty evidence)" (WHO 2020).	physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms. This is linked to terms used in the guideline with further explanation of the meaning.
Royal College of Physicians (RCP)	Guideline	034	1-20	**Recommendation 1.11.43-7 "Only offer cognitive behavioural therapy (CBT) to people with ME/CFS who would like to use it to support them in managing their symptoms of ME/CFS and to reduce the psychological distress associated with having a chronic illness. "…Do not offer CBT as a treatment or cure…it is deigned only to improved well being and quality of life"**	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to

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				"Aims to improve functioning and reduce the psychological distress associated with having a chronic illness" **"Exploring their personal meaning of symptoms and illness, and how this might relate to how they manage their symptoms** **"working together to adapt and refine self-management strategies to improve the person's functioning and quality of life, for example their sleep, activity and rest"** These three recommendations emphasise the role of CBT only as a route to help people to live with their condition of ME/CFS. They are negative descriptions which our experts believe do not address the more positive role of CBT which is typically aimed at helping people to become aware of when they make negative interpretations, and of behavioural patterns which reinforce the distorted thinking. CBT helps to develop alternative ways of thinking and behaving which aim, not only to reduce their psychological distress, but to gradually build up and resume regular daily activities, to identify and plan how to deal with any triggers that might cause symptoms to get worse – to learn how to manage and reduce the symptoms. Our experts note this may seem to be a nuanced difference, but the language is important to help people adopt more positive strategies about coping with their condition and its consequences. Our experts believe that the text on CBT is heavily biased by the committee's pre-conceived attitude towards this intervention Our experts are aware that access to good CBT is variable in the general hospital setting, but when it is present our	accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).

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				members provide good feedback about acceptability and engagement, especially when it is 'on site' and not in a distant mental health settings. Our experts consider CBT to be an essential part of a holistic approach rehabilitation and support for patients with ME/CFS and cannot understand why it is being devalued. Our experts note that danger of this recommendation is that it may not in future be made available even to those who would gain some benefit – which the PACE trial demonstrates is about 40% at one year. This would highly detrimental for many people.	
Royal College of Physicians (RCP)	Guideline	043	15	Our experts do not agree that patients with moderate CFS will necessarily have 'Reduced mobility', and this is not true for every moderate patient ((van der Werf JPsychosomRes 2000;49:373; King JPsychosomRes 2020)	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
Royal College of Physicians (RCP)	Guideline	066	11-15	**The committee agreed that people with ME/CFS may be more intolerant of drug treatment and have more severe adverse effects than people who do not have ME/CFS, so they decided to raise awareness of this. To reduce the risk of harm, the committee discussed using a cautious approach to medicines prescribing, which includes starting the medicine at a lower dose than in usual clinical practice and monitoring how the person responds before adjusting the dose**	Thank you for our comment and information. The committee had clinical and personal experience of people with ME/CFS being more intolerant of drug treatment, they acknowledged that 'more severe adverse effects' did not add further clarity to their point and deleted this text here and in the recommendation. When considering the evidence for pharmacological interventions the committee agreed that there was insufficient evidence of benefit to recommend any medicines but recognised

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				Our experts question what the evidence is for drug intolerance and note that it does not come from drug trials. All prescribed medications should be monitored for both effects and side-effects, but we know of no evidence that using lower doses (probably sub-therapeutic) doses of medication is an appropriate solution. Our experts believe that this will probably just serve to reinforce the notion that medications are ineffective.	that people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and could be discussed on an individual basis. The committee agreed it was important to have a section on medicines for symptom management to emphasise this. *Treatment and cure* The committee agreed to remove the word 'treatment' from the recommendations where treatment and cure 'is used to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Royal College of Physicians (RCP)	Guideline and Evidence Evaluation G	General	General	Our experts are concerned about the shift away from recommending interventions such as cognitive behavioural therapy (CBT) and graded exercise therapy (GET) for people with mild or moderate CFS/ME • The update cites a 'lack of evidence for the effectiveness of these interventions' despite the overall positive results of randomised evidence published since 2007, which are detailed on specific comments below. • It also emphasises the potential harms of exercise, (which are not borne out by the research evidence as detailed below) without acknowledging the potential benefits and the harms of immobility Our experts note that this decision seems to omit the views of frontline NHS clinicians and the silent majority of patient voices who have gained, and continue to gain, very substantially from these approaches. Our experts acknowledge that not all patients will benefit from these interventions but a significant proportion do	Thank you for your comment. *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). *GET/Physical activity and exercise* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the

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				- Trial evidence that was accepted for the 2007 guidelines seems to have been reanalysed and/or excluded on spurious grounds - Since the publication of PACE, additional trials, accumulation of anecdotal experience and data from the national outcomes database all support the use of CBT/GET as useful, beneficial and safe therapeutic interventions. - Although some patient groups describe adverse events from GET, this is not substantiated in any properly conducted, peer reviewed trial. - Our experts' concern is that the specialist ME/CFS services that do exist are based substantially on treatment approaches that include CBT and GET where relevant and appropriate. If the updated guidance removes these evidence-based interventions the rationale for a UK wide NHS CFSME service is seriously undermined. As noted earlier, our experts acknowledge that the problem has to some extent been exacerbated by NICE's approach to evaluating evidence, which breaks down complex interventions such as rehabilitation into individual component parts with a separate patient/population, intervention, comparison and outcomes (PICO) question for each. As a result of this piecemeal approach, patients with CFS/ME have often felt disbelieved by clinicians or have been offered inappropriate forms of exercise or other interventions that are not tailored to their individual needs. Our experts believe that this is not a reason to dismiss all forms of these interventions, so long as it is prescribed as previously recommended by NICE, as a flexible, patient-centred, intervention that is	reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.

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				symptom contingent, rather than in standardised regimens that have sometimes been used in RCTs to meet the requirements for 'consistency' Our experts believe a role for CBT/GET should be restored in this updated guideline.	Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed it was important people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *NICE methodology and complex interventions* Developing NICE guidelines: the manual. Chapter 4 *Developing review questions and planning the evidence review* addresses the topic about approaches to take when considering the design of studies to be included in a systematic review. In summary the effectiveness of an intervention is usually best answered by a RCT because a well-conducted RCT is most likely to give an unbiased estimate of effects. Where such evidence is not available (for example, where interventions it can be difficult or unethical to assign populations to control and intervention groups). In such cases, a non-randomised controlled trial might be a more appropriate way of assessing association or possible cause and effect. The Medical Research Council (MRC) has produced guidance on evaluating complex interventions (Craig et al. 2008) and using natural experiments to evaluate health interventions delivered at population level (Craig et al. 2011).

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					When developing the protocols for the intervention reviews, a RCT was agreed to be the most appropriate study design to evaluate clinical effectiveness. In recognition that the views of people with ME/CFS who had experienced the interventions was important a qualitative review was done with an accompanying call for evidence to identify any unpublished evidence. In clinical practice a holistic personalised approach to care may typically combine a range of physical, cognitive and psychological approaches depending on patients' needs, preferences and priorities. These may include elements of different intervention varied proportions, incorporated where possible into everyday activities. Current NICE methods do not discount any RCTs of this approach. In ME/CFS the protocol for non-pharmacological interventions includes combinations of treatments (including combinations with pharmacological treatments). Unfortunately, very few RCTs combining any treatments were identified. *Underrepresentation from patients who have recovered from ME/CFS* The committee membership had a broad range of professional and personal knowledge about the different experiences of people with ME/CFS and this was discussed and considered at all stages of the decision making. It is true that there is little representation in the literature of people who have recovered from ME/CFS and the committee hope that where this can be published it will be as this can only further inform the care and support of people with ME/CFS.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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Royal United Hospitals Bath NHS Foundation Trust	Appendix 1	009	17	**Appendix 1 Involving children and young people in developing a NICE guideline on ME/CFS: diagnosis and management** It appears that the children and carers recruited to this piece of work were recruited through Action for ME via email using their member directory. We can find no evidence that these participants definitely had ME/CFS. Only that they were on the members directory. Although the appendix says they had a diagnosis of ME/CFS, no evidence is provided on how that was obtained, whether other diagnoses were excluded, and whether they had PEM. As the guideline committee consider that a clinical diagnosis and the presence of PEM is essential for the evidence to be considered, we consider other qualitative data and trial data where a clinical diagnosis of ME/CFS and the presence of PEM can be confirmed should be placed above this evidence.	Thank you for your comment. In Appendix 1 the study authors set out the limitations of the consultation and acknowledge the limitations on recruitment and the representation of the sample. Despite limitations in recruitment (small sample, lack of involvement of third-party organisations), the sample was heterogenous in that it included a range of geographies across England, genders and condition severities (CYP reporting ME/CFS severity ranging from mild to severe did take part). Section 4 of Appendix 1 describes the committee's overview of the consultation. In this they noted it was unclear if all the sample were recruited from Action for ME potentially representing only one group of young people with similar views and if the participants were currently under NHS care and if the experiences reflected current care.it was unclear if the participants were currently under NHS care and if the experiences reflected current care. This was taken into account in the committee's decision making when considering how this contributed to the body of evidence and when making the recommendations. *PEM* See the methods chapter, evidence reviews D, G and H for further information on the assessment of indirectness and relevance. *Strength of the evidence* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose

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					activities, services or care will be covered by the guideline. This committee included members with clinical and personal experience of children and young people with ME/CFS. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). In the case of children and young people the themes and findings in the report were considered alongside all the other evidence and the committee took into account the limitations in their interpretation of all the evidence and in their decision making.
Royal United Hospitals Bath NHS Foundation Trust	Appendix 1	017		There is positive evidence of the experience of both CBT and GET from children and young people. This is consistent with the evidence synthesis 7, and provides further evidence that the guidelines should make CBT and GET optional for children and young people as some find it helpful.	Thank you for your comment. The management sections of the guideline include recommendations: • to support people with energy management • to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or programme into the management of their ME/CFS. • to offer CBT to help people manage their symptoms and reduce the distress associated with having a chronic illness

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					and are options for part of the care and support plan where appropriate and chosen by the person with ME/CFS. To accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. See evidence reviews G and H for the evidence and the committee discussion on these recommendations. *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in

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					this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed it was important that people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Royal United Hospitals Bath	Appendix 1	023	7-8	We do not think it is acceptable that this appendix with interviews with 14 young people who do not have a confirmed diagnosis of ME/CFS and for whom there is no record of PEM	Thank you for your comment. In Appendix 1 the study authors set out the limitations of the consultation and acknowledge the limitations on recruitment and

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NHS Foundation Trust				andfor whom there is no data on exclusionary diagnosis, was rated "the most applicable evidence for a number of topics." This evidence was rated above qualitative interviews of those with confirmed diagnoses (>70 participants all of whom had PEM) and trials of hundreds of participants with clearly defined diagnosis, where all or nearly all the children had PEM. This suggests a systematic bias in the way the guidelines were created.	the representation of the sample. Despite limitations in recruitment (small sample, lack of involvement of third-party organisations), the sample was heterogenous in that it included a range of geographies across England, genders and condition severities (CYP reporting ME/CFS severity ranging from mild to severe did take part). Section 4 of Appendix 1 describes the committee's overview of the consultation. In this they noted it was unclear if all the sample were recruited from Action for ME potentially representing only one group of young people with similar views and if the participants were currently under NHS care and if the experiences reflected current care.it was unclear if the participants were currently under NHS care and if the experiences reflected current care. This was taken into account in the committee's decision making when considering how this contributed to the body of evidence and when making the recommendations. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee included members with clinical and personal experience of children and young people with ME/CFS. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The

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					evidence from the report in Appendix 1 was not given a rating and was considered alongside all the evidence. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). In the case of children and young people the themes and findings in the report were considered alongside all the other evidence and the committee took into account the limitations in their interpretation of all the evidence and in their decision making.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G			The following papers match the protocol (Population and setting: people who have had interventions for ME/CFS) were available, and do not appear to have been included: BMJ Open. . 2017 Jan 13;7(1):e012633. Children's experiences of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME): a systematic review and meta-ethnography of qualitative studies Roxanne M Parslow [1], Sarah Harris [2], Jessica Broughton [2], Adla Alattas [1], Esther Crawley [1], Kirstie Haywood [3], Alison Shaw [4] "It'**s** not one size fits all"; the use of videoconferencing for delivering therapy in a Specialist Paediatric Chronic Fatigue Service. Haig-Ferguson A, Loades M, Whittle C, Read R, Higson-Sweeney N, Beasant L, Starbuck J, Crawley E.Internet Interv. 2018 Dec 23;15:43-51. doi: 10.1016/j.invent.2018.12.003. eCollection 2019 Mar.	Thank you for your comment. These references have been checked and where appropriate had been included in evidence reviews of this guideline. Therefore, despite not being part of evidence review G, all included studies were considered during the development of the present guideline recommendations. Specifically: The BMJ open paper by Parslow is a systematic review, the references of which had been checked for inclusion during development. The paper by Haig-Ferguson, although meeting the protocol for review G in terms of the population as stated in the comment, was excluded due to not having themes relevant to evidence review G but was included in evidence review C- Access to care (in the Barriers and facilitators to the care of people with ME/CFS review question) and therefore findings from this study were

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				BMC Health Serv Res . 2011 Nov 11;11:308. doi: 10.1186/1472-6963-11-308. What stops children with a chronic illness accessing health care: a mixed methods study in children with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) Carly M Webb [1], Simon M Collin, Toity Deave, Andrew Haig-Ferguson, Amy Spatz, Esther Crawley Adult patients' experiences of NHS specialist services for chronic fatigue syndrome (CFS/ME): a qualitative study in England. Broughton J, Harris S, Beasant L, Crawley E, Collin SM.BMC Health Serv Res. 2017 Jun 2;17(1):384. doi: 10.1186/s12913-017-2337-6. New qualitative papers that are relevant to the PICO are: "The child's got a complete circle around him". The care of younger children (5-11 years) with CFS/ME. A qualitative study comparing families', teachers' and clinicians' perspectives'. Brigden A, Shaw A, Barnes R, Anderson E, Crawley E.Health Soc Care Community. 2020 Nov;28(6):2179-2189. doi: 10.1111/hsc.13029. Epub 2020 Jun 9.	reviewed and taken into account by the committee during the development of the present guideline. The paper by Webb 2011 also did not contain themes relevant to review G, as findings did not relate to any specific intervention, but it did provide themes relevant to review C and was included there. This was also the case for paper by Broughton 2017 which has been included in evidence review C (both in the Barriers and facilitators to the process of diagnosing ME/CFS and in the Barriers and facilitators to the care of people with ME/CFS) as well as in evidence review B (both in the Information , education and support for health care professionals and in the Barriers and facilitators to providing information and support review questions) and in evidence review A- Information for people with ME/CFS. Therefore, findings from this study informed the committees decision making for recommendations relevant to multiple review questions/topics. Paper by Brigden 2020 was also included in evidence revie C.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G		Tables 3-7	These tables clearly describe the lack of adverse events (or that the rate of adverse events is less in the treatment groups compared to controls). The committee should adapt the language in the guidance suggesting that CBT and GET are associated with adverse events as this is not reflected in the published data or the evidence synthesis conducted by NICE.	Thank you for your comment. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on

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					how recommendations are developed). The committee has noted there are difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials and that it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. The wording regarding adverse effects has been removed from the guideline and is only included in the Evidence reviews when referring to outcomes extracted from studies. After reviewing the evidence available, together with their clinical experience, the committee agree that although CBT is not curative for ME/CFS, it is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation has been made to offer CBT to ensure this will be the case. Considering the worsening of symptoms reported in the qualitative evidence, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been acknowledged in the recommendations that have also included detail about the content of programmes involving physical activity or exercise, as well as for whom such programs should be considered. In developing recommendations on physical activity and exercise, the content, approach and delivery of physical activity management, the committee considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their experiences of these types of interventions.

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Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G		Table 25	This table provides good evidence from 131 children that internet delivered CBT is helpful. All these children had PEM. Therefore, therefore the quality of the evidence needs to be upgraded. These results are also consistent with the direction of evidence from the qualitative studies.	Thank you for your comment. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. Only published data was accepted for this analysis. The percentage of participants in this trial (FITNET) with PEM could not be found in any published articles, and participants were diagnosed using the CDC 1994 criteria which does not have PEM as a compulsory feature. Therefore, the committee was unsure if participants in this study had PEM, and the evidence remained downgraded for indirectness. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendix G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. However, this was not the only factor the committee used when making recommendations. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people

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					with ME/CFS that were identified as underrepresented in the literature. The committee acknowledged that some children with ME/CFS may benefit from CBT, and this is reflected in the recommendations for CBT. The full committee discussion of the evidence and rationale for the recommendations is in evidence review H.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G		Table 36	This table provides good evidence from 100 children that the Lightning Process in addition to specialist medical care was better than specialist medical care alone. This was downgraded because of risk of bias and imprecision presumably due to self report. However, self report is recommended in these guidelines. And in children, no other form of outcome has been recommended. This evidence is therefore stronger than a qualitative study of 9 children and the personal opinion of the committee members (who have, to our knowledge) not had the LP. Therefore, this appears to be a form of bias.	Thank you for your comment. As with all NICE guidelines, recommendations were developed using a range of evidence and other sources of evidence. When developing this guideline the committee considered evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The committee took great care to ensure that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).

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					The committee noted the clinical evidence you refer to was limited to one study and was of very low to low quality which impacted the committee's confidence in those findings. Both positive and negative experiences of the intervention emerged from the qualitative evidence and negative experiences including accounts about the secrecy surrounding the Lightning Process raised the committee's concerns about ethical considerations. After considering all the evidence available and their clinical experience, the committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G		Table 69	This table shows that data on the feasibility, acceptability of AM and GET was included in the evidence synthesis. This clearly describes the positive experiences children have had with GET. However this has not reflected in the guidance. A sentence needs to be added to the guidance to say that qualitative data suggests that the children who receive GET are positive about it. The main issue for children is the reduction of physical activity and this is an important factor that	Thank you for your comment. There was evidence of both positive and negative experiences with GET including reports of reductions in fatigue and tiredness, improved sleep but also experiences of no difference with treatment, uncertainty, or lack of impact, often related to school and cognitive activities emerging for children and young people. Positive experiences have been acknowledged in the committee's discussion and interpretation of the evidence (Evidence review G). The

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				should be discussed with children and families before starting treatment.	committee also noted there was no clear picture of benefit from the quantitative evidence, and the evidence was inconsistent. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Considering the worsening of symptoms reported in the qualitative evidence as well as their experience of the effects when people exceed their energy limits, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been reflected in the recommendations and based on clinical experience the committee concluded the same considerations were also applicable to children and young people.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G		Table 69	This table describes feedback from a survey of services where all patients will have a clinical diagnosis of ME/CFS. A described above, (see Collins paper) over 96% of UK patients accessing specialist ME/CFS services will have PEM. This qualitative data does not appear to be represented in the guidance.	Thank you for your comment. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. The same approach was taken for the qualitative review on experiences of

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					interventions. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendix G for the approach taken, the analysis and the impact on the results and interpretation of the evidence
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G		Table 69	The survey from patients seen in a specialist ME/CFS service (with confirmed diagnosis of ME/CFS) has limitations documented. However, the two surveys from charities (the ForwardME survey and Action for ME) do not have the most obvious limitation documented in the table which is that these surveys rely on a self report diagnosis of ME/CFS. They cannot confirm if a patient has ME/CFS or not or another diagnosis associated with fatigue. As <40% of members of patient support groups have ME/CFS [see Brimmer et al. BMC Research Notes 2013, 6:309]], many responses are likely to have been from members who do not have ME/CFS. This is an example of bias in favour of the charities, and against specialist services.	Thank you for your comment. We agree that this constitutes an important limitation. The Forward ME survey 2019 has been downgraded for concerns over methodological limitations due to concerns over the recruitment strategy used, the data collection method and concerns over data analysis as specified in the qualitative evidence table for the survey in Appendix D on Evidence review H. The diagnosis was however confirmed by a clinician and thus this has not been included in the limitations identified. Serious limitations have also been noted for the Action for ME survey relating to similar reasons that have now been updated to include the self-reported diagnosis. This has been accounted in the assessment of confidence of review findings that the survey contributes to. The limitations in the evidence have been brought to the committee's attention and taken into account in decision making. In addition to this, after considering stakeholder comments and address concerns over the representativeness of the population included in the evidence, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of qualitative findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported

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					would be downgraded for concerns over relevance. See evidence review H Appendix G on PEM-reanalysis for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The committee agreed that in order for this criterion to be adequately met, self-reporting of PEM would not be sufficient and 95% of participants need to have been diagnosed by a health professional as having PEM. The Forward ME 2019 survey did not meet this criterion as 98.5% self-reported their experience of PEM. As a result, evidence from the survey was further downgraded for concerns over the applicability of the population, which is reflected in the relevance rating component of the assessment of confidence in the findings. This resulted in further downgrading the confidence in the relevant review finding from Moderate to Low quality. Similarly, the ME Action survey has now been downgraded for moderate concerns over applicability due to the percentage of people reported to have PEM being self-reported. The committee agreed such shortcomings are important and this approach has been followed throughout the guideline to ensure these have been accounted for in the assessment of confidence in the evidence/ evidence quality which contributes to decision making along with the variety of factors including the different types of evidence, the balance between benefits and harms, economic considerations, equality considerations and the committee's clinical expertise (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G		Table 70	The significant positive findings from CBT have been described in this table and few negative findings are described. This positivity from the qualitative evidence is not reflected in the draft guidelines. The guidelines needs to be a more accurate reflection of what the evidence has found.	Thank you for your comment. There was evidence of both positive and negative experiences with CBT emerging from the qualitative findings. Both types of experiences have been acknowledged in the committee's discussion and interpretation of the evidence (Evidence review G).

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					As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). After reviewing the evidence available, together with their clinical experience, the committee agree that CBT is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation has been made to offer CBT to ensure this will be the case. The discussion of how the evidence informed the recommendations is detailed briefly in the rationale in the guideline, where the committee's consideration of people's positive experiences of CBT have also been acknowledged and in more detail in the discussion of the evidence sections in Evidence review G.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G		Table 72	We are pleased to see the positive reports which outweigh the negative reports. This is not reflected in the guidance. We believe the guidelines should reflect the evidence found by the NICE synthesis team	Thank you for your comment. There was evidence of both positive and negative experiences of interventions emerging from the qualitative findings. Both types of experiences have been acknowledged in the committee's discussion and interpretation of the evidence (Evidence review G). As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the

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					types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The evidence was therefore not the only information that the committee has considered, and it is important for all the information that underlined the committee's decision making to be reflected in the guidance. The discussion of how the evidence informed the recommendations is detailed briefly in the rationale in the guideline, where the committee's consideration of people's positive and negative experiences have also been acknowledged and in more detail in the discussion of the evidence sections in Evidence review G.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G		Table 78 Row 10	This table is based on one paper with only 13 patients, the very large majority of whom made a recovery. The words "some experienced an instant healing; some experienced a gradual improvement and some did not find the treatment helpful does not reflect the paper where the majority found the treatment helpful. This table does not reflect the themes from the paper and needs to be reviewed	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have across the evidence. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning process', Peer support', 'Goal setting', 'Practice and application' highlight aspects of the interventions that people had found helpful and the 'Relationship with the therapist' where as you state descriptions of staff as positive and encouraging have been included together with accounts of people who had a less positive experience. However, this was not representative of the

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					experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case and did not find the intervention helpful. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G		Table 80	Describes positive findings from children as well as issues experienced over limiting activities. This is not reflected currently in the guidance.	Thank you for your comment. There was evidence of both positive and negative experiences with interventions such as GET including reports of reductions in fatigue and tiredness, improved sleep but also experiences of no difference with treatment, uncertainty, or lack of impact, often related to school and cognitive activities emerging for children and young people as well as challenges of limiting activities as you mention. Positive experiences have been acknowledged in the committee's discussion and interpretation of the evidence (Evidence review G) but this was not the only information considered in decision making and it is important for all the

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					information that underlined the committee's decision making to be reflected in the guidance. The committee also noted there was no clear picture of benefit from the quantitative evidence, and the evidence was inconsistent. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Considering the worsening of symptoms reported in the qualitative evidence as well as their experience of the effects when people exceed their energy limits, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been reflected in the recommendations.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	009 - 061	Table 2	The committee has excluded studies or down graded studies on the basis of "serious population indirectness." We believe this is because these studies did not describe whether participants had the symptom of Post Exertional Malaise or PESE. In the UK, this symptom is almost universal in patients accessing specialist services. This is evidenced in epidemiological papers (Collin and Crawley) where over 96% of UK patients had symptoms of post-exertional malaise. If the committee wishes to create a new definition, they should a) contact the authors and ask for a reanalyses of the data	Thank you for your comment. No studies meeting the inclusion criteria of the review protocol, which had been developed before systematic searches for the evidence were conducted, were excluded due to concerns over population indirectness. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to

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				using PEM as part of the eligibility criteria, or b) exclude information from the committee (unless they can prove they have ME/CFS using the new definition) and exclude data from qualitative studies/personal opinion/survey data unless they can also demonstrate that they included the definition. Otherwise, to apply a definition to part of the evidence base, and not to another part of the evidence base is a serious form of bias, and suggests the committee selected the evidence to suit the opinions expressed in the introduction before the evidence was reviewed.	trials do not experience PEM they just don't know if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	062 - 071	Tables 3-7	The committee has downgraded trials because of the new definition but described the outcomes in these tables. As an example, these show positive benefit for thousands of patients in terms of fatigue. **However, this data synthesis does not**	Thank you for your comment. As with all NICE guidelines the committee used its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate

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				appear in the guidance. The committee has then described outcome data from qualitative studies, and the committee opinions without using the same definition as they required for trials (requiring PEM). In effect, the committee have used lower levels of evidence as it was consistent with their opinions and ignored the published evidence base. The committee should include all the evidence in the guidance. Otherwise, it appears they are excluding evidence based on the beliefs of a minority of committee members rather than a very substantial number of patients.	strength of the recommendation. The committee considered many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Studies were included if they met the criteria outlined in the review protocol. No studies were excluded on the basis of PEM reporting or diagnostic criteria used. The committee consider PEM to be an essential feature for a diagnosis of ME/CFS. This causes difficulty in interpreting the evidence from trials that do not use a criteria that has PEM as an essential feature (and therefore a 100% ME/CFS population) or where the percentage of people with PEM are not reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported, and numbers of people with PEM are rarely reported in the trials. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. The same approach was taken for the

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					qualitative review on experiences of interventions. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendix G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	253 -254	Both pages	This section is titled: **Narrative summary of review findings for children/young people who have had the Lightning process.** In this study, all the children and young people were offered specialist medical care, and half were randomised to receive the Lightning Process as well. In this narrative synthesis, many of the findings in the children and young people who received and are **discussing Specialist Medical Care and NOT to the Lightning Process** (for example line 25 "an informative team of experts". …tailored specialist medical care"….line 39 the CFS/ME service….and so on) This section therefore has the wrong title. If the reviewers are going to extract data in this way, they need to be completely clear which treatment participants are talking about.	Thank you for your comment. We agree with what you have raised. This study by Beasant, aimed was to understand the experiences of accessing and using a specialist service and it was unclear to which intervention arm the findings related to and findings seemed to be more relevant to the specialist service in general rather than the Lightning Process . This limited the extent to which conclusions about the Lightning Process could be drawn from the study. The study still met the protocol as it included participants from the SMILE trial, some of whom had received the Lightning Process, depending on which arm they were randomised to and timelines; however, this was not clear from the information reported in the paper. The focus of the paper on specialist services rather than the Lightning Process and the impact of this in the applicability of the findings has been brought to the attention of the committee and has been acknowledged in the discussion section of Evidence review G and it has also impacted the assessment of confidence in the findings emerging from this study.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	324 -325	All	In the Qualitative review of experiences of CBT. Please separate out the experiences of those with clinically diagnosed ME/CFS (the published data) who will have fulfilled the committee's definition of ME/CFS (with PEM) from the survey data or data collected in Appendix 1. Because this data is not from children with clinically diagnosed ME/CFS. Please can you also separate out children and young people from adults. This data clearly shows that the children and young people	Thank you for your suggestion. The committee agree that PEM is a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just don't

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				were positive about CBT and some of the qualitative data from adults was negative. This data from adults may have been from patient surveys so it is important to know if the data was from those with clinically diagnosed ME/CFS (and PEM as defined by the committee) or from patients clinically diagnosed with ME/CFS.	know if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. Evidence available for adults and children and young people has been stratified in the Qualitative review of experiences of interventions. After undertaking the PEM reanalysis, there was uncertainty

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					about the population in the studies included in the evidence for the experiences of CBT in adults and in children and young people. Thus, findings have not been separated further according to the inclusion of PEM.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	005	8-13	We do not feel it is appropriate for the introduction to start off with an answer. The guidance cannot assume there is no known cure until they have reviewed the evidence. It is unusual for the introduction to state that GET and CBT are controversial, when in fact they do not present evidence for this. This suggests the guideline committee was biased against these treatments before they started to write the guidance. The introduction should be neutral until the evidence has been reviewed.	Thank you for your comment. This is the introduction to the review and provides brief background information.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	005	13	"People with ME/CFS have reported worsening of symptoms with GET and no benefit from CBT". Again, the introduction should be more neutral. It could instead say, over 3000 patients have taken part in RCTs which have shown benefit, hundreds of children and young people have taken part in trials and qualitative research studies which have shown benefit. This statement is inconsistent with the evidence presented in the synthesis. Either the introduction should discuss **all the evidence, or none** rather than a biased version	Thank you for your comment. The wording has been changed to 'some people' to reflect that this does not apply to all people with ME/CFS.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	007	29	It appears that studies that did not include every outcome defined as critical (including mortality) were excluded. (i) Given how vulnerable patients with ME/CFS are, it would be impossible to conduct a treatment trial and measure all of these critical outcomes. This is particularly true for "specified exercise performance measures" and "cognitive function". This is therefore an inappropriate exclusion criteria.	Thank you for your comment. Individual studies were only excluded if they reported none of the outcomes listed in the review protocol. No studies were excluded for not reporting all of the outcomes, and if this were the case, no studies would have been included in the review. With regards to Cochrane reviews, three potentially relevant Cochrane reviews were identified but were not included in this

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				There is clear evidence (papers by Parslow) of the important outcome measures in children, described by children and young people which has been published, and the guideline committee should use these for children and young people.	review due to differences in the review protocols and methodologies. All included studies within these reviews were cross-checked for eligibility for inclusion in this review. Exclusion reasons are now clarified below and in the report. Larun 2017: This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity levels, return to school/work, exercise performance measures, and mortality. However, all studies included in this Cochrane review were included in our review. Also note that Cochrane has acknowledged issues with this review in terms of the methods used and the population definition and they plan to conduct a full update of this Cochrane review. Price 2008: This Cochrane review looked at CBT versus usual care or other interventions in adults with 'CFS'. The main reasons for exclusion are as follows: Studies with mixed populations where at least 90% of participants had a primary diagnosis of CFS were included. The committee agreed it was important that all participants in included reviews were diagnosed with ME/CFS. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the

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					review): cognitive function, pain, sleep quality, activity levels, exercise performance, and mortality. It is also worth noting that Cochrane has stated that this review is no longer current and should not be used for clinical decision making. Adams 2009: This review did not include any studies, as no studies that met all of the inclusion criteria were identified. An updated version of this review published in 2018 was withdrawn from publication. (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD006348.pub3/full
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	007	29	It also appears that the committee down graded published papers because they did not believe patients had ME/CFS. It appears that this is because the committee changed the definition for ME/CFS to include Post Exertional Malaise. However, it appears that the committee didn't use this definition for other forms of evidence (for example appendix 1 focus group, or the qualitative data or the opinions of the committee). This represents a form of bias. In addition, the evidence synthesis team did not check with the authors of the papers to find out if it was possible to identify the number of participants who would have fulfilled the committees new definition. If the committee had chosen a reasonable set of core outcomes, and contacted the authors about participants, these important reviews would not have been excluded or downgraded. This is important as these reviews represent the outcomes and views and risks of thousands of patients which have been systematically and unfairly excluded. This is a form of bias which undermines the guidelines.	Thank you for your comment. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence.

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					After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	198	28	Cost effectiveness suggests multidisciplinary rehabilitation was not cost effective compared to CBT and yet the guidance does not discuss this.	Thank you. 'Multidisciplinary rehabilitation' is a specific intervention that was not found to be cost effective. It is evident from the recommendations that the committee are not advocating this intervention. However, a "do not do" recommendation was not made, since there was no evidence that it is harmful to patients. This comment has now been added to "The committee's discussion and interpretation of the evidence".
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	198	43	The economic analyses demonstrates that GET is also cost effective, but this evidence has not appeared in the guidance. It therefore appears that evidence uncovered by NICE has been ignored by the guideline committee. There is a risk of bias if some evidence synthesis is included and some excluded based on the committees personal opinions	Thank you. At £23,000 per QALY gained, GET was not unequivocally cost effective. If something is to be recommended by NICE that is above £20,000 per QALY gained then there ought to be additional reasons to recommend it, such as the benefit in terms of quality of life has been under-estimated or that the intervention is particularly innovative. It is not clear that these

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					apply in this case. Conversely, the qualitative evidence and expert opinion reported that a number of patients perceived that they had been harmed by GET. This contributed to the committee's decision not to recommend GET.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	222	8-9	"most people reported high levels of satisfaction with treatment and in some cases felt that the treatment exceeded expectations." This is based on the qualitative data, however this finding is not reflected in the guidance. In addition, the evidence synthesis constantly refers to treatment (which we agree with). The word treatment should be used in the guidelines as this is consistent with the evidence synthesis.	Thank you for your comment. We agree your suggestion on the word treatment. After considering stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from recommendations suggesting interventions should not be offered as a 'treatment or cure' to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However, while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. The variability of positive and negative experiences with CBT, GET and other interventions examined in the current review, have been captured by the evidence summarised under different findings relevant for each intervention and have been discussed in the main body of the current report (see the committee's interpretation and discussion of the evidence, Evidence review G). The particular experience cited in the comment has been included in the 'Qualitative review of experiences of CBT' in the Committee's discussion and interpretation of the evidence. Experiences such as this have been taken into account by the committee who after reviewing the evidence available, together with their clinical experience, agree that CBT is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation has been made to offer CBT to ensure this will be the case.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	222	Line 4	It is not clear, which evidence is used in each part of the synthesis. As some of the evidence has come from clinical services with a confirmed diagnosis of ME/CFS and where patients are known to have PEM, and some has come from patient groups (where <40% will have ME/CFS (see Brimmer et al. BMC Research Notes 2013, 6:309])) we recommend the guidance identifies where the evidence has been extracted from.	Thank you for your comment. With the large amount of evidence included in the evidence report we appreciate it becomes very difficult to distinguish which studies have contributed to different findings. The quantitative studies relevant to each GRADE table have now been specified at the end of the table. Qualitative studies contributing to each review finding can also be determined from the references included in the 'Qualitative evidence synthesis section' as well as from the table footnotes in the 'Qualitative evidence summary' in Evidence review G. We agree that there often limitations in the recruitment strategy and inclusion of participants in studies and we carefully assessed these across both the quantitative and the qualitative evidence and accounted for potential limitations in the risk of bias assessment of the individual studies which then contribute to the overall assessment of confidence/ quality of the evidence emerging from them. The assessment of limitations in each study can be found in the Qualitative evidence tables (Appendix D, Evidence review H). Please note that after considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns

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					over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. This has also resulted in downgrading our confidence in the findings where diagnosis had been.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	230	15-16	The review authors do not appear to have reflected on the fact that much of this data has come from patient organisations where the diagnosis is one of patient self report. This reduces our confidence in the findings to low as <40% of patients in patient support groups have ME/CFS [see Brimmer et al. BMC Research Notes 2013, 6:309]]	Thank you for your comment. We agree that there often limitations in the recruitment strategy and inclusion of participants in studies and we carefully assessed these across both the quantitative and the qualitative evidence and accounted for potential limitations in the risk of bias assessment of the individual studies which then contribute to the overall assessment of confidence/ quality of the evidence emerging from them. The assessment of limitations in each study can be found in the Qualitative evidence tables (Appendix D, Evidence review H). Please note that after considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of

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					participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. This has also resulted in downgrading our confidence in the findings where diagnosis had been self-reported.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	254	38	The narrative summary concludes that for children, exercise is enjoyable. "most were positive about GET". However, this has not reflected in the guidance. This important information may reflect the differences between children and adults. We believe this should be in the guidance and the guideline committee should separate recommendations for children and adults.	Thank you for your comment. There was evidence of both positive and negative experiences with GET including reports of reductions in fatigue and tiredness, improved sleep but also experiences of no difference with treatment, uncertainty, or lack of impact, often related to school and cognitive activities emerging for children and young people. Positive experiences have been acknowledged in the committee's discussion and interpretation of the evidence (Evidence review G). The committee also noted there was no clear picture of benefit from the quantitative evidence, and the evidence was inconsistent. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The evidence was therefore not the only information

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					that the committee has considered, and it is important for all the information that underlined the committee's decision making to be reflected in the guidance. Considering the worsening of symptoms reported in the qualitative evidence as well as their experience of the effects when people exceed their energy limits, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been reflected in the recommendations and based on clinical experience the committee concluded the same considerations were also applicable to children and young people.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	255	37	The syntheses team has used the wrong wording. "Pacing benefits" is incorrect. This data is about Graded Exercise Therapy. Pacing should be changed to Graded Exercise Therapy. These positive findings should be reflected in the guidance.	Thank you for your comment. The findings summarised under this theme have been related to pacing in the study they emerge from. All the information extracted from the study can be found in the relevant Qualitative evidence table in Appendix D, Evidence review G. However this finding is indeed part of the evidence for Graded exercise. There was evidence of both positive and negative experiences with GET. Positive experiences have been acknowledged in the committee's discussion and interpretation of the evidence (Evidence review G). The committee also noted there was no clear picture of benefit from the quantitative evidence, and the evidence was inconsistent. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations,

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					resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The evidence was therefore not the only information that the committee has considered, and it is important for all the information that underlined the committee's decision making to be reflected in the guidance. Considering the worsening of symptoms reported in the qualitative evidence as well as their experience of the effects when people exceed their energy limitslimits, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been reflected in the recommendations and based on clinical experience the committee concluded the same considerations were also applicable to children and young people.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	256	1	The syntheses team has used the wrong wording "pacing challenges". This is Graded Exercise Challenges. The title needs to be changed. None of the children had pacing. This is important feedback that in children, we need to reduce excessive physical exercise to keep them safe. This is how specialist paediatric services deliver GET. This should be reflected in the guidance.	Thank you for your comment. The findings summarised under this theme have been related to this aspect of the intervention in the study they emerge from. All the information extracted from the study can be found in the relevant Qualitative evidence table in Appendix D, Evidence review G. However, this finding is indeed part of the evidence for Graded exercise. There was evidence of both positive and negative experiences with GET. Positive experiences have been acknowledged in the committee's discussion and interpretation of the evidence (Evidence review G). The committee also noted there was no clear picture of benefit from the quantitative evidence, and the evidence was inconsistent. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of

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					the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The evidence was therefore not the only information that the committee has considered, and it is important for all the information that underlined the committee's decision making to be reflected in the guidance. Considering the worsening of symptoms reported in the qualitative evidence as well as their experience of the effects when people exceed their energy limits, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. This has been reflected in the recommendations and based on clinical experience the committee concluded the same considerations were also applicable to children and young people.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	317	36	" the committee agreed that a population diagnosed with such criteria may not accurately represent the ME/CFS population." There is no evidence that this is the case. The epidemiological studies for the UK (Collin et al) clearly describe how "*Symptoms of post-exertional malaise (UK 96.5%, NL 87.5%), cognitive dysfunction (UK 94.1%, NL 92.1%), and sleep disturbance (UK 95.3%, NL 96.8%) occurred in almost all patients in both cohorts. These 3 symptoms were excluded from the primary and replication analyses, because they did not contribute to differentiation of latent classes.*" In these papers, the prevalence of PEM was so close to being universal	Thank you for your comment. The committee agree that PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM, they just don't know if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty. As

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				in this population, further analyses was not possible. Therefore NICE should conclude that > 96% of patients in specialist services in the UK will have PEM. This should change the way NICE considers data from specialist services given the definition NICE has created.	such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. To adequately account for concerns over PEM across studies the committee agreed this criterion would be applicable to all studies regardless of whether recruitment was from a specialist service as it there was a lack of information regarding the criteria used for diagnosis, the committee could not be sure about the relevance of the population. Through the PEM reanalysis the committee

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					aimed to ensure concerns limiting the relevance of the population in the studies have been addressed and considered in decision making.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	317	36	In addition, the studies in which the evidence was "down graded" because of this change in definition, have data on PEM or PESE. Almost all or all participants of these trials had PEM or PESE. The guidance group should have either used accepted definitions, or asked the authors to define how many participants had PEM/PESE or asked for a reanalyses.	Thank you for your comment. The committee agree that PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM, they just don't know if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding

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					applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. To adequately account for concerns over PEM across studies we looked for information regarding PEM across the included, excluded studies and publications associated with the included studies; but where there was a lack of published data with this information, the committee could not be sure about the relevance of the population. Through the PEM reanalysis the committee aimed to ensure concerns limiting the relevance of the population in the studies have been addressed and considered in decision making.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	317	36	As far as we can see, this definition (requiring PEM) was not used for the qualitative data or the survey data or to be sure those on the committee had ME/CFS. The patient surveys did not have clinician confirmed diagnosis of ME/CFS so are likely to be much more heterogenous. Excluding the evidence from randomised controlled trials and including survey data without the same stringent case definition appears to be a risky and biased process.	Thank you for your comment. No evidence meeting the inclusion criteria of the review protocol has been excluded. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the studies included in the quantitative and the qualitative evidence review, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not

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					be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. To adequately account for concerns over PEM across studies we looked for information regarding PEM across the included, excluded studies and publications associated with the included studies; but where there was a lack of published data with this information, the committee could not be sure about the relevance of the population. Through the PEM reanalysis the committee aimed to ensure concerns limiting the relevance of the population in the studies have been addressed and considered in decision making.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	317	40	"It was therefore agreed to downgrade the evidence for population indirectness." NICE should either use definitions in widespread use (rather than create a new definition and downgrade the trials), ask the authors for the percentage of participants who fulfil their new criteria or ask the authors to reanalyse the data rather than exclude the trials. The guideline committee should be consistent in their use of a definition across randomised controlled trials, qualitative studies and patient surveys.	Thank you for your comment. No evidence meeting the inclusion criteria of the review protocol has been excluded. The committee agree that PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM, they just don't know if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they

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					considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the studies included in the quantitative and the qualitative evidence review, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. To adequately account for concerns over PEM across studies we looked for information regarding PEM across the included, excluded studies and publications associated with the included studies; but where there was a lack of published data with this information, the committee could not be sure about the relevance of the population. Through the PEM reanalysis the committee aimed to ensure concerns limiting the relevance of the population in the studies have been addressed and considered in decision making.
Royal United Hospitals Bath	Evidence Review G	321	14	"In general, the committee placed greater weight on moderate confidence findings than low and very low confidence findings	Thank you for your comment. Guideline committees are formed to reflect as far as practically possible, the range of stakeholders

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NHS Foundation Trust				during discussion of the evidence, although they acknowledged that some lower confidence findings reflected their own experience and should not be disregarded." This sentence suggests the guidance is biased towards the committees experience rather than being based on the evidence. We believe the committee should have followed the evidence, and the outcome data and qualitative data that has been published. If they are to use their own experience, then we recommend NICE establishes if those on the committee have confirmed diagnosis of ME/CFS using the criteria created by NICE and pre-publish how they will interpret the data. This is particularly important for children and young people as their voices are not being heard as the evidence syntheses from the paediatric papers is not currently reflected in the guidelines.	and groups whose activities, services or care will be covered by the guideline. In addition to this, as with all NICE guidelines, recommendations were developed using a range of evidence and other sources of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. No findings were disregarded based on evidence quality but as with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee did not consider findings differently based on personal preference, but rather utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform their decision making. They may therefore place greater weight to a lower quality finding when this appears to be in line with what they see in their everyday encounters with people with ME/CFS, as these provide further support about the accuracy with which a finding represents the phenomenon of interest (i.e. the experience of people with ME/CFS). Evidence and evidence quality although very important, were not the only source of information informing decision making and the committee took great care to ensure

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					that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. The committee agree that the use of diagnostic criteria in the studies included in the evidence in important is this can determine the extent to which findings emerging from the studies are applicable to the review topic. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed to revisit the evidence for the intervention reviews, further

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					scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. Through the PEM reanalysis the committee aimed to ensure concerns limiting the relevance of the population in the studies have been addressed and taken into account in decision making.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	322	1	"serious adverse events were reported in one study with harm identified in the adaptive pacing group". This intervention is the same as energy management. It is different to GET and CBT. The fact that adverse events were not noted in this groups should be reflected in the guidelines.	Thank you for your comment. The committee discussion about the evidence for GET and CBT is in evidence review G and includes discussion on the benefits and harms. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. The energy management section of the guideline provides information on the principles of energy management and is clear

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					that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	323	26-32	The committee listed the negative but not the positive findings which can be found in the tables. The guidelines should reflect all the evidence (positive as well as negative findings).	Thank you for your comment. Guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. In addition to this, as with all NICE guidelines, recommendations were developed using a range of evidence and other sources of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. There was evidence of both positive and negative experiences of interventions emerging from the qualitative findings. Both types of experiences have been acknowledged in the committee's discussion and interpretation of the evidence (Evidence review G). As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what

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					recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The evidence was therefore not the only information that the committee has considered, and it is important for all the information that underlined the committee's decision making to be reflected in the guidance. The discussion of how the evidence informed the recommendations is detailed briefly in the rationale in the guideline, where the committee's consideration of people's positive and negative experiences have also been acknowledged and in more detail in the discussion of the evidence sections in Evidence review G.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	323	5	There is no evidence that pacing is the main management tool in the evidence synthesis, and little evidence that it is effective from trials or observational cohorts. The qualitative data that the committee used from patient surveys is unreliable because it is not clear if patients had a clinical diagnosis of ME/CFS or had PEM (which the committee required for trials. This is the committee's opinion and should be reflected with a degree of uncertainty in the guidelines.	Thank you for your comment. Guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. In addition to this, as with all NICE guidelines, recommendations were developed using a range of evidence and other sources of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. When making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering

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					many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Pacing was a component of various interventions examined both in the quantitative and qualitative studies. Apart from the findings emerging from those studies, the committee were able to utilise their clinical experience to inform their decision making. The committee agreed that PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM, they just don't know if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied

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					differently across the studies included in the quantitative and the qualitative evidence review, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. To adequately account for concerns over PEM across studies we looked for information regarding PEM across the included, excluded studies and publications associated with the included studies; but where there was a lack of published data with this information, the committee could not be sure about the relevance of the population. Surveys where the percentage of PEM was self-reported were also downgraded for concerns over relevance as self-reporting of PEM was not considered to adequately fulfil the PEM criterion set by the committee. Through the PEM reanalysis the committee aimed to ensure concerns limiting the relevance of the population in the studies have been addressed and considered in decision making.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	324	27-30	Line 27 – 28 is correct. There is benefit in fatigue, physical function, return to school and school attendance. Line 30 is incorrect "no clinically important difference was seen for return to school". Please correct this	Thank you for highlighting this. Benefit was seen for return to school (proportion of classes attended) for web-based CBT. No clinically important difference was seen for return to school (hours attended) for individual face-to-face CBT. The review has now been amended to clarify this.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	325	39	Overall – Cognitive behavioural therapy. The committee have discussed positive clinical and health economic data for children and entirely positive qualitative data. None of the data presented in the evidence review suggests anything other than positive effects of CBT for children with ME/CFS. The positive evidence (both in the trials and the qualitative data) should be reflected in the guidance.	Thank you for your comment. There was evidence of both positive and negative experiences with CBT emerging from the qualitative findings, including reports of reductions in fatigue and tiredness, improved sleep but also experiences of no difference with treatment, uncertainty, or lack of impact, often related to school and cognitive activities emerging for children and young people as well as challenges of limiting activities as you mention. Positive experiences have been acknowledged in the committee's discussion and interpretation of the evidence (Evidence review G) but this was not the only information considered in decision making and it is important for all the information that underpinned the committee's decision making to be reflected in the guidance. The committee also noted there was no clear picture of benefit from the quantitative evidence, and the evidence was inconsistent. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Please note that after reviewing the evidence available, together with their clinical experience, the committee agree that CBT is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation has been made to offer CBT to ensure this will be the case. The discussion of how the evidence informed the recommendations is detailed briefly in the rationale

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					in the guideline, where the committee's consideration of people's positive experiences of CBT have also been acknowledged and in more detail in the discussion of the evidence sections in Evidence review G.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	327	48	"in the committees experience CBT based interventions in young children"…..the conclusions that follow are <u>evidence of the lack of experience on the committee for delivering CBT for</u> children with ME/CFS. Did the committee seek advice from a paediatric ME/CFS specialist psychologist who has experience in delivering CBT for children with ME/CFS? If not, the guidance committee needs to consider expert opinion from those who have experience on how these interventions are delivered and what they are in different age groups or the guidance should be clear that they did not have this experience. If the guideline committee did NOT have this experience (specialist CBT work in children with ME/CFS) they should not use this experience to comment on delivering treatment.	Thank you for your comment. Guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. In addition to this, as with all NICE guidelines, recommendations were developed using a range of evidence and other sources of evidence, including that from, published peer review quantitative and qualitative evidence; a call for evidence for unpublished evidence (studies identified meeting the protocol have been included in Evidence review G), expert testimonies (see Appendix 3), and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature (Appendix 1: Children and young people; Appendix 2: People with severe ME/CFS) were also used to provide additional information to the committee (see ME/CFS methods chapter). These have also captured experiences of CBT. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).

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					There was evidence of both positive and negative experiences with CBT emerging from the evidence. Positive experiences have been acknowledged in the committee's discussion and interpretation of the evidence (Evidence review G) but this was not the only information considered in decision making and it is important for all the information that underpinned the committee's decision making to be reflected in the guidance. Please note that after reviewing the evidence available, together with their clinical experience, the committee agreed that CBT is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation has been made to offer CBT to ensure this will be the case. The discussion of how the evidence informed the recommendations is detailed briefly in the rationale in the guideline, where the committee's consideration of people's positive experiences of CBT have also been acknowledged and in more detail in the discussion of the evidence sections in Evidence review G.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	332	7	"The committee were aware that some children had been told not to discuss the therapy with their carer or parents". Our service does not offer the Lightning Process, however we assess over 500 Some children also try the Lightning Process outside NHS services. We believe the committee is mistaken. Children and young people are encouraged to talk to parents/carers and frequently they are present in the LP sessions. We believe it is important that NICE guidance reflects the reality of what happens, and not just the committee's views on what happen. It is important that NICE describes the truth, based on evidence or expert opinion.	Thank you for your comment. Guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. In addition to this, recommendations were developed using a range of evidence and other sources of evidence. When developing this guideline the committee considered evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The committee took great care to ensure that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed

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					briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Thank you for reporting the experience of people who have used your service. These have been considered by the committee who however cannot discount the negative experiences other people have had emerging from the qualitative evidence reviewed for the present guideline and concerns raised by the committee based on the evidence and their experience. After reviewing the evidence and considering the multiplicity of factors described above, the committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on

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					the principles of energy management and this therapy is at odds with these principles.
Royal United Hospitals Bath NHS Foundation Trust	Evidence Review G	333	11	Section Qualitative review of experiences of graded exercise therapy. The experiences of children and young people are very different to the experiences of adults. These should not be confused or described together. Please separate out the qualitative data for adults from the qualitative data for children and young people. There is good evidence that children and adults are different and their response to treatment shouldn't be confused. The tables and evidence review emphasise this difference. We need to hear the children's voice separately in the summary paragraphs and throughout.	Thank you for your suggestion. The discussion of findings relevant to Adults and children and young people have been separated under different headings in the qualitative review of experiences of graded exercise therapy.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	General	General	1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why. Encouraging all children with fatigue that has lasted longer than 4 weeks to be referred for assessment will be impossible to implement in either paediatric services or specialist paediatric ME/CFS services. It is likely to have unintended consequences on both the child, their family and other children as it will not be possible to appropriately triage patients and those who need urgent assessment and treatment will be delayed.	Thank you for your comment.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	General	General	2. Would implementation of any of the draft recommendations have significant cost implications? Yes. These guidelines will have significant cost implications as more children and young people will require treatment. Unfortunately, many of these children will get better	Thank you for your comment. The committee have now removed from the guideline reference to a provisional diagnosis of ME/CFS. For children, the duration of symptoms before diagnosis has not changed since the last guideline. The criteria for diagnosis is slightly stricter than in the

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				spontaneously but services will not be able to identify these children before assessment.	previous guideline. The committee have recommended referral to a specialist team to ensure that children and young people do not receive advice that would worsen their condition. The committee acknowledge that provision of specialist teams across the country will require investment in some areas. The committee anticipate that where children's symptoms resolve spontaneously, they will drop out of the system before or shortly after assessment by the specialist team.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	General	General	We believe NICE should have considered children separately from adults. Children are not the same as adults in terms of physiology, genetic risk or symptom presentation. NICE should have reviewed the epidemiological data before deciding to treat children the same as adults. For example: Chronic fatigue syndrome (CFS) or myalgic encephalomyelitis (ME) is different in children compared to in adults: a study of UK and Dutch clinical cohorts. Collin SM, Nuevo R, van de Putte EM, Nijhof SL, Crawley E.BMJ Open. 2015 Oct 28;5(10):e008830. doi: 10.1136/bmjopen-2015-008830. The evidence that children respond differently to treatment is also emphasised throughout the synthesis reviews conducted by NICE (and discussed in detail below).	Thank you for your comment. The committee agree that children are not the same as adults. Children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	027 - 028	Both pages	We are concerned about the statement "Do not advise people (page 27, line 21) with ME/CFS…… **any therapy based on physical activity or exercise** as a treatment or cure of ME/CFS." This is particularly important for children and young people. Our service provides assessment of over 500 new patient a year, and provides treatment to over 100 patients a week. In our experience, children and adolescents often want advice on physical activity and on exercise. This is important as over exercise, or the boom-bust pattern can maintain fatigue and disability (which the committee appears to agree with). This guidance is harmful as it may prevent children and young	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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				people accessing help when they need it. If a teenager or child is developing symptoms after physical activity, and wishes to have advice about this, we need to provide a programme based on stabilising physical activity, and making it safe. This recommendation is also inconsistent with other aspects of the guidance: (page 24, line 13) energy management which state: energy management is a self management strategy that can be applied to any activity. Page 28, line 12 discusses offering physical activity to those who want it. Our experience with children and young people is reflected in the evidence synthesis (Evidence review 7). Our recommendation is that the guidelines are changed to give patients with ME/CFS choice about accessing treatments. We also recommend that the guidance separates children and young people from adults with ME/CFS.	
Royal United Hospitals Bath NHS Foundation Trust	Guideline	007	1	NICE has recommended that people with severe or very severe ME/CFS "need a low-stimulus environment, for example a dark quiet room with interaction at a level of their choice." This advice is not differentiated between children and adult. However, *evidence* suggests that such sensory deprivation in combination with physical inactivity may have detrimental effects on health, and strongly increase the risk of disability (cf. for instance Khan & Khan, 2020; and Park et al, 2020). We are concerned that this recommendation will increase harm to patients.	Thank you for your comment. This section raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these symptoms and the support that may be needed to manage them, in this case hypersensitivity. The committee agreed that these recommendations could apply to children and young people with severe or very severe ME/CFS. The committee note that the level of support needed is individual to the person and agreed collaboratively as part of their personalised care and support plan with the health and social care professionals

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					involved in their care. An assessment of benefits and harms would be part of this.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	007	1	The guidance should separate adults from children for this recommendation (that patients with severe ME/CFS "need a low stimulus environment"). We are particularly concerned about children/adolescents, in whom, mental and social activities are pivotal for a normal development. For children and young people, this can be particularly problematic given their developmental and social needs. We are concerned that this is recommendation is unsafe.	Thank you for your comment. This section raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these symptoms and the support that may be needed to manage them, in this case hypersensitivity. The committee agreed that these recommendations could apply to children and young people with severe or very severe ME/CFS. The committee note that the level of support needed is individual to the person and agreed collaboratively as part of their personalised care and support plan with the health and social care professionals involved in their care. An assessment of benefits and harms would be part of this.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	007	7	Re: managing "sensitivity to touch". NICE's recommendations should include alternatives that are in standard use such as desensitisation or refer to the NICE guidance on pain management.	Thank you for your comment. The management of symptoms section of the guideline includes pain and referral to specialist pain services if appropriate.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	007	11	"unable to eat and digest food easily". This could be a red flag to other disorders. There is no evidence that this is a symptom of ME/CFS particularly in children. We are concerned that this is dangerous and may lead to other disorders being missed. NICE should recommend a detailed assessment to exclude other gastroenterological diseases or indeed eating disorders.	Thank you for your comment. Taking into account the range of stakeholder comments about the location in the guideline of this section the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. In response to your comment this now means that the criteria for suspecting and diagnosing ME/CFS and the assessment and care planning section precedes this recommendation providing clarity about the symptoms that are related to a diagnosis of ME/CFS and the importance of excluding and identifying other diagnoses.

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					The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist with ME/CFS and these should be investigated and managed in accordance with best practice.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	024	4	"be aware there is no current treatment or cure for ME/CFS." This is a confusing and potentially harmful statement. For example, section 1.11.4 describes how to establish an individual activity pattern (which we agree with). This is a form of treatment. We agree that none of them are guaranteed to be 100% effective. However, there is no evidence that there is "no cure" and NICE has not provided evidence that there is "no cure". We recommend this sentence is changed to "there is no current treatment that is guaranteed to be 100% effective". This is true for al treatment approaches and is less confusing.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. However the committee agree there currently isn't a cure for ME/CFS and it is important that people with ME/CFS are aware of this. For this reason, the committee have not further edited the recommendation.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	024	10	We recommend that the guidelines change "it is not curative" to "it is not always curative". The committee does not have sufficient evidence to say it is never curative.	Thank you for your comment. The committee agreed to keep, 'is not curative' at the beginning of the recommendation. In the rationale for managing ME/CFS the committee outline why it is important that it is clear there are not any cures for ME/CFS. In line with that it is appropriate to keep here that energy management is not curative.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	028	10	Re the statement: "Do not offer people with ME/CFS therapies derived from osteopathy, life coaching and neurolinguistic programming (for example the Lightning Process)." This sentence is in the wrong place as the Lightning Process is not based on exercise or physical activity. The Lightning Process is a psychological/coaching approach not an exercise based approach.	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer people with ME/CFS therapies based on the Lightning Process'.

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					The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H) After considering the stakeholder comments the recommendation on the Lightning Process has been moved to a separate subsection in the symptom management for people with ME/CFS section of the guideline.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	028	10	This sentence is not consistent with the ME/CFS evidence synthesis (Evidence review 7) This paper (https://bpspsychub.onlinelibrary.wiley.com/doi/abs/10.1111/j.2044-8287.2012.02093.x) was included in the evidence synthesis and describes how 7 children improved and 2 did not. The randomised controlled trial by our group (The SMILE trial, Crawley et al) showed significant clinical benefits. In addition, the ME association survey in 2010 described 25.7% greatly improved and 18.8% improved. The evidence synthesis does not provide sufficient evidence to "not offer" the Lightning Process. Much of the evidence provided for this recommendation appears to be based on the personal opinion of the committee not on the NICE evidence synthesis.	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer people with ME/CFS therapies based on the Lightning Process'. The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H) The NICE Policy on declaring and managing interests for NICE advisory committees sets out the processes for : • what interests need to be declared and when • how declared interests should be recorded • when a declared interest could represent a conflict of interest and the action that should be taken to manage this. As with any other guideline this Policy has been applied to this guideline. The Interests Register for the committee is published on the NICE website (https://www.nice.org.uk/guidance/indevelopment/gid-ng10091/documents) . The register has been updated

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					throughout the development of the guideline and includes the decisions and actions made on the interests declared.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	032	21	There are no paediatric dieticians who specialist in ME/CFS. This recommendation will therefore deny children access to dieticians. We suggest changed to "refer to a paediatric dietician".	Thank you for your comment. The committee agree there is a lack of paediatric dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The recommendation has been reworded to describe paediatric dietician as a 'paediatric dietician who has a special interest in ME/CFS', the committee recognised that currently paediatric dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are paediatric dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	033	4	There are no paediatric dieticians who specialist in ME/CFS. This recommendation will therefore deny children access to dieticians. We suggest changed to "refer to a paediatric dietician".	Thank you for your comment. The committee agree there is a lack of paediatric dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The recommendation has been reworded to describe paediatric dietician as a 'paediatric dietician who has a special interest in ME/CFS', the committee recognised that currently paediatric dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are paediatric dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better.

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Royal United Hospitals Bath NHS Foundation Trust	Guideline	034	5	There is no evidence that CBT is NOT curative, just as there is no evidence that it cures everybody. This should be changed to "there is no evidence that it is curative, or that there is limited evidence that it is curative." In children, there is evidence to suggest children are more likely to recover if they have CBT and this is another example of why the guidelines should separate out the guidance for children and adults.	Thank you for your comment. After considering the range of stakeholder comments the first recommendation in this section has been edited to remove the word treatment. The committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. The recommendation now starts with, 'explain to people with ME/CFS that cognitive behavioural therapy (CBT) may help them to manage their symptoms but it is not curative'
Royal United Hospitals Bath NHS Foundation Trust	Guideline	034	11	The statement here of "potential benefits and risks" is not consistent with the evidence synthesis which did not provide evidence of risks for CBT. This seems more appropriate as a guiding statement. If the guideline committee want to have a statement like this, they should have it for all the recommendations (activity management, dietetic advice and so on).	Thank you for your comment. It is good practice to discuss the risks and benefits of any intervention and CBT is no exception. This is one of the reasons it is important that CBT is only delivered to people with ME/CFS by healthcare professionals with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. They will be aware of the risks for the person and able to ensure the person with ME/CFS makes an informed choice.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	036	14	We disagree with merely referring children and young people to the same treatment as for depression for the following reasons: Children with ME/CFS and depression are not the same as children with depression. For example, (as the guidance defines) they are not able to function cognitively at the same level. The approach is different, as treatment for depression uses behavioural activation which contrasts with your recommendations here. For evidence on this see the papers by Loades and Crawley. Just giving children standard	Thank you for your comment. This section links to related NICE guidance on co-existing conditions. The first two recommendations in this section advise that when managing coexisting conditions in people with ME/CFS, the recommendations in the sections on principles of care for people with ME/CFS, access to care and energy management should be taken into account.

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				depression interventions is likely to be unhelpful, and possibly make their ME/CFS worse. As there is now sufficient evidence on this, we recommend the NICE guideline group considers further work (with child psychiatrists) on this important group of children and young people.	
Royal United Hospitals Bath NHS Foundation Trust	Guideline	036	14	In addition, the guidance should differentiate between those with co-morbid depression and those with depression as an exclusionary diagnosis which the guidance does not appear to do.	Thank you for your comment. This section links to related NICE guidance on co-existing conditions. Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms. Evidence review D- Diagnosis includes comprehensive lists of differential and co-existing conditions that are commonly associated with ME/CFS.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	039	27	Offering a review with children only every 6 months will not satisfy the home-schooling requirement for reviews in all regions of the UK	Thank you for your comment. The recommendation is 'at least every 6 months' allowing for more frequent reviews if necessary.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	042	10	The definition of exercise is confusing and could be detrimental for children. The guidance has defined Exercise as "planned, structured, repetitive and purposeful activity focused on improvement or maintenance of one or more components of physical fitness." This definition may apply to adults but it is not appropriate for children and young people as it is not a definition that is used in childhood, or in paediatric services. Children exercise all the time, at school, in their breaks and when they are at home. The main criticism of treatment programmes for ME/CFS for children (as discussed in the Evidence review 7) is in making children reduce exercise.	Thank you for your comment. **The Definitions for the terms 'Exercise' and 'physical activity' are based on those used by the World Health Organisation and are widely understood. We are not aware of any source that uses the term 'exercise' to describe break time play at school, which is more correctly described as either 'active play' or 'active recreation'.'**

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				NICE can choose to define a treatment programme in this way, but cannot define exercise in this way for children as it will provide extensive confusion for those providing services as well as parents and carers because it is so different to the reality for children.	
Royal United Hospitals Bath NHS Foundation Trust	Guideline	043	21	The guideline committee appear to have redefined Orthostatic intolerance incorrectly as: "Orthostatic intolerance is defined as "the inability to regulate blood pressure and cerebral blood flow when upright, usually when standing, but it can also occur when sitting. The guideline committee should use the correct definition to avoid confusion and potentially harm to patients. **A correct definition** (from Quantitation of Autonomic Impairment. PHILLIP A. LOW, CHRISTOPHER J. MATHIAS, in Peripheral Neuropathy (Fourth Edition), 2005 is: "Orthostatic intolerance (OI) is defined as the **development of characteristic symptoms while standing, which are significantly improved by recumbency**	Thank you for your comment. After considering the stakeholder comments the definition has been edited to, ''A clinical condition in which symptoms such as light-headedness, near-fainting or fainting, impaired concentration, headaches, and dimming or blurring of vision, forceful beating of the heart, palpitations, tremulousness, and chest pain occur or worsen upon standing up and are ameliorated (although not necessarily abolished) by sitting or lying down. Orthostatic intolerance may include postural orthostatic tachycardia syndrome (a significant rise in pulse rate when moving from lying to standing) and postural hypotension (a significant fall in blood pressure when moving from lying to standing).
Royal United Hospitals Bath NHS Foundation Trust	Guideline	048	23	"These overarching principles will improve consistency of best practice and do not need any additional resources to deliver." Reducing the length of time a child has symptoms before getting a diagnosis, will require a very large increase in additional service provision. We recommend NICE conducts further assessments on the impact on the NHS before making this recommendation.	Thank you for your comment. The committee are not recommending reducing the length of time a child has symptoms before diagnosis. The reference to a provisional diagnosis has been removed.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	049	18	"Based on their experience, the committee decided that people should be given a provisional diagnosis of ME/CFS if they have all the 4 key symptoms (debilitating fatigability, post-exertional symptom exacerbation, unrefreshing sleep and cognitive difficulties)." We believe the NICE guideline committee should use the evidence and not the experience of a small number of people. There is no evidence that this	Thank you for your comment. After considering the stakeholder comments on early diagnostic labels the committee have amended the wording to remove the recommendation on making a provisional diagnosis of ME/CFS**.** Diagnosis is now introduced at 3 months.

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				improves diagnosis. The only paper to have explored this is: Sullivan PF, Pedersen NL, Jacks A, Evengård B. Chronic fatigue in a population sample: definitions and heterogeneity.Psychol Med. 2005 Sep;35(9):1337-48. This paper shows that the number of symptoms are in a continuum and therefore this is an arbitrary decision. This is particularly important for children and young people. We believe this recommendation is not based on evidence and has the potential to be harmful.	
Royal United Hospitals Bath NHS Foundation Trust	Guideline	049	23	"for a minimum of 6 weeks in adults and 4 weeks in children and young people. The committee agreed it would be unusual for an acute illness, including a viral illness, to persist longer than 6 weeks in an adult and 4 weeks in a child or young person with all 4 key symptoms. They emphasised it is the combination and interaction of the symptoms that is critical in distinguishing ME/CFS from other conditions and illness." This recommendation is based on the experience of the committee (no evidence was presented in the evidence synthesis). However, (i) Epidemiological evidence provides the data showing a substantial spontaneous recovery rate in fatigue following infections, in particular during the first months after the preceding infectious event (Hickie I, Davenport T, Wakefield D, Vollmer-Conna U, Cameron B, Vernon SD, Reeves WC, Lloyd A. Post-infective and chronic fatigue syndromes precipitated by viral and non-viral pathogens: prospective cohort study. BMJ 2006; 333: 575-81. (ii) Labelling children and young people who are likely to get spontaneously better can be harmful. For example, it will prevent them entering some occupations (such as the armed forces in the UK).	Thank you for your comment. After considering the stakeholder comments including those on the risk of early diagnostic labelling, the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 6 weeks -'Provisional' diagnosis has been deleted. The committee agreed that the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. • Further investigation/differential diagnoses. Throughout the section on suspecting ME/CFS the committee have recommended that investigations should be done to exclude other diagnoses and this should continue where ME/CFS is suspected. They have now added some examples of tests to be done. If in any doubt specialist advice should be sought. The committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations.

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				(iii) There is some data that early diagnosis may increase the risk of long term disability, [Rob J Bakker [1], Elise M van de Putte, Wietse Kuis, Gerben Sinnema Effects of an educational video film in fatigued children and adolescents: a randomised controlled trial Arch Dis Child . 2011 May;96(5):457-60.] We believe NICE should use the evidence and not personal opinion in making recommendations, particularly when they have the potential to harm children.	Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Royal United Hospitals Bath NHS Foundation Trust	Guideline	049	23	Reducing the length of time required for a diagnosis will lead a large increase in ME/CFS cases that will overwhelm specialist services reducing the ability to triage and provide treatment for those that need it. This recommendation will increase referrals to paediatricians and specialist services.	Thank you for your comment. After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. Since the committee have now removed reference to a provisional diagnosis and made recommendations about testing for alternative conditions, the demand on paediatric and specialist services should not be so great. Furthermore, the

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					diagnostic criteria are slightly stricter than in the previous guideline.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	050	28-29	We disagree that the 4 different symptoms present will change the impact on services. The committee did not examine the symptom data from the services that was available to them. [See the Epidemiological studies from Collin and Crawley which describes the symptoms in UK patients accessing services. See also the Sullivan paper (reference above). There is no evidence that there is a change in symptoms for patients presenting early. There is evidence that many of these patients will get better spontaneously [Hickie paper, reference above]. The guideline committee is therefore making a recommendation that is not based on available evidence and has the potential to cause more harm than good. .	Thank you for your comment. The experience of the committee, which also reflects the experience of patients recorded in the qualitative evidence is that advice to exercise early in the course of their disease appeared to significantly deteriorate their symptoms. Therefore, the implication is that more appropriate management would improve outcomes. Text has been added to this section to clarify that referral to a paediatrician at 4 weeks is for further assessment to identify and exclude other conditions as well as to assess for ME/CFS.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	050	1	"the evidence and the committee/s experience suggested that managing symptoms early"…. Whilst it seems instinctive that offering help early is a good idea, we have looked carefully for evidence that early diagnosis and early intervention prevent patients getting worse and this is not the case for children and adolescents. We have examined this in in multiple epidemiological studies and trials and found no evidence in children that length of time to diagnosis is a predictor for outcome. In addition, there is one study in children to suggest that certain types of early intervention may be harmful [Rob J Bakker [1], Elise M van de Putte, Wietse Kuis, Gerben Sinnema Effects of an educational video film in fatigued children and adolescents: a randomised controlled trial Arch Dis Child . 2011 May;96(5):457-60.]. Children and adults are different. Please can the guideline committee either provide the evidence or change the recommendation for children as we believe this recommendation has the potential to be harmful. .	Thank you for your comment. **After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month.** The committee agree that children and adults are different and as such children need to be seen by a paediatrician after 4 weeks and then a paediatric specialist in ME/CFS if appropriate to receive the care that is best for them. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that advice prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term. In addition committee note that it is

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					important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and it would not cause harm to in the short term. The committee note that while clinicians are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement the guidance does not override the responsibility of healthcare professionals and others to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	050	23	We agree that this will increase the number who are referred to specialist services. We disagree that this will ensure they get better care. Suggesting children are referredl at 4 weeks will have a dramatic impact on services. This is likely to increase waiting time, and prevent triage for children and adolescents who need it. This could reduce the number of children who receive appropriate care and there is no evidence it will improve outcomes.	Thank you for your comment. After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	052	5-15	We agree with the committee (page 49 line 10 onwards) that there is no evidence for whether one criteria is better overall. And therefore, we disagree with the committee producing a new criteria and then using this to decide on which evidence to include. If the committee create a new diagnostic criteria, they should check whether this changes the evidence base by contacting authors before downgrading the evidence from trials and cohort studies. They should also apply the same diagnostic criteria to the qualitative data, and the patient survey data (where only approximately one third of patients will have ME/CFS [Brimmer et al. BMC Research Notes 2013, 6:309].	Thank you for your comment and information See evidence review D-diagnosis for the evidence and committee discussion on the diagnostic criteria. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS but the difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*.

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					As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. The committee no evidence that met the inclusion criteria for the review protocols was excluded. After considering the stakeholder comments the committee agreed to revisit the quantitative and qualitative evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population > 95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.)
Royal United Hospitals Bath NHS Foundation Trust	Guideline	053	2	"Earlier access to appropriate advice and care could prevent disease progression." There is no evidence for this. It could also overwhelm services unnecessarily as many will get spontaneously better within the first three months, it is also possible that this has a negative impact on disease progression (see Hickie I, Davenport T, Wakefield D, Vollmer-Conna U, Cameron B, Vernon SD, Reeves WC, Lloyd A. Post-infective and chronic fatigue syndromes precipitated by viral and non-viral pathogens: prospective cohort study. BMJ 2006; 333: 575-81 and Rob J Bakker [1], Elise M van de Putte, Wietse Kuis, Gerben Sinnema Effects of an educational video film in fatigued children and adolescents: a randomised controlled trial Arch Dis Child . 2011 May;96(5):457-60.).	Thank you for your comment. After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. See evidence review D-diagnosis for the evidence and committee discussion on the diagnostic criteria.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	054	5	"If assessment is carried out early and a care plan is implemented, it could reduce resource use in the longer term by preventing progression of disease." There is no evidence that early assessment will do this, and there is some evidence that it is harmful because many children and young people will	Thank you for your comment. After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to

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				recover spontaneously within the 3 months post illness onset. This recommendation therefore has the potential to overwhelm services and reduce service availability to those who need treatment. The NICE guidelines needs to be based on the available evidence and not on the personal opinions of the committee.	diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. The committee agree that children and adults are different and as such children need to be seen by a paediatrician after 4 weeks and then a paediatric specialist in ME/CFS if appropriate to receive the care that is best for them. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that advice prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and it would not cause harm to in the short term. The experience of the committee, which also reflects the experience of patients recorded in the qualitative evidence is that advice to exercise early in the course of their disease appeared to significantly deteriorate their symptoms. Therefore, the implication is that more appropriate management would improve outcomes. On that basis, one would expect some resource savings in the longer term, although not necessarily net cost savings overall. The rationale was already quite cautious but we have made it clearer by changing one sentence from "Earlier access to appropriate advice and care could prevent disease progression and therefore reduce resource use in the longer term" to "Earlier access to appropriate advice and care could prevent disease

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					progression and therefore might lead to some resource savings in the longer term." The committee note that while clinicians are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement the guidance does not override the responsibility of healthcare professionals and others to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	059	1	"care for most people with ME/CFS can be managed in primary care." This may be true for adults but is not true for children and young people where care should be delivered in paediatric services, particularly community paediatric services or primary care (if children and families choose this). This is because paediatric services provide general multidisciplinary care across a range of conditions. Please separate out the advice for adults and the advice for children and young people.	Thank you for your comment. The committee discuss further access to ME/CFS specialist teams in Evidence review I-Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	059	16	"however faster access to diagnosis and appropriate care will lead to better symptom management and to substantially better outcomes for people with ME/CFS and so might reduce health and care costs in the longer term." There is no evidence for this in adult studies that we are aware of. All the evidence in paediatric epidemiological or trial studies shows that this is not true for children.	Thank you for your comment. We acknowledge that there is not quantitative evidence that early diagnosis and intervention would have a positive effect on resources. But conversely, there is not evidence that the

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				(i) Epidemiological evidence provides the data showing a substantial spontaneous recovery rate in fatigue following infections, in particular during the first months after the preceding infectious event (Hickie I, Davenport T, Wakefield D, Vollmer-Conna U, Cameron B, Vernon SD, Reeves WC, Lloyd A. Post-infective and chronic fatigue syndromes precipitated by viral and non-viral pathogens: prospective cohort study. BMJ 2006; 333: 575-81. (ii) Labelling children and young people who are likely to get spontaneously better can be harmful. For example, it will prevent them entering some occupations (such as the armed forces in the UK). (iii) There is some data that early diagnosis may increase the risk of long term disability, [Rob J Bakker [1], Elise M van de Putte, Wietse Kuis, Gerben Sinnema Effects of an educational video film in fatigued children and adolescents: a randomised controlled trial Arch Dis Child . 2011 May;96(5):457-60.]	proposed changes to the diagnostic process would increase resource use. The experience of the committee, which also reflects the experience of patients recorded in the qualitative evidence is that advice to exercise early in the course of their disease appeared to significantly deteriorate their symptoms. Therefore, the implication is that more appropriate management would improve outcomes. On that basis, one would expect some resource savings in the longer term, although not necessarily net cost savings overall. The rationale was already quite cautious but we have made it clearer by changing one sentence from "Earlier access to appropriate advice and care could prevent disease progression and therefore reduce resource use in the longer term" to "Earlier access to appropriate advice and care could prevent disease progression and therefore might lead to some resource savings in the longer term." Furthermore, the committee are not now recommending reducing the length of time a child has symptoms before diagnosis. The reference to a provisional diagnosis has been removed.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	060	9	We agree work on core outcome sets is needed for adult studies. However, this research has already been done with over 70 children with ME/CFS [see multiple papers by Parslow]	Thank you for your comment and information.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	061	1	"based on their experience, the committee agreed that energy management is one of the most important tools that people with ME/CFS" This is not consistent with either the quantitative or the qualitative data in the data synthesis chapters [Evidence review 7]. This is based on the committee's experience which is no more or less valid than the	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to

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				outcomes and experience of thousands of patients in published papers as identified by the NICE synthesis team or the evidence and experience of thousands of patients accessing specialist services.	this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that all people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits.
Royal United Hospitals Bath	Guideline	061	19	We agree that self monitoring techniques are helpful. These are integral to CBT and to GET We are delighted that the committee have agreed that tools are important	Thank you for your comment.

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Royal United Hospitals Bath NHS Foundation Trust	Guideline	063	22-26	We disagree. We believe these guidelines reduce the treatment opportunities available to children and young people which they enjoy, value and want as can be seen in the evidence synthesis.	Thank you for your comment.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	063	7	We disagree that there is no evidence that physical activity or exercise therapy is effective or helpful. Qualitative evidence included by the NICE synthesis team (Evidence review 7) is clear that children and young people find GET helpful. We urge the committee to listen to the voices of children and young people with ME/CFS and allow children and young people to make an informed choice about their treatment.	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes

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					result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed it was important people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. This includes children and young people.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	063	9	The committee considered the evidence "identified in the qualitative evidence and their own experiences of these type of interventions." We disagree with this approach. (i) The committee should consider ALL the evidence including randomised controlled trials and epidemiological studies. If the	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to

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				committee is concerned about whether participants in these studies had PEM, they should have contacted the authors. If the committee is going to base these guidelines on their own opinions, and qualitative data, the committee should use the same diagnostic criteria to avoid a risk of bias. The committee should use all the evidence in making their recommendations and should follow the evidence identified in the evidence synthesis. In addition, the committee should separate out recommendations for children form those for adults.	this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The effectiveness of an intervention is usually best answered by a RCT because a well-conducted RCT is most likely to give an unbiased estimate of effects. The committee agreed there needs to be better reporting and long-term data collection of harms in RCTs. The difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials is not disputed (for example see https://bmjopen.bmj.com/content/9/2/e024537). Notwithstanding this, it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. Ideally this takes both a quantitative and qualitative approach and includes the

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					experiences and opinions of all people who have had the intervention, patient experience is invaluable. In recognition that the views of people with ME/CFS who had experienced the interventions was important a qualitative review was done with an accompanying call for evidence to identify any unpublished evidence. People with ME/CFS reported harms in the qualitative evidence. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume

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					that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G.' The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed it was important that people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. This includes children and young people.
Royal United Hospitals Bath	Guideline	064	5	There is considerable general evidence on managing and improving sleep which the committee could have referred to that would be helpful for patients with ME/CFS.	Thank you for your comment.

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NHS Foundation Trust					After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	067	9	We disagree that there is limited evidence on the efficacy of CBT in children. There is substantial evidence as discussed in Evidence synthesis 7. This evidence includes the randomised controlled trials and the qualitative data. We agree that patients should be properly informed, but the guidelines should adjust the wording around the evidence base.	Thank you for your comment. After considering the stakeholder comments the committee concluded that the recommendation could be edited to, 'only offer CBT to a child or young person with ME/CFS after they and their parents or carers have been fully informed about its aims and principles and any potential benefits and risks.'
Royal United Hospitals Bath NHS Foundation Trust	Guideline	068	3	We disagree that there is qualitative evidence that CBT can cause harm. (i) it is not possible to make these causal assumptions from qualitative studies and (ii) the NICE evidence synthesis was overwhelmingly positive about CBT (particularly in children). Please separate out the recommendations for children from those for adults.	Thank you for your comment. Evidence review G and H provide detail on the evidence and the committee discussion, these includes the benefits and harms that were reported by people with ME/CFS in the qualitative evidence. Children and young people are separated in the guideline. To note after considering the stakeholder comments the committee concluded that the recommendation could be edited to, 'only offer CBT to a child or young person with ME/CFS after they and their parents or carers have been fully informed about its aims and principles and any potential benefits and risks.'
Royal United Hospitals Bath	Guideline	071	15	The guideline group should use the most up to date meta analyses of prevalence studies [Lim 2020]	Thank you for your comment.

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NHS Foundation Trust					The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.
Royal United Hospitals Bath NHS Foundation Trust	Guideline	072	14	There is no controversy about CBT or GET as treatment approaches for ME/CFS for the thousands of patients who access specialist services and the clinicians who provide them. The guideline committee has not provided evidence for this. Whilst, the committee finds the treatment controversial, they need to follow the evidence rather than using opinion in making recommendations for children and young people with ME/CFS.	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline.
Salford Royal Foundation Trust	Evidence Review D	148	Table 14	It should be pointed out that the study by Hives L. et al 2017 was not aimed at developing a diagnostic test. The purpose of the research was to evaluate the efficacy of a screening tool to aid in the diagnosis of ME/CFS. The paper described that without the use of any other clinical data such as case history and symptom picture, 86% of the patients were correctly diagnosed. As panel members will be aware, there are no stand-alone diagnostic signs for ME/CFS but the findings of this paper serve to aid the clinician in their evaluation of the patient so as to make the correct diagnosis. These signs described in the Hives paper, are not being evaluated as an alternative to the standard clinic methods but as an adjunct and a cost effective, easy to use and effective aid to screening for ME/CFS These signs are not being taken account in the draft guidelines. **We ask the committee to review the paper and consider that these signs are not forgotten and are explored further as a screening tool when clinically assessing patients with suspected ME/CFS.**	Thank you for your comment. The review question was, 'what are the predictive accuracies of specific clinical symptoms/signs, to identify those who will subsequently be given a clinical diagnosis of ME/CFS?' and not about the effectiveness of screening tools. This is a different question with a different reviewing approach and for this reason the paper was excluded from this review on specific signs and symptoms. In addition, the paper did not include the signs and symptoms the committee had identified to evaluate. The protocol sets out the process for how the committee agreed on the signs and symptoms to be included in this review.

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Salford Royal Foundation Trust	Guideline	General	General	It is essential that the final version of the NICE 2021 guidance recognises that the person with ME/CFS is in charge of the aims of their management plan. The plan should be mutually agreed and based on the person's preferences and needs; skills and abilities in managing their condition; hopes, plans and priorities symptom severity; physical and cognitive functioning. **Osteopathic techniques are currently available in some NHS trusts for musculoskeletal conditions. Emerging evidence suggests that some ME/CFS patients benefit from this therapy and therefore patients may choose to self fund it as part of their personalised management plan.** As no treatment works in all patients with ME/CFS, priority must be given for patient choice guided by a clinician with an interest in ME /CFS to decide on their specific management plan, which may include approaches not currently funded by the NHS, if the patient is suitable and other treatments have been unsuccessful or are not appropriate. **Finally, I would like to point out that as a clinician working in a tertiary ME/CFS service, all of our multidisciplinary team welcome any contributions that can be made in relation to assessment and management of the patient with ME/CFS whether from an osteopath or from other legitimate therapists whether based in the NHS or the private sector.**	Thank you for your comments. The committee agree and this is reflected in the recommendations in the assessment and care planning section. *Osteopathic techniques* The guideline reflects the evidence for best practice and the decision on whether to recommend an intervention is based on the evidence reviewed. The committee agreed there was insufficient evidence of benefit to recommend osteopathy techniques for people with ME/CFS (Evidence review G- non pharmacological management.)
Salford Royal Foundation Trust	Guideline	026	16	We wholeheartedly support the offering of treatment and gentle techniques that aim to improve overall joint mobility, muscle flexibility, postural and positional support, muscle strength / endurance and cardiovascular health as mentioned in the draft guidance (with perhaps the inclusion of an aim to improve lymphatic health) and we wish to inform the committee that these aims are all part of what many allied health professionals,	Thank you for your comment. To note after considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice

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				including physiotherapists and osteopaths, attempt to achieve with the application of manual therapy developed specifically for ME/CFS, as for example in The Perrin Technique. Incidentally, a nationwide survey by the ME Association in 2010 entitled *Managing my ME* examined the treatments and strategies that were most recommended by British patients with ME/CFS. This placed pacing first, second was relaxation/meditation and third was the Perrin Technique in a list of 25 treatment approaches.	on maintaining and preventing the deterioration of physical functioning and mobility.
Salford Royal Foundation Trust	Guideline	028	10	We ask that the committee review the section 1.11.16 and **omit the words "derived from osteopathy"** in the 'do not offer section' of the guidance. Also with reference to section 1.11.11 (page 26) **offering treatment and gentle techniques that aim to improve overall joint mobility, muscle flexibility, postural and positional support, muscle strength and endurance and cardiovascular health should remain as in the draft and not mention specific disciplines or professions in the final version of guidance,** to maintain health equality. These aims are all part of what Allied Health Professionals attempt to achieve with the application of some forms of manual therapy.	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer people with ME/CFS therapies based on the Lightning Process'.
Salford Royal Foundation Trust	Guideline	028	17	In the latest NICE guidelines for low back pain and sciatica (last updated 11th December 2020) there are no particular professions singled out as better than another allied health profession in the manual treatment of the back. This present guidance for ME/CFS singles out advice and management from physiotherapists and occupational therapists without any mention of osteopaths who are also recognised members of the allied health profession by the NHS. This perceived bias is potentially discriminatory, which is also implied in the previous	Thank you for your comment. After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. However no evidence was identified to support recommending treatments and osteopathy services for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy.

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				section 1.11.16 of the draft document which specifically advises "Do not offer - therapies derived from osteopathy"	
Scottish Government	Evidence Review G	General	General	*As per comment no. 4. (included below)* While there are details of outcome measures, consideration could be given to agreeing standardised assessment tools. Outcome measures may be less meaningful without more consistent initial assessment.	Thank you for your comment. The committee noted that there was inconsistency in outcomes used in trials for ME/CFS and have made a research recommendation for the development of a core outcome set (see Evidence Review H Appendix L).
Scottish Government	Guideline	General	General	**Draft NICE Guideline for ME/CFS** The Scottish Government is pleased to have the opportunity to respond to the consultation on the draft NICE guideline for diagnosis and management of Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome (ME/CFS). We recognise that ME/CFS can be a distressing and debilitating condition. We are committed to ensuring that all people living in Scotland with ME/CFS are able to access the best possible care and support, and to benefit from healthcare services that are safe, effective and put people at the centre of their care. We are working with service providers, the third sector and patient groups to identify care and support gaps for people living with ME/CFS. The Scottish Government welcomes the person-centred approach NICE has taken in producing this guideline, which has aimed to incorporate patient experience into the process and which recognises that people with ME/CFS may feel stigmatised by their condition. The guideline promotes a multidisciplinary approach to care, and it is encouraging to see that it contains specific consideration of people whose condition is severe/very severe and for children and young people. While there are details of outcome measures, consideration could be given to agreeing standardised assessment tools. Outcome measures may be less meaningful without more consistent initial assessment. We are aware that	Thank you for your comment. We note that when the ME/CFS guideline is published on the NICE website it includes a tab that includes 'Information for the public' to provide a clear overview of the guideline.

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				patient organisations have welcomed some of the key recommendations, in particular those around physical activity therapies. We are also conscious that some clinical professional bodies harbour concerns about the methodology used and the potential impact of some recommendations upon guidance for other long term conditions. We hope that NICE will continue to work closely with both clinical and patient organisation stakeholders in progressing towards the final guideline. St Andrew's House, Regent Road, Edinburgh EH1 3DG www.gov.scot αβχδε αβχ α We would also ask the Committee to consider the health literacy needs of the patient population and ensure the final guideline is as accessible as possible. An accompanying quick reference guide may be helpful in this respect; also for engaging use among nonspecialist clinicians. The Scottish Government has made GPs and Chief Executives of health boards in Scotland aware of the draft guidance, but will await the final publication before considering how to implement its recommendations.	
Scottish Government	*Guideline*	*General*	*General*	*Scottish Government recognises that ME/CFS can be a distressing and debilitating condition. We are committed to ensuring that all people living in Scotland with ME/CFS are able to access the best possible care and support, and to benefit from healthcare services that are safe, effective and put people at the centre of their care. We are working with service providers, the third sector and patient groups to identify care and support gaps for people living with ME/CFS.*	Thank you for your comment.
Scottish Government	Guideline	General	General	The Scottish Government welcomes the person-centred approach NICE has taken in producing this guideline, which has aimed to incorporate patient experience into the process and which recognises that people with ME/CFS may feel stigmatised by their condition.	Thank you for your comment.
Scottish Government	Guideline	General	General	The guideline promotes a multidisciplinary approach to care, and it is encouraging to see that it contains specific	Thank you for your comment.

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				consideration of people whose condition is severe/very severe and for children and young people.	
Scottish Government	Guideline	General	General	The Scottish Government has made GPs and Chief Executives of health boards in Scotland aware of the draft guidance, but will await the final publication before considering how to implement its recommendations.	Thank you for your comment.
Scottish Government	Guideline	020 - 029. Also general.		We are aware that patient organisations have welcomed some of the key recommendations, in particular those around physical activity therapies. We are also conscious that some clinical professional bodies harbour concerns about the methodology used and the potential impact of some recommendations upon guidance for other long term conditions. We hope that NICE will continue to work closely with both clinical and patient organisation stakeholders in progressing towards the final guideline.	Thank you for your comment.
Scottish Government	Guideline	001	Box	We would also ask the Committee to consider the health literacy needs of the patient population and ensure the final guideline is as accessible as possible. An accompanying quick reference guide may be helpful in this respect; also for engaging use among non-specialist clinicians.	Thank you for your comment. NICE also publish the ME/CFS information for the public alongside the guideline.
Scottish Government	Guideline	046 060 Also general.	Lines 1-3 Lines 9-17.	While there are details of outcome measures, consideration could be given to agreeing standardised assessment tools. Outcome measures may be less meaningful without more consistent initial assessment.	Thank you for your comment. Research recommendations can only be made where the evidence has been searched for within the guideline. Assessment tools were not included in the scope of this guideline as a topic to consider, and therefore the committee are unable to make research recommendations on this topic. This refers to the development of core outcomes sets for research, to date one for ME/CFS has not been developed. See https://www.comet-initiative.org/
Sheffield ME and	Guideline	General	General	The new Guideline is broadly welcomed by our members and is considered to be a significant improvement on the 2007 Guideline. In particular, members hugely welcome the	Thank you for your comment.

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Fibromyalgia Group (SMEFG)				removal of graded exercise therapy (GET) as a recommended treatment. The revision which describes CBT as a supporting therapy rather than a treatment, was also considered by our members to be an important change from the 2007 Guideline. Whilst long overdue, these substantial changes were unanimously welcomed by our members.	It should be noted that the committee have clarified that CBT is not a cure for ME/CFS but can be offered to support people manage their symptoms.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	General	General	In line with changes made in the US in 2015, the recognition in the UK of ME/CFS as a physical health disorder was considered to be of great importance by our members. Members hold a strong belief that services should be led medically, and should no longer be underpinned by a psycho-social model.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	General	General	Our members strongly recommend that resources currently provided for ME/CFS specialised services be reallocated to meet the new service priorities and away from previous priorities, with appropriate and suitably trained staffing.	Thank you for your comment and your suggestion. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS.

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				It is recommended that a national register for ME/CFS is considered in order to support on-going care and assist in improving understanding of the epidemiology of this disorder.	The committee agree that a national register for people with ME/CFS would be helpful in supporting on-going care and assist in improving understanding of the epidemiology of this disorder but were unable to recommend one in the context of the remit and scope for this guideline.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	General	General	People with ME/CFS are at risk of severely exacerbating their symptoms and potentially taking an extremely long time to recover if they contract the flu virus. Many have been refused the vaccine despite requesting it from their GP. **Amendment to guideline** Insert People with ME/CFS and their carers should be offered access to the flu vaccine as a priority vulnerable group.	Thank you for your comment. The administration of vaccines for people with ME/CFS was not prioritised by stakeholders during the development of the scope or by the committee when finalising the evidence review questions. As such evidence on vaccines has not been searched for or reviewed and the committee were unable to make any recommendations on this topic.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	General	General	Our members call for a review of the model for specialist services. They believe that these services need to be revised in the light of the amended Guideline, with consideration given to how future services are more fully co-ordinated with primary health and other local services to improve on-going support to people with this chronic health condition.	Thank you for your comment and your suggestion. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	004	016	Our members strongly support this statement. It is very powerful to find our experiences acknowledged and validated by this guideline.	Thank you for your comment.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	005	007	In our experience family members and carers have sometimes been excluded from conversations. This comment is strongly supported.	Thank you for your comment.

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Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	005	018	Our members emphasise that it is not always possible to sustain involvement in an action plan and so being able to resume one aspect when this is feasible is important, rather than being rejected for care due to severity of symptoms. We question the use of the word 'intervention' here as that sounds like an externally driven intent to achieve change, rather than support to manage symptoms. **Amendment to guideline** Delete 'intervention' and replace with 'support programme'.	Thank you for your comment. The management and management of symptoms sections of the guideline set out the strategies and treatments to support people with ME/CFS with managing their symptoms. Intervention has been replaced with treatment to match the rationale and impact section for these recommendations.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	006	006	**Amendment to guideline** Always ensure the child or young person's chosen carer in present.	Thank you for your comment. This recommendation includes, 'may need their parents or carers to help them'. In addition after considering stakeholder comments this recommendation has been edited to include, ' with or without their parents of carers as appropriate' to provide further clarity.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	007	016	**Amendment to guideline** Add new bullet point ' may struggle to regulate their temperature and may need help with keeping warm or cool	Thank you for your comment. This section highlights the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. It is supported by Appendix 2, Evidence review C – access to care and the committee's experience. The committee acknowledge there are other symptoms that could be included and any list is not meant to be exhaustive. Hypersensitivity is included in the previous recommendation describing the symptoms that may be experienced.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	009	021 - 023	Our members are of the view that the initial assessment should be very thorough and include a full physical health assessment in order to identify/exclude other conditions and to identify co-morbidities. **Amendment to Guideline** - The Guideline should be amended to including details of the full assessment, including	Thank you for your comment. The committee agrees and a full assessment and the exclusion or identification of other diagnosis is recommended in section 1.2 and again in section 1.5. Referral to a specialist for advice on sleep is recommended in the section on rest and sleep in the management section of the guideline.

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				tests to be performed to exclude other conditions and to identify co-morbidities.. Our members have reported that sleep apnoea has sometimes been mistaken for unrefreshing sleep with insufficient investigation undertaken of sleep problems. **Amendment to Guideline** - Assessment should consider a potential referral to a sleep clinic to consider a differential diagnosis of sleep apnoea.	
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	009	017 - 019	The importance of early intervention is considered of significant importance to our members.. Early intervention has not been addressed in the guideline. Often people are often very unsure what to do on diagnosis and they suffer a lot during the whole period until they access support. A lot of people with ME/CFS try to fight the illness through being active, which only makes them worse. Hence the importance of early intervention. Intervention at the moment does not happen early enough, so people get worse by not managing their condition in the right way, and their hopes decrease over time. **Amendment to Guideline**· the guideline should be amended with specified short timescales for access to initial support following diagnosis **and** with the importance of early access to services stressed.	Thank you for your comment. Advice for people with suspected ME/CFS is included in section 1.3 of the guideline.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	010	002	The term 'appropriate specialist' needs defining further. **Amendment to guideline** 'appropriate specialist physician with experience and understanding of ME/CFS	Thank you for your comment. Appropriate specialist here refers to expertise in supporting the interpretation of signs and symptoms where there is uncertainty and a possible alternative diagnosis. Throughout the guideline where a specialist refers to a ME/CFS specialist this has been made clearer by including ME/CFS before specialist.
Sheffield ME and	Guideline	010	015	So many of our members have talked about wishing they had been given the right advice when they were first ill. This section is extremely welcome and strongly supported.	Thank you for your comment. The committee did not agree that this added further clarity to the recommendation, personalised advice would be given at the time

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Fibromyalgia Group (SMEFG)				**Amendment to the guideline** insert word 'immediate' to read 'give people immediate personalised advice'	of the consultation and for that reason have not added your suggestion.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	011	013 - 014	Our members are concerned that the role of specialist services with regards to the on-going care of people with ME/CFS is unclear. Patients are usually referred to specialist services by their GP, and assessment and initial support/treatment is provided. However, patients are then discharged to GP care. Many GPs are untrained to support people with ME/CFS and are not able to provide support when issues relating to the ME/CFS diagnosis arise. Therefore, when a patient who has been discharged by a specialist service has issues in the future, perhaps following a change in their condition, GPs will often re-refer them to the specialist service. Patients are then dealt with as new patients and assessed and offered the same programmes again. There is no route for people with ME/CFS to access appropriate support following discharge from a specialist service, without being re-referred, and often having a lengthy wait to access that service. If they need specific help, for example, physiotherapy, they are not able to access it directly and often not at all. A direct referral to experienced ME/CFS professionals would be very beneficial to people with ME/CFS to meet changing needs as they arise. People with ME/CFS can therefore feel as if they are on a merry-go-round being passed between GP care and specialist care, neither of which can necessarily help and neither of which currently provide physiotherapy, dietary or other support.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee highlight where access to a ME/CFS specialist services is required. They have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. The committee recommended a named contact in the multidisciplinary care section of the guideline. The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no one single model of care. Some of the committee members described experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support.

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				Given that people with ME/CFS generally do not have access to support post discharge from a specialist centre, often they are unable to receive support to meet their changing needs. They may therefore have to find information themselves, or work out for themselves, how to manage debilitating symptoms, how to manage day to day activities, and how to conserve energy. Access to practical advice when its needed could significantly impact on lives. The revised services need to identify how patients could access services in a more streamlined manner in the future, and how they might more easily get the practical help they might need as their condition changes without waiting for a re-referral to a specialist centre. **Amendment to Guideline -** the Guideline should contain more details about the roles of the specialist service and the GP, and clarity on where responsibilities lie for on-going case management, monitoring and responding to changing needs..	The review in primary care section of the guideline recommends a review of the care and support plan at least once a year.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	012	010 - 012	The proposal that all patients have a management plan is welcomed by our members. However, clarity is needed on who would develop this plan and who will support patients on an on-going basis with the plan. Such a plan should be reviewed regularly with the patient with on-going support available from specialised staff. This should include an Annual Review for patients, with a reassessment of their condition and a review of their management plan and their changing needs.Some of our severe members have maybe one GP consultation in a year, only 7 minutes - this is inadequate. **Amendment to Guideline -** further details should be included to specify where responsibility would lie for on-going monitoring of care plans. A requirement for an Annual Review of all patients with this chronic condition should be included.	Thank you for your comment. The care and support plan is developed by the ME/CFS specialist team and is based on the holistic assessment in the previous recommendation. The committee recognised certain parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. The multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse. The review

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					in primary care section of the guideline recommends a review of the care and support plan at least once a year.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	012	029 - 030	'details of the health and social care professionals involved in the person's care, and how to contact them' One of the problems with the current arrangements is that no ongoing care is available for people with ME/CFS. Our members describe how, once discharged by a Specialist Service, there is no other on-going support from professionals trained in ME/CFS care. To get further support from the Specialist Centre requires a new referral by GP to the service and a long wait to get access to a suitably trained professional. What is needed is a named Care Co-ordinator, to enable access to suitable support when needs arise. **Care Co-ordinator/ Link Workers** Consideration should be given to the provision of Care Co-ordinator/ Link Workers for those moderate/severely affected, to provide people with ME/CFS with a named professional they could contact with any issues and who could provide on-going support. The professional background of a Link Worker would need to be determined, possibly a specially trained nurse, or a multi-professional team could work together, but with a named individual assigned to each patient. Link Workers would be specialist in ME/CFS, and may be able to provide a range of generic support including nursing support, advice on medication, movement and occupational therapy, dietary advice and more general support and guidance. **Amendment to Guideline** - The guideline should include a proposal for a Care-Coordinator/Link Worker role, so that all patients have on-going support	Thank you for your comment. The multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse.

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Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	013	009 - 010	Care Co-ordination for patient care following discharge from Specialist services is lacking, as other than GP care in response to demand no other on-going support is available to patients.	Thank you for your comment. The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no one single model of care. Some of the committee members described experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support. The review in primary care section of the guideline recommends a review of the care and support plan at least once a year.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	016	007	**Amendment to guideline**: A safeguarding assessment should only be carried in circumstances where safeguarding concerns are clearly evident. this should be carried out or overseen by health and social care professionals with training and experience in ME/CFS.	Thank you for your comment . After considering the stakeholder comments this section has been reordered and the now second recommendation has been edited to,' *If* a person with confirmed or suspected ME/CFS needs to be assessed'. To clarify this point.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	016	011	**Amendment to guideline** - add: ME/CFS is not a mental disorder. (For purposes of clarity)	Thank you for your comment. It is clear at the start of the guideline in the principles of care section of the guideline that ME/CFS is a complex chronic medical condition affecting multiple body systems. In addition the text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3)' has been added to the context section of the guideline. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. This point you make is clear in other parts of the guideline and for this reason your suggestion has not been added to the recommendation.

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Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	016	013	**Amendment to guideline** - add after 'is needed' 'due to a co-morbid mental disorder'	Thank you for your comment. The recommendation is to raise awareness about the need to involve health and social care professionals who have training and experience in ME/CFS and your suggestion does not add further clarity to the recommendation and for this reason your suggestion has not been added.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	018	006 - 007	Our members have described how hospital in-patient admission can be very difficult for those with ME/CFS and often lead to a severe worsening of symptoms. Improvement is needed in this area, in terms of the environment,(light,sound,temperature, bed clothes, chemicals and more) and staff practice eg limiting numbers at a time in a room, no loud knocking and otherwise responding to a patient's sensitivities. Staff also need improved knowledge and understanding of ME/CFS.	Thank you for your comment and information. The committee note these are examples in the recommendations and as with any list of examples these cannot be exhaustive.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	028	012	While very strongly supporting the wording of section 1.11.15 and 1.11.16, we are concerned that section 1.11.17 now implies there can be such a thing as a physical activity 'programme'. People should have access to advice and support wth managing their physical activity as part of the energy management section. A separate section implies there can be a treatment 'programme', which is not the case. The principles of energy management already cover this. **Amendment to guideline:**Move sections 1.11.15 and 1.11.16 to be situated earlier in the section 1.11 under energy management. Delete all references to 'physical activity programme' and replace with 'advice and support in managing physical activity'	Thank you for your comment. Based on the quantitative and qualitative evidence* and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F

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					and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	032	009	**Amendment to guideline** insert after losing 'or gaining' weight	Thank you for your comment. This recommendation has been edited to include 'weight gain'.
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	034	001 - 005	The Sheffield ME&Fibromyaliga Group fully support the revised approach to CBT, with CBT rightly no longer considered curative. However we are concerned that this raises CBT above other therapeutic approaches that may be of benefit, despite a very low quality evidence base to do so. Any professional delivering CBT to people with ME should be specifically trained in accordance with this guideline, and in particular that CBT is not a cure. We would like to see a more flexible and varied psychological support recommended in this guideline, with clarity about what any approach to psychological support for people with ME should look like, not just CBT.	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee

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					concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	040	011 - 023	Training of healthcare professionals **1.** Our members consider the proposed approach to training to be too general and aimed at all health and social care professionals involved in the care of those with ME/CFS. More emphasis needs to be placed on transformation, and this should involve being more explicit about the changes that need to be made and with a greater focus on ME/CFS as a medical condition, which would require a change in mind-set. **2.** Specifically, GPs as the first point of contact for patients, should have specific, targeted training which is focused on helping GPs understand ME/CFS as a physical health condition. **3.** The services should be medically-led by those with knowledge of physical health care, and no longer dominated by mental health professionals as previously. **4.** Training for staff needs to be in treatments and support that is evidence-based. **Amendment to the guideline**. The guideline should propose that health care professionals working with people with ME/CFS should undertake accredited training to ensure that	Thank you for your comment. The committee discussed the level of detail that should be included in training programmes and agreed on a general description to avoid a prescriptive interpretation of the content allowing the recommendations to remain relevant as research in the area develops. The final recommendation in this section is clear that training should reflect current knowledge so that health and social care professionals can maintain continuous professional development in ME/CFS relevant to their role so that they provide care in line with this guideline.

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				the previous myths and misconceptions are no longer circulated. This training should be made available or even required of professionals at all levels in the system.	
Sheffield ME and Fibromyalgia Group (SMEFG)	Guideline	041	019	It is not clear why the distinction is made between paid and unpaid carers? **Amendment to guideline** Remove 'unpaid'.	Thank you for your comment. There is a distinction between paid and unpaid carers and the regulations that apply to paid carers. To clarify, 'This is distinct from care workers who are paid to provide support' has been added to the definition.
South London and Maudsley NHS Foundation Trust	Evidence Review G	200	6	*"Population and setting People who have had interventions for ME/CFS.* *Context Experiences of people that have had interventions for ME/CFS and the benefits and harms they experienced*." Which makes it hard to understand why important qualitative studies and meta-syntheses of patients' experiences of referral to and treatments in NHS specialist services have not been included. See: Broughton et al Adult patients' experiences of NHS specialist services for chronic fatigue syndrome (CFS/ME): a qualitative study in England https://doi.org/10.1186/s12913-017-2337-6 McDermott, et al Patients' hopes and expectations of a specialist chronic fatigue syndrome/ME service: a qualitative study https://doi.org/10.1093/fampra/cmr016 Bayliss et al Overcoming the barriers to the diagnosis and management of chronic fatigue syndrome/ME in primary care: a meta synthesis of qualitative studies. BMC Family Practice. 2014 http://www.biomedcentral.com/1471-2296/15/44 Peters et al. Challenges of nurse delivery of psychological interventions for long-term conditions in primary care: a qualitative exploration of the case of chronic fatigue syndrome/myalgic encephalitis. https://link.springer.com/article/10.1186/1748-5908-6-132	Thank you for your comment. These have all been included in the review. Thank you for your comment. All references except for Peters were included in the evidence reviews. The study by Peters has now been checked. Themes emerging from this study are relevant to review C for which a large number of papers were identified and in line with NICE processed for developing qualitative evidence reviews, inclusion of papers was halted as data saturation was reached. As a result findings similar to those emerging from Peters for example about the training needs of therapists, the individual characteristics of the therapist, the complexity of primary care, patients' personal attitudes and beliefs or individual circumstances have been already included in the evidence reviewed by the committee and the recommendations made.

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				This omission of several important qualitative studies of patients attending NHS services like these diminishes the confidence that healthcare professionals will have in these guidelines, relying as they are so heavily on qualitative studies, so why exclude studies that do include perspectives on different interventions, as well as overall satisfaction measures.	
South London and Maudsley NHS Foundation Trust	Evidence Review I	023	10-13	Page 23: *"The committee noted services are led by a variety of specialities, 10 including psychiatry, psychology, infectious diseases, immunology, neurology, physiotherapy 11 and occupational therapy. The committee commented that this has led to misunderstanding 12 when people with ME/CFS have been referred to some services feeling there is a mismatch 13 between their illness experience and the speciality."* The committee's conclusion from the expert testimony here is that the different specialties involved in services for ME/CFS has led to misunderstanding when people with ME/CFS have been referred to some services feeling there is a mismatch between their illness experience and the speciality. However, this does not follow from the evidence provided in the expert testimony (which is based on our service). We are concerned the committee is suggesting that psychology and psychiatry led services lead to people with ME/CFS feeling a mismatch between their experience and the speciality given that our service is psychology and psychiatry led. The evidence of anonymous patient feedback we have provided in comments 47 and 48 highlight that people with ME/CFS using our service have very positive experiences and	Thank you for your comment. The comment on mismatch was part of the committee discussion that was prompted by Dr Husain's presentation and it is not attributed to him. To clarify, 'The committee noted this was not a specific comment about SLAM.' has been added to this paragraph. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then

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				demonstrates no evidence of people feeling there is a mismatch. We are concerned the committee's personal experiences are outweighing the many people with ME/CFS who benefit from CBT and GET and discounts the views and feedback they have provided.	through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed).
South London and Maudsley NHS Foundation Trust	Guideline	General	General	We applaud the release of the updated ME/CFS NICE guidance, and particularly approve of the use of the service user's voice in coming to a patient-centred approach to care. There is much in the way of helpful guidance in the document, which will help service users and professionals work together to ensure they receive the right care for their condition. However, we were somewhat surprised, and concerned with many of the findings and recommendations. Our service has treated patients with ME/CFS for approximately 20 years with a range of therapies that are entirely collaborative, and prioritise patients' goals. We offer both cognitive behavioural therapy (CBT), and graded exercise therapy (GET) from specialist therapists, who have accrued a tremendous amount of experience in treating this often debilitating illness over time. As you would expect from a tertiary care service, our methods include robust staff supervision, alongside a strenuous evaluation of both methods and outcomes, as funding agencies understandably wish to see value in their investments. We note that psychiatrists were not part of the NICE committee for these guidelines, which we find surprising given the need for a multidisciplinary approach to treating ME/CFS, our experience in this area, and the evidence base around	Thank you for your comments and information. *Committee composition* The committee composition was agreed during the scoping phase as appropriate for the expertise for the guideline scope. Great care was taken to ensure the committees was formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. The committee membership does reflect the multidisciplinary approach to treating ME/CFS and includes medically qualified clinicians and allied health professionals who lead and work in specialist ME/CFS services. A clinical psychologist with experience in delivering CBT to people with ME/CFS was recruited to the committee. In addition, Dr Husain was invited to give his reflections on the different models of multidisciplinary care, including team composition, for people with ME/CFS (Appendix 3- Expert testimonies). In the discussion section of Evidence review I-Multidisciplinary care the committee have acknowledged the historical context in the variation in how ME/CFS services are led in the NHS and added further text about the composition of ME/CFS specialist teams. *Tone of the guideline*

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				such treatment. In addition the high prevalence rates of depression and anxiety cannot be ignored. The bleak outlook presented in the guidance appears at odds with the many patient voices that have benefited from our input (as you will see from our patient feedback data). Our outcomes are broadly in line with the higher quality evidence in the area summarised in the Cochrane review for treatments for ME/CFS. We are concerned that the repeated statement that there is no treatment is at odds with how we define and describe treatment in all other long term conditions. This gives people with ME/CFS little hope for improved quality of life or recovery. We note that there is a disparity in the views of our patients as demonstrated by the qualitative feedback from patients who have used our service, compared with much of the qualitative feedback from the patient experts on the panel. It is essential to hear and engage with critical voices but it is also important to ensure the guidance reflects the views of all patients. Those who have improved with treatment could be underrepresented in patient groups. To avoid potential bias it is essential to include the views of people with ME/CFS who are less likely to be part of groups involved in the NICE consultation. Please find attached our views on the document. Our comments are predominantly weighted to our patient feedback, collected over several years, rather than directly representing our own views on the matter. We would respectfully ask that it be weighed against the qualitative	When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.) In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. *Cure or treatment* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' in the recommendations where it is alongside 'cure' to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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				comments that have formed some of the recommendations, in order to obtain as balanced a view as possible to better serve future and current suffers of this condition. Regarding the outcomes and feedback we report on in our patients, it should be noted that we used CDC 1994 criteria throughout this period. Diagnostic assessments were carried out by a team highly experienced in using these criteria. We have a comprehensive assessment procedure for all patients to identify alternative medical and/or psychiatric diagnoses. Our patients are similar to all other ME/CFS populations in that they have post-exertional malaise, high rates of disability, evidence of neuroendocrine and immune system function (underactive HPA axis, and high levels of type 2 cytokine producing cells – see Skowera et al Clin Exp Immunol. 2004 Feb; 135(2): 294–302) Please see: • Comment Number 23 for data on clinical outcomes and patient satisfaction for people with ME/CFS who had Cognitive Behaviour Therapy in our service. • Comment Number 27 for data on clinical outcomes and patient satisfaction for people with ME/CFS who had Graded Exercise Therapy in our service. • Comment Number 50 for anonymous qualitative feedback from people with ME/CFS who had Cognitive Behaviour Therapy in our service. • Comment Number 51 for anonymous qualitative feedback from people with ME/CFS who had Graded Exercise Therapy in our service.	

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
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South London and Maudsley NHS Foundation Trust	Guideline	General	General	In summary, we appreciate that patients with ME/CFS do not always feel that health services understand their condition. Whilst it is vital that these guidelines address these concerns and potential inequalities in the treatment they receive, we believe it is vital that this is not at the expense of denying patients access to potentially highly beneficial and evidence based treatment programmes.	Thank you for your comment. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of ME/CFS services across the NHS. This guideline highlights areas where resources should be focussed and this will ensure that people with ME/CFS will receive the appropriate care.
South London and Maudsley NHS Foundation Trust	Guideline	037 - 038	037 lines 1-24 p38 lines 1-21	"1.13 Managing flares and relapse" Page 37, line 9 recommends temporarily reducing activity which can sometimes be helpful. But there is nothing in this section on managing flares or relapse on how to support people with ME/CFS to increase activity again. Managing flares and relapses only by reducing activity and establishing a lower baseline will lead to poorer functioning and worse patient outcomes, without a structured plan on how to return to physical activity.	Thank you for your comment. This section is about managing a flare up* and relapse and the strategies to address this. The recommendation includes that people should not return to their usual activity levels until the flare-up has resolved. There is specific reference to people adjusting their physical activity levels during and after a flare up in the physical activity and exercise section of the guideline. Both sections advise the person to seek support if needed. *After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
South London and Maudsley NHS Foundation Trust	Guideline	004	004 - 006	*"1.1.1 Be aware that ME/CFS is a complex, chronic medical condition affecting multiple body systems and its pathophysiology is unclear"* The opening definition describes ME/CFS as a multi-system disorder. Whilst it does involve multiple symptoms there is not enough evidence to support it being described as multi-system which implies pathophysiology in multiple organ systems as seen in, for example, some autoimmune conditions. The risk factors associated with ME/CFS are multifactorial and include biological, psychological and social risk factors. It would be	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. People with ME/CFS do experience changes and symptoms in multiple body systems. This bullet point has been edited to,' and its pathophysiology remains under investigation' to clarify that there is not enough evidence to make any conclusions about the pathophysiology of ME/CFS and this is an active area of research.

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				more accurate to describe ME/CFS as a complex condition, with multiple symptoms associated with a range of biological, psychological and social risk factors.	
South London and Maudsley NHS Foundation Trust	Guideline	004	010	*"1.1.1 Be aware that ME/CFS affects each person differently and varies widely in severity – in its most severe form it can lead to substantial incapacity"* The guideline states that the severity of the illness varies widely. We would add that the duration of illness can also vary widely and this is important for patients to know at the outset. The evidence suggests that people with ME/CFS can and do recover which is important information to include here.	Thank you for your comment. The committee agree and in the information about ME/CFS section of the guideline the variation in long-term outlook is highlighted and includes that a proportion of people recover.
South London and Maudsley NHS Foundation Trust	Guideline	004	016	*"1.1.2 Recognise that people with ME/CFS may have experienced prejudice and disbelief and feel stigmatised by people who do not understand their illness"* We are pleased to see the inclusion of this section on the stigma, disbelief and prejudice people with ME/CFS may have faced. We would add that people with ME/CFS can also face these issues in the workplace, education, amongst friends and family as well as in healthcare and social care. An important part of CBT is to allow people to express those experiences and concerns in a safe and supportive environment.	Thank you for your comment.
South London and Maudsley NHS Foundation Trust	Guideline	005	005	*"1.1.3 Health and social care professionals should take time to build supportive, trusting and empathetic relationships"* We fully agree with the need to spend time with patients to build a therapeutic relationship. The 2007 guidance used the terms supportive, collaborative and person-centred. We agree	Thank you for your comment.

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				that additionally stressing the need for trusting and empathetic therapeutic relationship and the need for time to build these is helpful.	
South London and Maudsley NHS Foundation Trust	Guideline	005	007	"*1.1.3 Health and social care professionals should involve family members and carers (as appropriate) in discussions and care planning if the person with ME/CFS chooses to include them.*" We support the early mention of involvement of family and carers (as appropriate) where the person with ME/CFS wants this. This is an improvement on the 2007 guidance in which engagement with family is mentioned but less prominently.	Thank you for your comment.
South London and Maudsley NHS Foundation Trust	Guideline	005	015	*"1.1.5 Explain to people with ME/CFS and their family or carers that they have the right to decline or withdraw from any part of their management plan and it will not affect other aspects of their care. They can begin or return to an intervention if they feel able to resume."* We fully agree all patients have the right to withdraw from treatment and treatments should only be provided with informed consent. These are common principles in all areas of healthcare, for example in the General Medical Council's Good Medical Practice. We question the need to highlight this specifically in ME/CFS guidance when it is not highlighted in the same way in other NICE guidelines. It appears to imply that patients are routinely not given the right to withdraw from treatment. It is our experience, the vast majority of healthcare professionals within the NHS are caring individuals who work in a collaborative manner with the aims of building a trusting	Thank you for your comment. This recommendation is supported by the evidence and the committee's experience. Some people with ME/CFS reported negative reactions from health and social care professionals when they did not want to follow the advice given (see Evidence review A, Appendices 1 and 2). The committee agreed it was important to make a recommendation supporting people's choices and involvement in their care. The committee agree that a collaborative approach to care and treatment is important and recommend person centred care and personalised care throughout the guideline.

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				and empathetic therapeutic relationship. If the panel wish to include this comment, for balance, it may be appropriate to include in the earlier section (p5, Lines 3-8), "take a collaborative approach to treatment".	
South London and Maudsley NHS Foundation Trust	Guideline	005	020	*"1.1.6 Be aware of the impact on children and young people with ME/CFS who have experienced prejudice and disbelief by people they know and who do not understand the illness (family, friends, health and social care professionals and teachers). Health and social care professionals should understand this experience may result in a breakdown of the therapeutic relationship, lack of trust and hesitation to engage further in health and social care services."* This applies to adults as well.	Thank you for your comment. The committee agree and this is addressed earlier in this section on principles of care.
South London and Maudsley NHS Foundation Trust	Guideline	006	026 - 027	*"1.1.8 Be aware that people with severe or very severe ME/CFS may experience some of the following symptoms that significantly affect their emotional wellbeing, communication, mobility and ability to interact with others and care for themselves - postural orthostatic tachycardia syndrome (POTS) and postural hypotension"* We are surprised by the inclusion of postural orthostatic tachycardia syndrome (POTS) postural hypotension in this guidance. Our understanding is this condition is poorly understood, and potentially overlaps with several other recognised syndromes. It runs the risk of conflating established clinical services, with services that are essentially still in the research stage.	Thank you for your comment. Orthostatic intolerance is described as a commonly associated symptom that people with ME/CFS experience and is identified in four of the reviewed diagnostic criteria. The committee agreed it was important to recognise this in the guideline (see evidence review D- diagnosis).

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South London and Maudsley NHS Foundation Trust	Guideline	006	004	*"1.1.7 Ensure the voice of the child or young person is always heard by taking into account that children and young people may find it difficult to describe their symptoms and may need their parents or carers to help them"* We fully agree with the need to take a child centred approach for children and young people with confirmed or suspected ME/CFS. In addition to recognising that children and young people may find it difficult to describe their symptoms and may need their parents or carers to help them it should also be mentioned that children and young people may be reluctant to mention everything of relevance with their parents or carers present. We would suggest adding "a child or young person may need to be seen on more than one occasion with parents/carers and without, if appropriate, in order to gain trust" (this phrase is used in other NICE Guidance).	Thank you for your comment. After considering stakeholder comments this recommendation has been edited to include, ' with or without their parents of carers as appropriate' to provide further clarity.
South London and Maudsley NHS Foundation Trust	Guideline	007	022 - 026	*"1.1.11 Risk assess each interaction with a person with severe or very severe ME/CFS in advance to ensure its benefits will outweigh the risks to the person (for example, worsening their symptoms). For people with very severe ME/CFS, think about discussing this with the person's family or carer on their behalf."* We agree with the need to However, the phrasing of this recommendation suggests that any intervention that worsens symptoms should be discouraged. It does not allow for a balance between long and short term risks and benefits to be discussed with the patient in accordance with goals they may have. Approaches which involve some tolerable short term worsening of symptoms with	Thank you for your comment. 'Worsening their symptoms' is an example of what may happen as a result of an interaction and that this should be assessed. As an example there is no judgment on the whether an interaction that has an impact on symptoms is discouraged. As you note weighing up risks and benefits of interactions are discussed with the person with ME/CFS in a collaborative manner.

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				the aim of working towards a person's goals can be beneficial and desirable. The phrasing here discourages having these conversations in a collaborative manner and would make it very difficult to provide support involving gradual increases in activity.	
South London and Maudsley NHS Foundation Trust	Guideline	007	001 -003	*"1.1.9 Recognise that symptoms of severe or very severe ME/CFS may mean that people:* *need a low-stimulus environment, for example a dark quiet room with interaction at a level of their choice (this may be little or no social interaction)."* We are very concerned to see this recommendation about a dark, quiet room with little or no social interaction. This has the potential to harm patients. A low stimulus environment should not involve no social interaction at all. The description provided here suggests sensory deprivation. If this guidance is followed to the letter it could put people with severe ME/CFS at further risk of depression, delirium, isolation and loneliness.	Thank you for your comment. This section raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these symptoms and the support that may be needed to manage them, in this case hypersensitivity. The committee note that the level of support needed is individual to the person and agreed collaboratively as part of their personalised care and support plan with the health and social care professionals involved in their care. An assessment of benefits and harms would be part of this.
South London and Maudsley NHS Foundation Trust	Guideline	008	008	*"1.2.2 If ME/CFS is suspected carry out an assessment, which should include: psychological well being assessment"* We advise that the guidance should add screening for mood disorders to exclude depression in particular. Depression and other mental health diagnoses are easily the commonest differential diagnosis (a condition which needs to be excluded before making a diagnosis of ME/CFS) to consider when assessing a new patient – not mentioning this risks health professionals missing this important condition and patient being incorrectly diagnosed and treated. At present depression is mentioned only in section 1.12.4 on managing co-morbid conditions (page 36, lines 12-21).	Thank you for your comment. The committee agree at this stage the person has not been diagnosed with ME/CFS or any other condition and as you comment it is important to investigate the possibility of other diagnosis and co-existing conditions. The committee note the assessment recommended describes the routine examinations and assessments when a patient has an undiagnosed illness. To clarify this the recommendation has been edited from 'comprehensive clinical history' to 'medical assessment (including relevant symptoms and history, comorbidities, overall physical and mental health).

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				Page 8 line 8 recommends investigations to exclude physical health conditions. This section must also recommend excluding mental health conditions. The draft guidance stigmatises against mental health by stating investigations should be undertaken to exclude other (physical health) diagnoses but not stating assessment should assess for mood disorders as well. The term psychological wellbeing assessment is not specific enough and risks being misunderstood. As well as being a key differential diagnosis, depression is common in long-term conditions including ME/CFS and it is treatable. It can exacerbate and make it harder for people to manage symptoms of ME/CFS. It is associated with risk of self-harm and suicide and there is evidence to suggest a higher rate of suicide in people with ME/CFS.	
South London and Maudsley NHS Foundation Trust	Guideline	009	012	*"1.2.4 Be aware that the following symptoms may also be associated with, but are not exclusive to, ME/CFS: intolerance to alcohol, or to certain foods, and chemicals"* Intolerance to chemicals is too vague to be helpful	Thank you for your comment. These are examples of symptoms that people may experience and the committee note that any list of examples is not intended to be exhaustive.
South London and Maudsley NHS Foundation Trust	Guideline	011	015	*"1.5.1 After confirming a diagnosis of ME/CFS, carry out and record a holistic assessment. This should include:…"* A holistic assessment should include the impact of symptoms of education and / or employment, social life, relationships and activities of daily living (not mentioned in the bullet points under this recommendation)	Thank you for your comment. These are the minimum areas to be considered in the assessment the list is not meant to be exhaustive and does not exclude the areas you have mentioned.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
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South London and Maudsley NHS Foundation Trust	Guideline	012	010 - 030	*"1.5.2 Develop a personalised management plan with the person with ME/CFS (and their family members or carers, as appropriate) informed by the holistic assessment. Based on the person's needs, include in the plan:…"* We are extremely concerned to find that cognitive behaviour therapy and graded exercise therapy are not included as options in the management plan for people with ME/CFS. Reviewing how the committee looked at the evidence base it appears key randomised controlled trials involving hundreds of participants have been downgraded on the basis of the committee's opinions about diagnostic criteria. Yet no evidence to support those opinions has been provided. And yet surely this must be available? As a result qualitative evidence and personal experience of the committee has taken precedence. It is of note that the steps outlined in this section (1.5.2) are very much in keeping with a CBT-based approach to care.	Thank you for your comment. The management sections of the guideline include recommendations: • to support people with energy management • to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or programme into the management of their ME/CFS. • to offer CBT to help people manage their symptoms and to reduce the distress associated with having a chronic illness and are options for the management plan where appropriate. To accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. See evidence reviews G and H for the evidence and the committee discussion on these recommendations. See the methods chapter, evidence reviews D, G and H for further information on the assessment of indirectness and relevance. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review

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					quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
South London and Maudsley NHS Foundation Trust	Guideline	013	012	*"1.1.5 Offer home visits to people with severe or very severe ME/CFS to carry out their holistic assessment and develop their management plan."* The addition of a recommendation on home visits is helpful for people with ME/CFS who may be housebound, particularly important at assessment.	Thank you for your comment.
South London and Maudsley NHS Foundation Trust	Guideline	014	019 - 021	*"1.6.4 Explain that ME/CFS often involves periods of remission and relapse, although it is less common to have long periods of remission (see the section on managing flares and relapse)."* The explanation of ME/CFS here appears somewhat bleak. We see no evidence that the committee has provided or reviewed prospective long-term data on those who present at three months with significant fatigue that meets 'caseness' for disorder (i.e. significant impairment in work and social	Thank you for your comment. After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS. See evidence review A for the committee discussion on information about the long term outlook for people with ME/CFS.

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				function). Given the absence of such, we worry about the implications for people who may read such guidance at the onset of their diagnosis. This is especially relevant, as the guidance suggests that we should be thinking of the possibility of ME/CFS diagnosis as early as the 6 or 4-week stage in adults and children's respectively. Should the committee be unable to provide evidence on recovery from reliable prospective studies, we would suggest the paragraph be written as "varies in long-term outlook from person-to-person. A proportion of people recover or have long periods of remission, and a proportion will need to adapt to living with ME/CFS". We feel such an approach instils hope, whilst retaining acknowledgement of the potential long-term chronic nature of the condition.	
South London and Maudsley NHS Foundation Trust	Guideline	014	028 - 029	"*"1.6.4 Explain that ME/CFS can be worsened by particular triggers, for example new infections, physical injury or stressful events*" Again, this statement seems at odds with some of the document's comments on CBT as a therapy. CBT aims to potentially reduce the severity, impact, and frequency of symptoms, primarily fatigue. Here there is an acknowledgement that stressful events can be triggers for relapse. CBT provides an opportunity to facilitate the understanding of the patient-specific potential triggers, and then work collaboratively to put in place management strategies in anticipation.	Thank you for your comment. After considering the range of stakeholder comments on this bullet point it has been edited to,' can be worsened by particular triggers – these can be known or new triggers or in some cases there is no clear trigger'. The section on CBT is clear that it may help people to manage their symptoms. After considering the stakeholder comments recommendation 1.12.29 has been edited to,' Explain that CBT for people with ME/CFS aims to improve quality of life, including functioning, and reduce the distress associated with having a chronic illness'.
South London and Maudsley NHS Foundation Trust	Guideline	014	029	*"1.6.4 Explain that ME/CFS can be worsened by particular triggers, for example new infections, physical injury or stressful events, including childbirth."*	Thank you for your comment. There were several stakeholder comments about the examples of triggers that worsen ME/CFS. Some of the examples as suggested in your comment were considered potentially

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				We are concerned to see a recommendation that people should be advised that childbirth can worsen the symptoms of ME/CFS. This could lead to people with ME/CFS avoiding pregnancy and planning families. Furthermore, there is evidence suggesting this is not the case (A Comparison of Pregnancies That Occur Before and After the Onset of Chronic Fatigue Syndrome - Schacterle, R; Komarof, A. JAMA 2004)	misleading information and not always a trigger and there are comments that gave other examples that could be added. After considering the stakeholder comments the committee agreed to delete the examples and not provide any examples in the recommendation recognising the variation in triggers in people with ME/CFS.
South London and Maudsley NHS Foundation Trust	Guideline	021	004	*"1.9.1 Advise people with ME/CFS that: there may be times when they are unable to continue with work or education"* To begin the section on education with a statement that people with ME/CFS should be advised they may be unable to continue with education or work is damaging and risks worse patient outcomes. Leaving work or education should be a last resort where all other possibilities have been explored.	Thank you for your comment and information. After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support. ' and discuss with' has been added to the recommendation.
South London and Maudsley NHS Foundation Trust	Guideline	022	008 - 012	*"1.9.6 Advise children and young people with ME/CFS (and their parents and carers) that: training or education should not be the only activity they undertake they should aim to find a balance between the time they spend on education or training, home and family life, and social activities."* We agree with the need for a balance in the activities young people with ME/CFS undertake and are pleased to see this remains part of the guidance. Supporting people to achieve this balance is one of the goals of treatment in CBT.	Thank you for your comment.
South London and Maudsley NHS Foundation Trust	Guideline	024	004 -005	*"1.11.1 Be aware there is no current treatment or cure (non-pharmacological or pharmacological) for ME/CFS"*	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any

<table>
<tr><th>Stakeholder</th><th>Document</th><th>Page No</th><th>Line No</th><th>Comments</th><th>Developer’s response</th></tr>
<tr><td></td><td></td><td></td><td></td><td>We find this comment ‘no current treatment or cure’ perplexing. The management of any condition, especially long-term conditions always involves (1) investigations and (2) treatment. Treatment should not be conflated with cure. An example might be the management of hypertension which will involve investigation of potentially reversible causes and an assessment of impact of the condition, and then treatment with a suitable antihypertensive. This is a well-established concept in medicine, and we can see no reason why ME/CFS should be exempt.

We feel this statement implies a bias against our holistic methods of management, that leads to improvement in our patient population.

Specifically, in relation to our service, our patients report this experience to be extremely helpful.

For instance:

In an audit of our service of 995 patients receiving cognitive behavioural therapy for ME/CFS (confirmed on formal assessment; average duration of symptoms 6.7 years; dropout rate 14%) the service had the following outcomes on self-report measures of function following CBT (Adamson et al 2020).

<table><tr><td>Measure</td><td>Assessment</td></tr><tr><td>Chalder fatigue Scale</td><td>24.2
(n=977</td></tr></table></td><td>misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

Self-reported outcomes

Risk of bias was assessed using Randomised Controlled Trial: Cochrane RoB (2.0) in the studies and then using GRADE in evaluating the quality of the evidence (as described in Developing NICE guidelines: the manual.) The risk of bias for subjective outcomes in unblinded studies needs to be acknowledged, however, this doesn’t mean these outcomes shouldn’t be assessed or aren’t important. The role of the committee is then to discuss this limitation and the impact it has on the results and then in turn on the making any recommendations about practice. The decision making for developing recommendations is multifaceted and complex.

Energy management
Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits.

In addition the management sections of the guideline include recommendations:</td></tr>
</table>

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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<table>
<tr><th>Stakeholder</th><th>Document</th><th>Page No</th><th>Line No</th><th>Comments</th><th>Developer's response</th></tr>
<tr><td></td><td></td><td></td><td></td><td>
<table>
<tr><td>Work and Social Function scale</td><td>25.0 (n=989)</td><td>19.49 (582)</td></tr>
<tr><td>SF-36</td><td>47.6 (768)</td><td>57.5 (441)</td></tr>
</table>

Additionally, on self-reported measures of improvement using the Clinical Global Impression (CGI) scale 53% reported themselves as 'very much or 'much better' by the end of treatment; 2% reported themselves as a little worse; 0.5% reported themselves as very much worse. Three hundred and sixty five patients provided outcome data at follow up

We note prior comments on queries on the validity of some of the scales used in ME/CFS, so to put these findings in context the Clinical global impression (CGI) scale is used in virtually all FDA-regulated trials, with the sole requirement that its scoring rationale is understood. Scoring is based on the presenting pathology in question (but with an overview of the entirety of what is known clinically about the patient). It is known to correlate well with standard well-known drug efficacy scales in a variety of conditions, shows reasonable inter-rater reliability and good correlation with self and observer-rated tools.

We note that the committee seems to think that there is a particular problem in using self-reported outcomes in ME/CFS studies. We do not agree. We draw attention to the fact that NICE recognises that patient recorded outcomes are essential in assessing subjective experiences such as fatigue, pain and depression provided that well validated measures are used. This is not a reason for regarding such outcomes as fundamentally flawed, as the Committee seems to believe.
</td><td>
• to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or programme into the management of their ME/CFS.
• to offer CBT to help people manage their symptoms and reduce the distress associated with having a chronic illness
and are options for part of the care and support plan where appropriate and chosen by the person with ME/CFS. To accompany this the committee have made recommendations that set out how CBT and physical activity and exercise should be delivered for people with ME/CFS. See evidence reviews G and H for the evidence and the committee discussion on these recommendations.

GET
The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy 'based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that use are based on deconditioning and exercise avoidance theories of ME/CFS, or
</td></tr>
</table>

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Additionally, a separate audit on patient satisfaction with treatment (for those who received CBT) from our service revealed the following:	that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. The committee recognised that although graded exercise therapy is not recommended it was important that people with ME/CFS have access to a ME/CFS specialist team to provide support with physical activity and exercise programmes as outlined in the guideline where appropriate.

	n	
ery satisfied	61	43.0
oderately satisfied	50	35.2
ightly satisfied	16	11.3
either	6	4.2
ightly dissatisfied	2	1.4
oderately dissatisfied	3	2.1
ery dissatisfied	4	2.8
otal	142	100.0

In our view, these finding mirror some of the data presented in some of the randomised controlled studies to evaluate the efficacy of CBT for ME/CFS. However, they may also be viewed as offering a real-world validity to this treatment, as the patients referred represent the types of patients who are seen day-to-day by clinicians from various areas of the UK. The findings do not support the comment

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				that there are no treatments for this condition. Furthermore, the guidance then goes on to describe management strategies which are effectively treatments as commonly understood in long term conditions. However, the strategies listed have far less of an evidence base for improving outcomes in ME/CFS than CBT and GET. NB. Regarding the data presented in this comment we used CDC 1994 diagnostic criteria throughout the collection period. Diagnostic assessments were carried out by a team highly experienced in using these criteria. We have a comprehensive assessment procedure for all patients to identify alternative medical and/or psychiatric diagnoses. Our patients are similar to all other ME/CFS populations in that they have post-exertional malaise, high rates of disability, evidence of neuroendocrine and immune system function (underactive HPA axis, and high levels of type 2 cytokine producing cells – see Skowera et al Clin Exp Immunol. 2004 Feb; 135(2): 294–302)	
South London and Maudsley NHS Foundation Trust	Guideline	024	14-15	*"1.11.2 Discuss with people with ME/CFS the principles of energy management, its role in supporting them to live with their symptoms, the potential benefits and risks and what they should expect. Explain that it: helps people understand their energy envelope so they can reduce the risk of overexertion worsening their symptoms"*	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have

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				There is no evidence for the concept of the energy envelope as a management strategy or treatment for ME/CFS. Advocating a treatment without evidence has the potential to be harmful. Pacing (which is similar to the use of an energy envelope concept to limit activity) has been shown not to improve outcomes for patients with ME/CFS. This part of the guidance focuses too heavily on conserving energy rather than a rehabilitative approach aimed at gradual change to support people to achieve their goals and improve their functioning. The energy envelope approach minimises the possibility of change or improvement. We are concerned that a treatment with no evidence is being proposed as a key tenet in supporting people with ME/CFS.	while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS. *Pacing* The committee discussed the use of the term pacing agreed that it means something different to different people with many different versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.

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South London and Maudsley NHS Foundation Trust	Guideline	025	4-6	*"1.11.3 Carry out an assessment to help people with ME/CFS develop an energy management plan with realistic expectations and goals that are meaningful to them."* The energy management plan described here is encompassed within the rubric of our specialist CBT intervention. We reiterate a suggestion that the document fails to understand what CBT provides, and has downplayed the evidence in this area in a manner that will be of detriment to those wanting to receive care within our service and other similar services.	Thank you for your comment. The section on CBT includes recommendations to offer CBT to help people manage their symptoms and reduce the distress associated with having a chronic illness and is an option for part of the care and support plan where appropriate and chosen by the person with ME/CFS. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Both CBT and energy management are included in the care and support plan as tools to support people with ME/CFS if they choose to use them.
South London and Maudsley NHS Foundation Trust	Guideline	025	25-26	*"11.11.6 Advise people with ME/CFS to reduce their activity if increasing it triggers symptoms, or if they have fluctuations in their daily energy levels."* We are concerned about the recommendation to advise all people with ME/CFS to reduce their activity if increasing it triggers symptoms, or if they have fluctuations in their daily	Thank you for your comment. After considering the stakeholder comments this has been edited to,' Advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).'

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<tr><td></td><td></td><td></td><td></td><td>energy levels. This standalone statement runs counter to the need for a flexible, patient centred approach described elsewhere. If followed strictly it will make it impossible to support people to increase their activity as part of their management plan.

There is also little advice in the guidance on how to increase activity except with caveats, for example about risks of worsening symptoms or challenges. In our experience most people we see with ME/CFS are more likely to ask how to increase valued activities safely and identify these as treatment goals. As the guidance stands people reading this will see reducing activity as essential and increasing activity as something to be undertaken only with extreme caution - this is unlikely to lead to people achieving their goals or improving their quality of life.</td><td></td></tr>
<tr><td>South London and Maudsley NHS Foundation Trust</td><td>Guideline</td><td>025</td><td>18</td><td><i>"1.11.4 Based on the person's assessment, establish an individual activity pattern within their current energy envelope that minimises their symptoms. For example: reduce activity as the first step"</i>

Regarding the recommendation 'Reduce activity as the first step'. Although we agree a reduction in activity agree is sometimes part of the plan collaboratively developed with the patient, it is specifically to help an individual develop a more consistent approach to activity before building up slowly.

Our patient outcome data on GET suggests patients improve:
<table><tr><td>Scale</td><td>Assessment</td></tr><tr><td>Chalder Fatigue Scale (range</td><td>25.8 (n=67)</td></tr></table></td><td>Thank you for your comment.
After considering the stakeholder comments this bullet point has been edited to, agree a sustainable level of activity as the first step, which may mean reducing activity.'

<i>Included data</i>
All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. Any evidence that met the protocols or the call for evidence was included in the evidence reviews.</td></tr>
</table>

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<table>
<tr><td>Work and Social Function scale</td><td>25.3
(n=66)</td><td>21.5
(n=66)</td></tr>
<tr><td>SF-36
(range 0-100)
Higher scores denote better health</td><td>45.4
(n=49)</td><td>54.4
(n=49)</td></tr>
</table>
<p>NB. our service has fewer GET therapists than CBT therapists hence the reduced numbers</p>
<table>
<tr><td>ery satisfied</td><td>9</td><td>32.1</td></tr>
<tr><td>oderately satisfied</td><td>11</td><td>39.3</td></tr>
<tr><td>ightly satisfied</td><td>4</td><td>14.3</td></tr>
<tr><td>either</td><td>3</td><td>10.7</td></tr>
<tr><td>oderately dissatisfied</td><td>1</td><td>3.6</td></tr>
<tr><td>otal</td><td>28</td><td>100</td></tr>
</table>
<p>We do wonder if outcomes from specialist services that offer such interventions were fully taken into consideration when producing such recommendations, and feel that any such omission of the attached outcome data would represent a bias in the evidence base in the use of GET in ME/CFS.</p>
</td><td></td></tr>
</table>

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				NB. Regarding the data presented in this comment we used CDC 1994 diagnostic criteria throughout the collection period. Diagnostic assessments were carried out by a team highly experienced in using these criteria. We have a comprehensive assessment procedure for all patients to identify alternative medical and/or psychiatric diagnoses. Our patients are similar to all other ME/CFS populations in that they have post-exertional malaise, high rates of disability, evidence of neuroendocrine and immune system function (underactive HPA axis, and high levels of type 2 cytokine producing cells – see Skowera et al Clin Exp Immunol. 2004 Feb; 135(2): 294–302)	
South London and Maudsley NHS Foundation Trust	Guideline	026	1-3	"*1.11.8 Refer people with ME/CFS to a specialist ME/CFS physiotherapy or occupational therapy service if they have had reduced physical activity or mobility levels for a long time*" We agree that patients with reduced activity or mobility levels should be referred to specialist services especially if they have had symptoms for a long time. However, it is also important that patients are referred earlier on in the illness journey to avoid further deterioration. One of the biggest changes that has happened across medicine over the last five decades is the realisation that in every condition ever studied, or after any important trauma, accident, life event or illness, the longer people remain on bed rest, immobile or with restricted activity levels, the worse the outcome. The trend over the decades is to reduce the time of restricted activity to the safest minimum,	Thank you for your comment. After considering the stakeholder comments this recommendation has been edited to ,'refer people with ME/CFS to a physiotherapist or occupational therapist working in a ME/CFS specialist team if they: • have difficulties caused by reduced physical activity or mobility or • feel ready to progress their physical activity beyond their current activities of daily living or • would like to incorporate a physical activity or exercise programme into managing their ME/CFS.

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				knowing that anything longer does more harm than good. Prevention is better than cure. The committee does not define 'long'. However, we suggest that even in the short term rehabilitation services should be considered.	
South London and Maudsley NHS Foundation Trust	Guideline	027	21, 24	*"1.11.16 Do not offer people with ME/CFS:…"* We are very concerned that the strong, prescriptive 'do not' statements opening this section will result in health professionals avoiding any advice incorporating physical activity or exercise which would run counter to the advice on a person-centred care and flexibility expressed elsewhere in the guidance. This is also at odds with the favourable outcome data we have for our service for those who undertake graded exercise therapy (see comment 27 above).	Thank you for your comment. After considering the stakeholder comments, the committee have added exercise into the recommendations on considering a physical activity programme to clarify where these apply to exercise. The recommendation describes the types of physical activity or exercise programmes that should not be offered to people with ME/CFS. The previous recommendation in the energy management section includes that people who would like to incorporate a physical activity or exercise programme into managing their ME/CFS (see the section on physical activity and exercise) should be referred to a physiotherapist or occupational therapist working in a ME/CFS specialist team. The following recommendation in the physical activity section reinforce this and includes that if a physical activity or exercise programme is offered, it should be overseen by a physiotherapist in a ME/CFS specialist team. *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the

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					reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy 'based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.

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					Underrepresentation of people who have benefited from GET. The committee membership had a broad range of professional and personal knowledge about the different experiences of people with ME/CFS and this was discussed and considered at all stages of the decision making. There is little representation in the qualitative literature of people who have benefited from GET. The committee hope that where this can be published it will be as this can only further inform the care and support of people with ME/CFS.
South London and Maudsley NHS Foundation Trust	Guideline	028	8	*"1.11.6 Do not offer people with ME/CFS: structured activity or exercise programmes that are based on deconditioning as the cause of ME/CFS."* Deconditioning may not be the cause of ME/CFS but it is an important factor which can exacerbate symptoms, functioning and make reduce the likelihood of improvement or recovery. This is the case for any illness which involves long periods of immobility or rest and there is no evidence suggesting we should consider ME/CFS as different in this respect. We advise that the role of deconditioning as a modifiable factor contributing to ME/CFS be included. Without this people with ME/CFS are denied the possibility of support with a modifiable perpetuating or exacerbating factor in their illness (see page 28 line 9 and page 63 line 15).	Thank you for your comment. The committee have concluded that therapies based on deconditioning and exercise avoidance theories of chronic fatigue syndrome should not be offered to people with ME/CFS. These therapies assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. The committee recommended that strategies to maintain and prevent deterioration of physical functioning and mobility be included in support plans for people with ME/CFS . To note after considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.
South London and Maudsley	Guideline	028	19	*"1.11.19 Tell people about the risks and benefits of a physical activity programme. Explain that some people with ME/CFS have found that physical activity programmes can make their*	Thank you for your comment.

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NHS Foundation Trust				*symptoms worsen, for some people it makes no difference and others find them helpful."* This seems like a more balanced, appropriately positioned statement on increasing activity. We would add that where symptoms do appear to be consistently worsening the plan can be reviewed and advice / management adapted accordingly.	The personalised collaborative physical activity or exercise programme includes the recognition and management of flare ups and relapses.
South London and Maudsley NHS Foundation Trust	Guideline	028	27	*"1.11.20 If a physical activity programme is agreed with the person with ME/CFS, it should be personalised and should start by reducing the person's activity to within their energy envelope."* Again, we know of no evidence suggesting that programmes incorporating activity should always begin with a reduction in activity. Our view is that this depends on the patient. This recommendation goes against the flexible, person-centred approach we would normally take.	Thank you for your comment. This is to ensure the person starts the programme at a level that does not worsen symptoms and to ensure this level is maintained until flexible adjustment are agreed. As you note this is a personalised collaborative physical activity or exercise programme and would be agreed with the person and reviewed regularly.
South London and Maudsley NHS Foundation Trust	Guideline	029	10-13	*"1.11.21 Agree with the person how to adjust their physical activity after a flare or relapse. This should include:* • *reducing physical activity within the person's current energy envelope to stabilise their symptoms* • *only once symptoms stabilise and the person feels able to resume physical activity, establishing a new physical activity baseline."* This is too prescriptive and goes against the flexible approach, person centred approach we take. There is no evidence that all relapses / flare ups should be managed by a rapid reduction in activity. Similarly stating that increases in activity should	Thank you for your comment. The recommendation does not include a rapid reduction in activity but a reduction to stabilise symptoms. . As you note this is a personalised collaborative physical activity or exercise programme and would be agreed with the person and reviewed regularly.

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				only occur once symptoms have stabilised is not appropriate as a blanket statement. This could lead to long periods of decline and disability before something is done.	
South London and Maudsley NHS Foundation Trust	Guideline	030	14-16	*"1.11.27 Refer to the following for advice on treating pain:* - *NICE guideline on neuropathic pain in adults 15* - *NICE guideline on headaches in over 12s."* This section should also include a recommendation to refer to the NICE guidance on chronic pain. We are aware this is being reviewed. As noted in section 1.1.8 pain in ME/CFS can be muscular, arthritic or have neuropathic features so it is important all relevant NICE guidance is included.	Thank you for your comment. The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion.
South London and Maudsley NHS Foundation Trust	Guideline	031	6	"*1.11.29 Do not offer any medicines or supplements to treat or cure ME/CFS"* We wonder if it would be helpful to list some of the medication that should not be prescribed as a treatment for ME/CFS as we find that people with ME/CFS and health professionals frequently contact our service asking for advice on these. In the 2007 guidance a list of medications which should not be prescribed as a treatment was given. We would suggest this list include antibiotics, antiviral agents, steroids and hormonal treatments, immunological treatments, supplements and Vitamin B12 injections.	Thank you for your comment. The committee discussed whether a list of medicines should be included but concluded that any list would be incomplete and could be interpreted and used differently. The committee decided it was clearer to have a do not offer recommendation for all medicines or supplements to cure ME/CFS.
South London and Maudsley NHS Foundation Trust	Guideline	031	13	*"1.11.31 Take into account when prescribing that people with ME/CFS may be more intolerant of drug treatment and have more severe adverse effects. Consider starting drug treatments at a lower dose than in usual clinical practice"*	Thank you for your comment.

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				We agree that starting appropriate medication (for example to treat co-existing depression) at lower than normal doses can be helpful, particularly where there is a history of previous poor tolerance of medication or concern about the potential for adverse effects.	
South London and Maudsley NHS Foundation Trust	Guideline	034	2	*"1.11.43 Only offer cognitive behavioural therapy (CBT) to people with ME/CFS who would like to use it to support them in managing their symptoms of ME/CFS and to reduce the psychological distress associated with having a chronic illness. Do not offer CBT as a treatment or cure for ME/CFS"* We were surprised by this recommendation. The definition of therapy is a "treatment intended to relieve or heal a disorder". Reducing psychological distress and managing symptoms describes a treatment. The evidence from our service (see above) and from RCTs shows that CBT can lead to improved functioning and reduced symptoms. The current paragraph potentially reads as stigmatising in trying to partition off the complex interplay of mind and body that leads to disorder, in any known medical condition. We wonder where this statement originated from, and whether similar statements exist (for instance in hypertension guidance in NICE). Should they not be there, we would suggest removal of this current statement as it is potentially stigmatising against psychological medicine interventions. We view psychological therapies in this condition as similar to those provided for chronic pain, where there may be variable improvements in fatigue, but reliable improvements in functioning. Improvements in disability are often seen to a level where patients no longer meet 'caseness' for the disorder.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.

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South London and Maudsley NHS Foundation Trust	Guideline	034	13	*"1.11.45 Explain that CBT for people with ME/CFS is designed to improve wellbeing and quality of life."* We find this comment that CBT is designed to improve well-being and quality of life at odds with prior statements within the document that it is not a treatment.	Thank you for your comment. After considering the range of stakeholder comments the first recommendation in this section has been edited to remove the word treatment. The committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.
South London and Maudsley NHS Foundation Trust	Guideline	035	1-13	*"1.11.47 CBT for people with ME/CFS should include the following components:* • *developing a shared understanding with the person about the main difficulties and challenges they face* • *exploring their personal meaning of symptoms and illness, and how this might relate to how they manage their symptoms* • *working together to adapt and refine self-management strategies to improve the person's functioning and quality of life, for example their sleep, activity and rest* • *developing a self-management plan* • *reviewing their plan regularly to see if their self-management strategies need to be adapted, for example if their symptoms or functioning change* • *developing a therapy blueprint collaboratively with their therapist at the end of therapy."* We thank the committee for outlining clearly the approach to cognitive behavioural therapy for ME/CFS. Given the observation that therapy is defined as a treatment intended to relieve or heal a disorder, we	Thank you for your comment. After considering the range of stakeholder comments the first recommendation in this section has been edited to remove the word treatment. The committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.

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				find the accurate description of CBT's approach in this section, at odds with the preceding statement that it is not a treatment for ME/CFS. This is particularly the case as this section specifically mentions a "therapy blueprint". CBT for ME/CFS is designed to treat fatigue though not associated distress.	
South London and Maudsley NHS Foundation Trust	Guideline	036	14-20	*"1.12.4 For recommendations on identifying and treating associated or comorbid anxiety, depression or mood disorders see the: NICE guideline on depression in adults; NICE guideline on depression in adults with a chronic physical health problem; NICE guideline on depression in children and young people; NICE guideline on generalised anxiety disorder and panic disorder in adults; NICE guideline on common mental health problems."* Screening for mood disorders should be part of the every initial ME/CFS assessment. The assessment section mentions asking about psychological wellbeing but not depression (see above comment 13 to page 8, line 8). We are concerned listing depression only as a co-morbidity risks it being missed and undertreated in people with ME/CFS.	Thank you for your comment. *Inclusion of mental health assessments in the guideline.* An assessment of mental health is included in the medical assessment in the section on suspecting ME/CFS in addition to an assessment of the impact of symptoms on psychological wellbeing. This is then repeated in the holistic assessment carried out by the ME/CFS specialist team to confirm a diagnosis and develop the care and support plan. The review section of the guideline includes an assessment of a person's condition and an assessment of their psychological wellbeing. Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms. No differentiation is made on physical or mental health conditions. With all assessments clinical judgment is exercised to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer. This would include considering whether there are mental health concerns. Also to note that after taking into consideration the stakeholder comments the committee have reviewed the list of differential

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					diagnosis in Evidence review D and added, mental health conditions: anxiety, depression or mood disorders to reflect the managing co-existing section of the guideline.
South London and Maudsley NHS Foundation Trust	Guideline	036	9-11	*"1.12.3 For recommendations on multimorbidity, thyroid disease and coeliac disease refer to the: NICE guideline on multimorbidity; NICE guideline on thyroid disease; NICE guideline on coeliac disease."* These conditions should also be mentioned as part of the assessment of suspected ME/CFS not just as a co-morbidity. They are treatable causes of fatigue (although they can also be co-morbidities).	Thank you for your comment. Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms. After considering the stakeholder comments the committee have now included examples of investigations that might be carried out to identify or exclude other conditions in the suspecting ME/CFS section of the guideline. Evidence review D- Diagnosis includes comprehensive lists of differential and co-existing conditions that are commonly associated with ME/CFS.
South London and Maudsley NHS Foundation Trust	Guideline	037	6-13	"1.13.2 Respond promptly to a flare in symptoms by…" Flare-ups are very common in patients with ME/CFS. At these times patients are encouraged to reduce exercise a little. However, they are not encouraged to stop activity altogether.	Thank you for your comment. The committee agree and temporarily reducing activities is included in the recommendation.
South London and Maudsley NHS Foundation Trust	Guideline	037	6-7	*"1.13.2 Respond promptly to a flare in symptoms by identifying possible triggers, such as acute illness or overexertion (in some cases there may be no clear trigger)"* Triggers for flare ups include psychosocial stressors which should also be listed here.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
South London and Maudsley	Guideline	040	16 - 23	*"1.15.2 Ensure that training programmes on ME/CFS:*	Thank you for your comment.

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NHS Foundation Trust				*provide evidence-based content and training methods (developed and supported by specialist services with input from people with ME/CFS) represent the experiences of people with ME/CFS, using video and other resources."* We are pleased to see a section on training particularly highlighting the need for input from service users and for training to include the use of video or other resources to represent the views of people with ME/CFS.	
South London and Maudsley NHS Foundation Trust	Guideline	047	11	"1.15 Training for health and social care professionals" We agree that the teaching on ME/CFS needs to be improved across the healthcare profession. We view this guidance as an opportunity to provide such teaching. However, the tone of the current guidance as outlined in many of the points we have raised do not seem to lend themselves well to an integrated model of care incorporating aspects of rehabilitation, with a biological, psychological, and social context. Specifically, excluding the psychological / behavioural component of care in a treatment approach will worsen the impact the condition has on individuals. As it currently stands, we feel the guidance lacks the nuance in understanding of therapy and treatment.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this.
South London and Maudsley	Guideline	049	10-17	*Page 49: "The committee acknowledged there is ongoing discussion in the ME/CFS community about which*	Thank you for your comment and information.

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NHS Foundation Trust				*diagnostic criteria should be used to diagnose ME/CFS. Based on both the evidence and their experience, the committee agreed that the Institute of Medicine's 2015 criteria had the best balance of inclusion and exclusion of all the reviewed criteria, but it needed to be adapted for optimal use. In particular, the committee felt that the 6-month delay should be reduced so that management could start earlier, and that fatigue and post-exertional symptom exacerbation should be defined clearly to make it easier to interpret the revised criteria."* Regarding the diagnostic criteria, we accept that this should be clarified. However, in pragmatic terms, all diagnostic criteria are defined by the extent to which symptoms impact on social, private and occupational activities. The individual is therefore unable to function adequately. We feel the guidance would be enhanced, in this condition in particular (given the lack of clear aetiology), if due recognition is given to this. Additionally, it feeds back into the concept and aim of therapy - should a person continue to experience fatigue but able to maintain social relationships, or occupational function, as they would desire, such an individual would not meet criteria for the disorder. This additionally highlights how we might define improvement, and 'recovery' in a more objective way for this condition. This is especially pertinent given the comments on an absence of consensus criteria for this disorder.	

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South London and Maudsley NHS Foundation Trust	Guideline	051	7-9	Page 51: "*…the committee made a recommendation to give people advice on symptom management drawn from their own knowledge and experience.*" (regarding the section titled "advice for people with suspected ME/CFS (Recommendations 1.3.1 and 1.3.2). We agree (consistent with our own experience) that patients treated early, tend to improve far more than those who have suffered several years with the condition. However, especially in this group, we have concerns that the advice suggested that "only a 'small' proportion recover" is unhelpful given the lack of research evidence in this area. The best evidence in this area suggests that patients should receive CBT or GET early. We feel this omission may seriously impact on recovery in those who potentially have the best prognosis. (see eg. Candy et al, Journal of Psychosomatic Research 2005)	Thank you for your comment. *Advice for people with suspected ME/CFS* The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. Taking into account the views of people with ME/CFS in the qualitative evidence the committee agreed it was important to make recommendations for support at this stage while acknowledging there is a lack of trial evidence to support that advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS. The committee agreed the advice would not be harmful in the short term either to people that are later diagnosed with ME/CFS or those that are diagnosed with another condition. To note after considering the stakeholder comments the committee edited the wording on prognosis to,' a proportion of people recover'.
South London and Maudsley NHS Foundation Trust	Guideline	053	8-10	Page 53: "*The committee agreed that the key to managing ME/CFS symptoms successfully is 8 having a personalised management plan, which should be developed as soon as the 9 person's diagnosis is confirmed.*" We are surprised the committee has prioritised a 'personalised management plan' over the large evidence base for CBT or GET. This seems inconsistent with NICE's function of commenting only on	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) The care and support plan would include detail on any strategies for managing ME/CFS or treatments for managing symptoms.

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				areas where there is sufficient evidence. If we wish to adhere to a strong evidence base, is worth saying that well conducted CBT and GET is always personalised.	
South London and Maudsley NHS Foundation Trust	Guideline	060	2-8	Page 60: *"Overall, the evidence for non-pharmacological and pharmacological interventions for ME/CFS was heterogenous and inconclusive, with limited evidence for any one intervention, and this supported the committee's experience. The committee was aware of claims that have been made about cures for ME/CFS and that there is often a financial cost to people with ME/CFS when they pursue these. To address this, the committee agreed to raise awareness in the recommendations of the current lack of treatment or cure for ME/CFS."* It is our view here that the committee has missed and discounted essential evidence. Most of the studies have adopted the use of a broad scorecard of (both clinician, and patient self-rated) measures that indicate improvement. This is also the case for our day-to-day clinical work. Additionally, we continue to develop and adapt our approach based on patient qualitative feedback which we present below. Please note this feedback indicates our approach is more than patients simply 'liking' the intervention or 'wanting someone to talk to', which would be more consistent with the term support or	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. Any evidence that met the protocols or the call for evidence was included in the evidence reviews.

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				supportive counselling. The feedback is far more specific indicating that the treatments help manage (i.e. reduction in severity of fatigue; improvement in physical function) their disorder. Given this is cumulative feedback over five years, from a large number of patients, we wonder on the committee's justification for the disregard of the evidence for CBT. Additionally, given the average length of time our sufferers have experienced disability prior to coming to our service, this is unlikely to reflect spontaneous recovery. We have one-year follow up data that indicates the gains are broadly maintained. Patient feedback from South London and Maudsley NHS Foundation Trust's Chronic Fatigue / Persistent Physical Symptoms Service: **Comments from people with ME/CFS who had Cognitive Behaviour Therapy** **the following comments are CONFIDENTIAL** NB. Regarding the feedback presented in this comment we used CDC 1994 diagnostic criteria	

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				throughout the collection period. Diagnostic assessments were carried out by a team highly experienced in using these criteria. We have a comprehensive assessment procedure for all patients to identify alternative medical and/or psychiatric diagnoses. Our patients are similar to all other ME/CFS populations in that they have post-exertional malaise, high rates of disability, evidence of neuroendocrine and immune system function (underactive HPA axis, and high levels of type 2 cytokine producing cells – see Skowera et al Clin Exp Immunol. 2004 Feb; 135(2): 294–302)	
South London and Maudsley NHS Foundation Trust	Guideline	061	1-10	*Page 61: "The committee listed the components of energy management and what an assessment and plan would include, noting that the key component is understanding the principle of the 'Energy envelope'."* We are surprised NICE feels they can make recommendations regarding an 'energy envelope' without a robust, systematic evaluation in the context of a trial. The main concern might be whether such an approach may cause harm. Indeed, the PACE trial showed this was less effective than CBT or GET. Whilst we applaud the caring concern that such an attempt implies, our view is it is very difficult to include such recommendations, given NICE's recognised status as the lead on evidence-based clinical	Thank you for your comment and information. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or

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				practice. To be weighed against this viewpoint, we provide some qualitative feedback on the use of exercise (specifically GET) and how it has benefited some of our users over the years, in response to a question 'what does recovery mean to you. The body of data may suggest the views and experience of the committee members may not be entirely representative. Patient feedback from South London and Maudsley NHS Foundation Trust's Chronic Fatigue / Persistent Physical Symptoms Service: NB. Regarding the feedback presented in this comment we used CDC 1994 diagnostic criteria throughout the collection period. Diagnostic assessments were carried out by a team highly experienced in using these criteria. We have a comprehensive assessment procedure for all patients to identify alternative medical and/or psychiatric diagnoses. Our patients are similar to all other ME/CFS populations in that they have post-exertional malaise, high rates of disability, evidence of neuroendocrine and immune system function (underactive HPA axis, and high levels of type 2 cytokine producing cells – see Skowera et al Clin Exp Immunol. 2004 Feb; 135(2): 294–302)	downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS.

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				PLEASE NOTE, ESPECIALLY IN RELATION TO THE ABOVE FEEDBACK, WE WOULD BE INTERSTED IN THE PANEL'S VIEWS ON THE IMPACT THIS WOULD HAVE IN LIGHT OF THE FEEDBACK ABOVE.	
South London and Maudsley NHS Foundation Trust	Guideline	063	2-12	The comments here on a physical activity program (e.g. GET) seem counterintuitive, and at odds with any other approach to recovery that is usually provided in a neurorehabilitation setting. For instance, patients who have suffered spasticity in the context of a stroke, are also known to suffer from (centrally mediated) fatigue, alongside centrally mediated muscle atrophy, yet they receive planned systematised rehabilitation despite the observation that their contractures are neurologically caused. We are concerned the comments here reflect a bias, based on those who do not recover.	Thank you for your comment.
South London and Maudsley NHS Foundation Trust	Guideline	068	1-3	We feel in adherence with the strict standards of NICE, that if the committee should provide more specific (qualitative) feedback on how their members found CBT useful.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence

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					reviews G and H for the evidence and the committee discussion on these recommendations).
Stonebird	Appendix 2	General	General	Unfortunately with the term ME/CFS, any research findings will be vague because ME/CFS is vague and undefined itself. Severe ME covers a wide range of symptom severity, which will be different for each person and there is still a wide range of physical and cognitive capability within this group. So the experience of the most ill will not be here. Some will have neurological ME others may not, within the umbrella term ME/CFS. Without clarifying in greater detail who diagnosed the person with Severe ME, what specific medical role, if any, they had and what criteria were used, it is uncertain what illness the contributors have. This is not a criticism of them or what they have shared, which is clearly valuable but unlikely to be a total representation of the wider group of Very Severe ME. It is a failing of the system. .Questions could have been more specific to get better understanding of who was answering the questionnaire. 59 questions in such a short space of time for anyone with severe Cognitive dysfunction is impossible. We are glad to see it recognised that people with Very Severe ME are unlikely to have been included in this survey. This highlights the fact that none of the guidance has been informed by the most severely disabled and ill people diagnosed with ME. And therefore NICE has failed to consult the most ill and importantly has not consulted with this group of extremely vulnerable people as required, in order to make the recommendations that it has done. This guideline cannot be said to be for people with Very Severe ME.	Thank you for your comment.
Stonebird	Appendix 2	007	006	Add : "However 2% of people have Very Severe ME and are at extreme risk of harm, if this severity is not recognised and understood specifically"	Thank you for your comment. Appendix 2 is the report written by the University of Manchester Centre for Primary Care.

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Stonebird	Appendix 2	007	007 - 008	The disease is not curable, or treatable and there are no reliable or safe treatment protocols, universally advocated. "Lasting many years" is a typical understating and diminishing of the reality of Severe and Very Severe ME. This description comes nowhere near to describing the high level, continuous severity of	Thank you for your comment. Appendix 2 is the report written by the University of Manchester Centre for Primary Care.
Stonebird	Appendix 2	007	011 - 012	It is not just that "symptoms are reported" they should be medically recognised. Justifiably, reasonably people have difficulty accessing services.	Thank you for your comment. Appendix 2 is the report written by the University of Manchester Centre for Primary Care.
Stonebird	Appendix 2	007	017	Unfortunately this Consultation was only focused upon people with Severe not Very Severe ME. There were far too many questions and not enough time for people with Very Severe ME to contribute. Therefore the Guideline cannot be said to be safe or representative for people with Very Severe ME – because this Group has not been consulted. In this context, exactly what does "ME/CFS symptoms" mean? Were these people diagnosed with "Severe ME" specifically? We are surprised to hear, given the severity of symptoms in Severe ME that "most cannot work part time", implying some can. "ME/CFS" covers a very wide range of illnesses and therefore will not provide the specific information required to safely convey more than just generalised information on what may or may not be ME. It serves no one to have a vague description, especially when there are no criteria that adequately describe the symptoms in the first place.	Thank you for your comment. In Appendix 2, section 2.5.1 the study authors describe why they decided on an on line survey for this population. They also set out the limitations of the consultation, acknowledging there are limitations on using an online survey, on the recruitment and the representation of the sample. These include the points your raise about the survey and diagnosis. In section 4 of the appendix the committee also noted the sample was a self-selected group and the diagnosis was self-reported sample and this was taken into account in the decision making.
Stonebird	Appendix 2	007	033	There was minimal time allowed to include the most ill and have a voice.	Thank you for your comment. In Appendix 2, section 2.5.1 the study authors describe why they decided on an on line survey for this population. They also set out the limitations of the consultation, acknowledging there are limitations on using an online survey, on the recruitment and the representation of the sample. These include the points your raise about the time.

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Stonebird	Appendix 2	008	005 - 014	It needs recognising that these findings do not include people with Very Severe ME.	Thank you for your comment. In Appendix 2, section 2.5.1 the study authors describe why they decided on an on line survey for this population. They also set out the limitations of the consultation, acknowledging there are limitations on using an online survey, on the recruitment and the representation of the sample. These include the points your raise about the survey and diagnosis. In section 4 of the appendix the committee also noted the sample was a self-selected group and the diagnosis was self-reported sample and this was taken into account in the decision making.
Stonebird	Appendix 2	008	048	What "Pacing therapies" specifically? We would question that any form of pacing would be called a "treatment".	Thank you for your comment. Appendix 2 is the report written by the University of Manchester Centre for Primary Care.
Stonebird	Appendix 2	009	011	We understood the updated NICE Guideline to be about Management, not "Treatment"? How can you specifically recommend treatment for an unspecified group of people with different illnesses, because "ME/CFS" is an umbrella term not a specific disease?	Thank you for your comment. Appendix 2 is the report written by the University of Manchester Centre for Primary Care.
Stonebird	Appendix 2	009	023 - 026	This list of symptoms does not fully represent Severe or Very Severe ME. Physical Paralysis, for example, following sleep or during the day, partial or total, recurring or permanent is an important symptom that is being unacceptably ignored as part of the disease Myalgic Encephalomyelitis leaving people misinterpreted as having FND. It is important to understand the triggers, the best way to approach and support people,	Thank you for your comment. Appendix 2 is the report written by the University of Manchester Centre for Primary Care.

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				what not to do. This is a whole area for proper recognition and research. Specifically co-morbid conditions should not be ruled out.	
Stonebird	Appendix 2	009	040 - 045	The time constraints, both of the Research Projection and this Consultation feedback on the Draft Guideline have made it impossible for anyone with Very Severe ME to contribute. A lengthy questionnaire is not a suitable way to access information from this group of people. We do not consider that people with Very Severe ME have been properly included in gaining essential information on their experience. Without any clarification of what "ME/CFS" actually means or what illnesses are included under this umbrella term, any information gathered remains general rather than specific.	Thank you for your comment. In Appendix 2, section 2.5.1 the study authors describe why they decided on an on line survey for this population. They also set out the limitations of the consultation, acknowledging there are limitations on using an online survey, on the recruitment and the representation of the sample. These include the points your raise about the survey and diagnosis. In section 4 of the appendix the committee also noted the sample was a self-selected group and the diagnosis was self-reported sample and this was taken into account in the decision making.
Stonebird	Evidence Review G	General	General	We welcome that the committee found the evidence for GET to be of low to very low quality. We welcome that the committee recognised the implications of the underlying narrative in CBT negating the person's experience and the wrongness of associating illness with' wrong illness beliefs. We are pleased to see finally that GET is not recommended as curative or as treatment, also the Lightning Process. We welcome the recommendation to not offer GET.	Thank you for your comment.
Stonebird	Guideline	General	General	Despite the use of the name, this Guideline is not about the WHO-classified neurological disease Myalgic Encephalomyelitis (ME) and is unable to offer safe advice, treatment and support to patients. The language throughout is still overtly psychosocial. A complex physical disease, ME requires a biomedical pathway, however the overall emphasis of this Guideline is on mental health assessment, psychological therapy and psychosocial interpretation. The fundamental problem is that this is a Guideline not on	Thank you for your comments and feedback on the consultation documents. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly*

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				'ME" but upon "ME/CFS", a vague umbrella term, encompassing countless, disparate, fatigue conditions, which even the Guideline itself does not seem able to define. Without identifying pathology, no one is safe within an "ME/CFS" cohort. Rather than clarify the issues, as promised, for a new appropriate ME service, the Guideline continues to feed into the current discredited, unwanted Fatigue Service paradigm, which helps no one identify what is wrong with them or get their needs safely met. For people who hoped that NICE would go in a biomedical direction, with a properly defined disease, would abandon the psychosocial pathway and would separate out different sub groups for much better diagnosis, treatment and support, this Guideline is a massive let down. Its baseless pretence that improvement can be achieved through psychosocial therapy, which negates the physical reality and unimaginable physical suffering of ME is not just a crushing disappointment but is also profoundly irresponsible and dangerous, particularly to people with Severe and Very Severe ME. The debilitating cognitive difficulties and the sheer physical barriers to processing and commenting that make CBT, which is at the core of this Guideline, an impossibility for the most ill, are just not recognised in this document. But, how could they have been, given how the voice of the most severely affected is entirely missing from this document?	*defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'* The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3)' has been added to the context. *People with severe or very severe ME/CFS* When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. One of these reports focused on people with severe or very severe ME/CFS (see appendix 2 for details of the research and the recruitment methods used). The guideline committee included members that had experience of people with severe or very severe ME/CFS. Taking into account the range of stakeholder comments the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline. In this section the symptoms, their impact and the need for risk

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				It contains no input whatsoever from people with Very Severe ME and that is its fatal flaw. It also fails to recognise that there will be a range of abilities, cognitive difficulties and tolerances within the wider Severe ME group. Some will cope better with interactions and assessment procedures than others. We had hoped to provide a detailed response, from a Very Severe ME perspective, however, coming up to Christmas and in the midst of a pandemic, the consultation time has been poorly timed and no extensions were permitted, so our response is frustratingly limited. The Guidelines show no awareness at all of the crucial difference in illness and symptom experience, between the 25% of the patient population with Severe ME and the 2% with the much more extreme Very Severe ME. It is very troubling how the Guideline consistently under describes Severe ME and completely fails to describe Very Severe ME. It includes the same guidance for Severe and Very Severe ME, not recognising the extreme vulnerability and intense symptom experience of those in the Very Severe category, whom can be harmed long term, by even the slightest move, wrong noise or contact. They need specific care provided in an incredibly sensitive, skilled and flexible way. The specific skills and approach required of carers do not appear to be listed in the draft guideline. People with Very Severe Myalgic Encephalomyelitis need in depth understanding in order to safely approach, if at all. Values and underlying attitudes need more input. The layout of the Consultation Form is confusing. It is impossibly hard to follow for anyone with cognitive difficulties. It is inexcusable, for example, that after clicking on a hyperlink,	assessment are recognised for people with severe or very severe ME/CFS As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). *Consultation period* The consultation period was the standard length for consultations on NICE guidelines as set out in [Developing NICE guidelines: the manual.](#) An e-mail was sent to all stakeholder groups in August 2020 to confirm the consultation dates when they were amended. We are grateful to your organisation for engaging with the consultation and for the comments you have submitted.

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				there is no facility to turn back to the exact line or section on the Guideline, that one was on previously. Instead, one is returned to the head of the Guideline Document and forced to scroll down and search, wasting valuable time and energy and impacting visual and cognitive difficulty. The research that was conducted which was presumably carried out an heterogeneous group, was done far too quickly for people with Very Severe ME to participate in, was not in an accessible format. It did not recognise the difficulty of answering questions and accessing information in the most severely ill. 59 questions would have way too much for some people, whose input was essential. No wonder their voice is missing. The Guideline's uncritical assumption that the current system of Fatigue Specialists and "ME/CFS" experts who, up to now have been providing a psychosocial-based service, one based on the premise that there is no underlying pathology to ME, should not only continue but greatly expand its role in offering assessment, management strategies, care support and training is absurd and potentially harmful, especially for the most ill, who are so incredibly vulnerable to harm, through the slightest wrong or unaware approach, practice or intervention. The fact that none of the Guidance has been informed by the most severely ill and disabled people diagnosed with Very Severe ME, whom NICE has failed to consult with, despite saying it must, means that this Guideline cannot be said to be for people with Very Severe ME. People with ME have tragically been let down again and have not been listened to or heard.	

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Stonebird	Guideline	040 - 041	011 - 023 001 - 004	It is a concern if training will be provided by people and services that have previously promoted the Biopsychosocial interpretation of ME as having no underlying Pathology and not understood or accepted the WHO classification of ME as a neurological disease with CNS dysfunction. Attitudes, values, beliefs fundamentally influence service provision and interactions and interventions with people with ME. How will the existing "specialist services" now gain the correct knowledge , attitudes, beliefs and practices,required to offer training to reassure the ME community that they have changed their fundamental beliefs and approach? Who is going to train the trainers? People who have an ME/CFS diagnosis, will likely have varying causes of illness, due to poor diagnostic criteria, lack of clarity surrounding the name and the disease, lack of in-depth investigation, so they will not all have the same illness which will not help provide accurate training, and understanding; because ME/CFS and ME are not the same. Training should be based on biomedical knowledge and expertise and on an understanding the true nature of the disease and how it affects particularly the most ill. It should be based outside of the current psychosocial services and should come from people who have lived the experience for years and gained valuable insight and understanding. How can current services who have not followed a biomedical interpretation suddenly be used as experts to provide training? It is hoped that there will not be wrong training of people concerning Very Severe ME, given that the symptom	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline.

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				recognition is not full enough, the language in this document under describes the Severe ME experience and does not identify or specify clearly Very Severe ME at all., the words used to describe symptoms are understated like smells instead of chemical and perfume sensitivity. How can training be safe or correct, when the document itself does not identify it well enough nor appear from the recommendations to understand the reality. We have been left with a sense that carers are not considered equals, rather they are potential clients. And not considered capable of fully understanding jargon or information unless it is minimal, which is offensive given many carers have been fighting for many years to get proper biomedical not psychosocial services and know a lot and should be at the forefront of training themselves. Health and Social Care professionals will be influenced by the quality of the Training and the interpretation of ME on offer, which can never be good enough, under the "ME/CFS" umbrella.	
Stonebird	Guideline	001	006	We do not consider that "Encephalopathy/Chronic Fatigue Syndrome" is helpful in idenifying clear guidance for people with Myalgic Encephalomyelitis. There is no such WHO Classification as "Myalgic Encephalopathy", we do not understand why it is being used.	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental.*

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					For consistency, the abbreviation ME/CFS is used in this guideline.' The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10.
Stonebird	Guideline	001	009	We are not comfortable with the term "ME/CFS" as it is a conglomorate term covering many different conditions and does not specifically help or identify people who in fact have the WHO classified neurological disease Myalgic Encephalomyelitis. We do not understand how, without the document clarifying specifically exactly what "ME/CFS" means or represents, "awareness and understanding" can possibly be improved.	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'* The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10
Stonebird	Guideline	004	001	We would agree that "ME/CFS", an umbrella term, with no specific definition, could be a "complex medical condition", however Myalgic Encephalomyelitis is a specific WHO classified Neurological Disease with multisystem dysfunction and central nervous system disruption and should have its own separate pathway. The wider term "ME/CFS" helps no one identify the specific disease they have and can only enable general guidance. All the time "ME/CFS" is undefined it does not clarify the differences between the myriad illnesses and conditions included within the generalised label or even	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain*

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				acknowledge that this is the case. This is not good enough to safeguard people with Myalgic Encephalomyelitis.	*inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'* The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10.
Stonebird	Guideline	004	016	We totally agree that people with ME have exeprienced prejudice an are very pleased to see this being recognised.	Thank you for your comment.
Stonebird	Guideline	004	018	The issue is how to take disbelief and prejudice into account. It requires validation and respect by the Practitioner, especially if the Practitioner has contributed to this. We would suggest adding "and totally respect and validate their experience". Anyone, for example, who says "I recognise that you feel that" as oppose to "I recognise that is true" , is stll subtly disrespecting the person. Language, attitudes, values and beliefs may be very different depending upon your ultimate belief on what ME is and what causes it.	Thank you for your comment. The following recommendation addresses validation and is clear that health and social care professionals should acknowledge to the person the reality of living with ME/CFS and how symptoms could affect them.
Stonebird	Guideline	005	012	Although regular review is important it needs to be recognised that this is not necessarily that easy for the most severely ill person to tolerate, particularly those with Severe and Very Severe ME especially while their symptoms are worsening. Direct contact would be very difficult for this group of people.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.

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Stonebird	Guideline	005	024	Add “may justifiably result”.	Thank you for your comment. The current wording ‘ may result ’ addresses this and your suggestion does not add further clarification. For this reason the recommendation has not been edited.
Stonebird	Guideline	006	009 - 010	Why is “emotional wellbeing” the first point? This statement should read “Symptoms that significantly affect their physical health.”	Thank you for your comment. After considering the stakeholder comments the beginning of this recommendation has been edited to ‘including activities of daily living, mobility, the ability to interact with others and care for themselves and emotional wellbeing’ to match recommendation 1.1.1 describing the impact of ME/CFS.
Stonebird	Guideline	006	014	It is not just “smell” it is chemicals, perfumes and other odours like smoke. Need to add “any exposure to any of these hypersensitivities may trigger severe to profound deterioration of other symptoms i.e. noise can trigger paralysis, perfume can trigger breathing difficulties and other severe symptoms and also affect all the person’s systems- so there is a doubly-layer effect. ALL THESE SYMPTOMS HAVE PROFOUND IMPLICATIONS FOR HOW YOU APPROACH CARE AND INTERACT WITHOUT CAUSING DETERIORATION IN THE SEVERE AND VERY SEVERE ME POPULATION.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Stonebird	Guideline	006	017	Add “for a possible range of physical causes” An overall comment is that this list of symptoms do not appear to be grounded in any possible underlying physiology that would cause them.	Thank you for your comment. This section raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed and not the cause of the symptoms. It is supported by Appendix 2,Evidence review C – access to care and the committee’s experience. The committee agreed it was important to raise awareness about these symptoms and the support that may be needed to manage them.
Stonebird	Guideline	006	018	This is badly understated, for Very Severe ME. We would add “causing no ability to communicate, in the most severe cases, particularly when paralysed” Communication is not just about taking in written and verbal communication but also the difficulties the person has communicating their needs. Add	Thank you for your comment. This section raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed and not the cause of the symptoms. It is supported by Appendix 2,Evidence review C – access to care

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				"difficulty accessing memory, difficulty articulating expression, limited language, impacts word expression, difficulty connecting thoughts to speech, massive difficulty answering questions and retrieving information (particularly relevant for CBT).	and the committee's experience. The committee acknowledge that any descriptions in a recommendation will not cover every person's experience and are not meant to be exhaustive.
Stonebird	Guideline	006	024	This is a very limited list. Add "other neurological symptoms" because Severe Pain and Cognitive Difficulties are part of the ICC Criteria Neurological Symptoms. A General Point is that not all the symptoms listed have been acknowledged as Neurological neither has ME itself, in the document, as opposed to "ME/CFS" been acknowledged as a WHO classified Neurological Disease. Some of the more severe symptoms, such as paralysis, severe muscle spasms, or numbness have not even been added to the list. ALL THESE SYMPTOMS HAVE HUGE IMPLICATIONS FOR CARE AND PARTICULARLY HOW IT IS APPROACHED AND CARRIED OUT.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Stonebird	Guideline	007	002 - 003	For Very Severe this may mean little or no interaction at all, including profound difficulties in meeting need safely for the person. Just saying "no social interaction" is an inadequate description. Every interaction can be affected, not just the social ones. How do you get your benefits, your shopping, your care needs, your creative expression needs met?	Thank you for your comment. This section raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed and not the cause of the symptoms. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee acknowledge that any descriptions in a recommendation will not cover every person's experience and are not meant to be exhaustive.
Stonebird	Guideline	007	004	Add "needs significant or total support".	Thank you for your comment. This section raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed and not the cause of the symptoms. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee acknowledge that any descriptions in a recommendation will not cover every person's experience and are not meant to be exhaustive.

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Stonebird	Guideline	007	006 - 007	Add "and all other hypersensitivities"	Thank you for your comment. This section raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed and not the cause of the symptoms. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee acknowledge that any descriptions in a recommendation will not cover every person's experience and are not meant to be exhaustive.
Stonebird	Guideline	007	008	The aids that are needed are understated. People may be too hypersensitive to tolerate motion and use a wheelchair even though it is needed. Wheelchairs may need very specific modification to provide safe movement, if movement is tolerable or possible.	Thank you for your comment. After considering the range of stakeholder comments bullet points 2 and 4 have been combined and edited to, 'are housebound or bed-bound and may need support with all activities of daily living, including aids and adaptions to assist mobility and independence in activities of daily living (for example wheelchairs)'. The section on aids and adaptions provides further information. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Stonebird	Guideline	007	014 - 016	There is so much more to it than this. Remove the word "brain fog" and add "severe to profound cognitive dysfunction". It is not just "concentration" add "processing, comprehension ,understanding, difficulty reading, difficulty comprehending reading, difficulty following and comprehending speech or remembering what they have been told. There is also an issue about if someone is providing you with information, how slowly they speak, the tone of voice they use, how much time it takes to understand.. There are far more subtle things going on than what is written here, that have an impact.	Thank you for your comment. This section raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed and not the cause of the symptoms. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee acknowledge that any descriptions in a recommendation will not cover every person's experience and are not meant to be exhaustive.

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Stonebird	Guideline	007	019	This is great in principle but does not give pertinent information for people new to care. Need to add "A consistency of care provided by safe, known, sensitive practitioners and carers who know how to care and approach care, is preferred."	Thank you for your comment. This recommendation raises awareness about the importance of continuity of care and as such your suggestion does not add any further clarity and for that reason has not been added.
Stonebird	Guideline	007	021	You might be aware of the person's needs but you also need a commitment to learn what they are for they may change over time, they may need to be flexible and meet the need in the moment. They just don't need to be aware of the person's needs they need to take them into account in all their actions and interactions. A General Point – the impact of offering flexible, moment-to-moment care that takes into account the actual needs of the person and the difficulties they have tolerating interaction would have a significant cost and training implication. More time would have to be allowed and a more flexible approach developed to help those most ill.	Thank you for your comment. The training for health and social care professionals section of the guideline recommends that all staff that deliver care to people with ME/CFS should have training that is relevant to their role so that they provide care in line with this guideline. The committee agree that flexibility in accessing and receiving services is important to all people with ME/CFS and address this in the access to care section of the guideline.
Stonebird	Guideline	007	022 - 026	We would advocate a Risk Assessment with every practitioner who is involved with someone with Very Severe ME, that respects the person's realty and enables accountability and responsibility. This needs an extremely careful, sensitive approach. Risk Assessment is a very important tool that should protect people with Severe and Very Severe ME from harm if appropriately done.	Thank you for your comment.
Stonebird	Guideline	008	008	Unfortunately because ME has not been properly described or recognised as a WHO Neurological Disease and the focus is primarily upon Fatigue there seems to be an unnecessary psychological aspect to diagnosing ME. What physical disease has a primary psychological assessment to determine physical illness? Psychological assessment should be part of Mental Health services not ME, unless it is secondary. This leads to the continuing misinterpretation of ME as psychological.	Thank you for your comment. To note that after considering stakeholder comments the text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3)' has been added to the context. Thank you for your comment. The committee note that the assessment recommended describes the routine examinations and assessments when a

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					patient has an undiagnosed illness. At this stage the person has not been diagnosed with ME/CFS or any other condition and as you comment it is important to investigate the possibility of other diagnosis and co-existing conditions. Psychological wellbeing has been edited to, 'an assessment of the impact of symptoms on psychological and social wellbeing' to clarify this assessment.
Stonebird	Guideline	008	017	Add "Sleep Paralysis" to unrefreshing sleep.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Stonebird	Guideline	009	013 - 014	Add "movement, motion and vibration". Instead of "smell" add "chemicals and perfumes". Add "increased menstrual pain".	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Stonebird	Guideline	010	007	This needs to be a biomedical clinician who understands the organic nature of the disease Myalgic Encephalomyelitis.	Thank you for your comment and information.
Stonebird	Guideline	010	015 - 016	Unfortunately the impression one gets is that it possible to manage fatigue, sleep and pain and live "within your energy envelope" this is just not the experience or reality of people with Very Severe ME. The presentation of Severe and Very Severe ME s so much worse than is represented under the "ME/CFS" Guidance. We would recommend a separate pathway for Myalgic Encephalomyelitis that is not based upon Fatigue Management by practitioners that up to now have been pushing CBT and GET.	Thank you for your comment and information.
Stonebird	Guideline	010	020	It is important to acknowledge that people with Severe or Very Severe ME may NEVER be able to rest. Rest can make symptoms worse for people. For some lying down may feel much worse than sitting up. To say "rest" is far too minimal.	Thank you for your comment and information.

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				Every person's experience will be different and unique to them. The general, bland term "rest" is not adequate nor does it show understanding of the complex and painful implications for people.	
Stonebird	Guideline	012	004	We are very concerned with the explicit psychosocial emphasis here which has never been proven to be appropriate (the PACE Trial was discredited and the FINE Trail a failure). NICE themselves have recognised that the quality of research is poor. In what context is the information here to be used? The underlying attitude of the Practitioner will surely influence how they use the information and how they see the Client.	Thank you for your comment. After considering the range of stakeholder comments this bullet point has been edited to, 'the impact of symptoms on psychological, emotional and social wellbeing'.
Stonebird	Guideline	012	002 - 003	Not only is mental health mentioned, but also "emotional stress". 'Physical functioning" - if you go and do a physical functioning test, you may not be able to repeat it. Physical Functioning must be put in context. If the person with ME says they are unable to do something, this must be recorded as a physical disability, not a psychosocial factor.	Thank you for your comment and information.
Stonebird	Guideline	012	008	Add "this must not be misinterpreted psychosocially but acknowledged for the desperate difficulties people have eating food'. The physical issue underlying the restrictive diet needs to be recognised as valid. The overarching issue is this: how can anyone with the neurological disease Myalgic Encephalomyelitis trust a psychosocial clinic to access them accurately, if at all?	Thank you for your comment. In the committee discussion in Evidence review G-non pharmacological management the committee note the importance of understanding the impact that ME/CFS symptoms can have on eating (in particular, resulting in weight loss and weight gain and that these are not necessarily the result of an eating disorder) and that any assessment should be undertaken by a dietician that has this understanding.
Stonebird	Guideline	012	024	Physical maintenance" must be understood in the context of severe to profound physical symptoms, their nature and impact. For example, someone experiencing transient or periodic paralysis should not be physically moved because of potential damage to muscles and tendons. The extreme pain needs recognised. For people with Very Severe ME any touch, movement can be catastrophic. this document does not seem	Thank you for your comment and information.

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				to recognise that level of extreme sensitivity and impossibility.	
Stonebird	Guideline	012	025	We do not consider the Symptom Management to be adequate or representative particularly of the most severely ill.	Thank you for your comment.
Stonebird	Guideline	013	011	Before any professional enters the home of a person with Severe and especially Very Severe ME, they need to have learned what are the hypersensitivities and other very severe symptoms that the person experiences, to ensure that they do not exacerbate them or cause deterioration by their presence or interaction or make wrong assumptions or poor recommendations. A Risk Assessment prior to engagement consulting as appropriate with the person and/or their advocate would be essential to understand the risks of engagement. Accountability and responsibility of practitioners is essential.	Thank you for your comment and information.
Stonebird	Guideline	013	General	People with Severe and Very Severe ME need access to other health providers through home visits, in particular, a full dental service, consultants from other specialisms, biomedical ME consultants only, all GP's and other medical practitioners such as phlebotomists,	Thank you for your comment. This guideline applies to all health and social care professionals working in the NHS providing care to people with ME/CFS.
Stonebird	Guideline	014	008 - 014	Though we agree that appropriate information is needed, especially for those new to understanding ME, it will be very different subtly if not overtly, if written by Psychosocial practitioners. Who will write this information? What will their underlying background, attitudes, beliefs and views on ME be? We advocate a MOMENT approach to care that is flexible, person centred, respectful of the physical nature of the disease, recognises the way the care is provided and must demonstrate awareness of the risk of deterioration and the direct impact of the carer on creating the best possible interaction. Safety must be a priority.	Thank you for your comment and information.
Stonebird	Guideline	014	019 - 021	Adults with Very Severe ME to our knowledge do not have periods of remission. Very Severe ME is an extreme constant state of physical illness and disability with continuous high	Thank you for your comment and information.

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				level symptoms. The risk of deterioration and long time harm is massive.	
Stonebird	Guideline	014	025 - 027	For People with Severe and Very Severe ME, the disease will ALWAYS have a major impact upon all aspects of their live. They will definitely need to make complex adjustments in order to cope with such extreme symptom experience, necessary isolation and require the greatest of understanding, not judgement or misinterpretation.	Thank you for your comment.
Stonebird	Guideline	015	012 - 015	Carers should be treated as equals, not clientised in anyway by professionals. Unfortunately the power held by practitioners tends to be unequal and potentially judgmental. Carer services may be patronising, not recognising the skills nor knowledge and life experience or previous status of the carer. If the practitioner has a psychosocial agenda or approach it will undermine the assessment process and the relationship. Any Psychosocial judgment about ME whether overt or covert, will impact upon carers negatively. We do not consider that any service that is based fundamentally on a Psychosocial Approach to be appropriate for people with the WHO disease Myalgic Encephalomyelitis or their carers. Any training, any assessment should be done through creating a new biomedical service for people that totally honours the organic nature of the disease and the long term implications of living with it and understand the disease ME as opposed to the umbrella term ME/CFS	Thank you for your comment and information.
Stonebird	Guideline	018	015 - 016	Remove 'fear of' and add "likelihood" of relapse or symptom exacerbation. There are many more issues likely to impact the person with Severe or Very Severe ME. Being very severely disabled, noise, movement, motion,, light sensitive, being unable to move, being partially or totally paralysed, being harmed by the environmental impact.. Here the stark reality is understated once again.	Thank you for your comment. After considering stakeholder comments about the word fear this recommendation has been edited 'risk that their symptoms will worsen may prevent people from leaving their home'.

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Stonebird	Guideline	020	026	People with Severe and Very Severe ME MUST have aids and adaptations. It needs acknowledging that people with Very Severe ME, although they need a wheelchair or stairlift in principle, may not be able to use them, because of the severity of their symptoms. Also people with Very Severe ME require additional to the norm aids and equipment such as noise-reducing curtains, sound-reducing glass and the creation of new aids to help people with profound noise and light sensitivity. New thinking is required. Basic aids are not going to be good enough.	Thank you for your comment and information.
Stonebird	Guideline	022	013 - 022	We do not see any specialist medical input here. ME is not a fluctuating fatigue condition, that just needs management, which is the implication here. It requires medical management and monitoring.	about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.
Stonebird	Guideline	023	005 - 006	This gives far too much power and involvement to what appears to be an "ME/CFS" psychosocial team. People may not want an ME/CFS psychosocial specialist team involved in their care with their GP. The fatigue clinics have not demonstrated the right attitude or interpretation of ME to have earned that status automatically. People with Severe and Very Severe ME would not necessarily welcome their involvement if it is CBT and psychosocially oriented. People are very clear that they want biomedical clinics, a biomedical pathway and biomedical respect.. This is not what is on offer still. ME must be better defined for this.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section

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					After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. This includes the choice to participate in CBT.
Stonebird	Guideline	024	021 - 024	This sounds alarmingly like Graded Activity Management, which is not appropriate for people with Severe and Very Severe ME. People with Severe and Very Severe ME are unlikely to have "improved symptom experience". Even if there are better moments, this does not mean the person is well enough to push themselves any further. We consider this to be extremely dangerous to be recommending.	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have

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					while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). This is not graded activity management. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline.
Stonebird	Guideline	024	001 - 011	We welcome the statement that there is no current treatment or cure for ME/CFS - but how could there possibly whilst ME/CFS covers a wide heterogeneous group?	Thank you for your comment. To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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Stonebird	Guideline	025	001 - 002	What is meant by a "long Term approach" – is this about long term input for practitioners to enable Graded Activity Management? What is the implication of this? What are the covert messages? The concept of "Energy Envelope" appears to be new to NICE Guideline, so how can practitioners who have been teaching GET , teach about an Energy Envelope that is discerned by the person? Is the long term approach a practitioner or person approach? We would be very concerned about anyone with Severe or Very Severe ME, even being expected subtly to "stabilise", "increase tolerance or activity".	Thank you for your comments After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms. Concept is widely recognised in the ME/CFS field
Stonebird	Guideline	025	011	It does not seem appropriate for a physical disease to focus upon "social activity and relationships". Why is this being recorded? How is it being interpreted? What are the implications? In what other physical illness would you record social interaction and relationships? There are psychological implications here that we would say are inappropriate.	Thank you for your comment. The committee disagree a holistic personalised approach has been recommended throughout the guideline and this includes social activity and relationships.
Stonebird	Guideline	026	009 - 011	Awareness and knowledge of Very Severe ME does not seem to be in evidence in this document. Developing an "energy management plan" for someone with Very Severe ME seems to imply there is enough energy to manage. There is no mention of the complex communication and symptom issues that would negate this even being possible	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits.

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					This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led approach that is flexible and tailored, so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline.
Stonebird	Guideline	026	012 - 015	Realistically someone with Very Severe ME is just coping with terrible symptom experience, talking about "changes in activity" or "any increase in activity" shows zero understanding of Very Severe ME (the 2%). There is no mention of the huge risk of harm. An appropriate, aware Risk Assessment would show this to be a nonsense alongside the danger of deterioration.	Thank you for your comment. The section for people with severe or very severe ME/CFS includes a recommendation on risk assessment for each interaction.
Stonebird	Guideline	033	004	Add "great consideration needs to be taken as to how you approach assessment and interaction to ensure that the person's health does not deteriorate from the process of assessment itself or from unaware practitioners." As a General point any professional involved in Severe and Very Severe ME	Thank you for your comment. The training for health and social care professionals section of the guideline recommends that all staff that deliver care to people with ME/CFS should have training that is relevant to their role so that they provide care in line with this guideline.

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				must approach assessment and monitoring with ME AWARENESS NOT JUST GENERAL AWARENESS of the issues. Great understanding is required in Very Severe ME. There appears to be no awareness in this Guideline on the importance of HOW you approach, interact, access, monitor, respond to he most ill. There must be an emphasis on an ME Aware approach of the most severe illness and how it impacts. Consideration must be given to how EVERYTHING can trigger unimaginably profound deterioration. Practitioners must demonstrate they understand this. It is not enough to make any recommendation, if they do not know the likely outcome, because of the nature of Very Severe ME in which people's physical reactions do not necessarily correlate to what is expected under normal circumstances. This is why it so hard to help people. A recognition of the difficulties the most ill face in getting even basic need met, needs recognising, rather than the bland implication that practitioners can monitor, access, make suggestions easily, without real realisation of how impossible, how dangerous this can be.	
Stonebird	Guideline	033	003 - 011	Surely anyone with swallowing difficulties should be accessed by a Speech Therapist or a Gastroenterologist? The most severe may be experiencing throat paralysis.	Thank you for your comment. The guideline does not exclude referral to a speech Therapist or a gastroenterologist where this is appropriate.
Stonebird	Guideline	034	001 - 008	How can you ensure that CBT will not be linked to goal-setting, activity management or illness denial? Can you confirm that practitioners who up to now have used CBT alongside GET, will be retrained to ensure there is no covert or explicit expectation on the patient to unrealistically improve or deny their reality? Services who have previously been offering CBT linked to GAT and GET, need to be retrained in appropriate attitudes and values before being allowed to continue offering CBT. There needs to be some proof, for the ME Community that the existing services have changed. As far as we know there is no one with expertise in CBT, linked to Energy	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.

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				Envelopes, a new concept, in the Clinics. So who will retrain them?	
Stonebird	Guideline	034	009 - 029	It is all very well saying "discuss with the person", however with Severe and Very Severe ME this can be extremely difficult, if not impossible – to understand, never mind engage in the process. How can CBT possibly be deemed to "manage symptoms" unless there is an underlying assumption that the symptom is exaggerated by underlying psychological factors? There needs to be a recognition that symptoms are symptoms and thinking different thoughts are NOT going to make them better. How can CBT "improve quality of life" if the symptoms are untreated or ignored? How can CBT "improve functioning" unless it is ignoring the physicality of the disease? This is still a psychosocial misinterpretation of a serious physical disease with multi system dysfunction. We are concerned there is still a potential denial by suggesting you can create "meaningful goals and priorities", particularly if you are very severely affected. This potentially sets people up to fail and potentially denies their reality. "Working closely with the therapist" , for someone who cannot bear anyone in the room , is completely unrealistic if you have Severe or Very Severe ME. Any engagement can have a deteriorative effect.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). The committee agreed that it was important that CBT should be available for all people with ME/CFS but that is was important to highlight the additional caution needed for people with severe or very severe ME/CFS. The recommendations on the awareness of severe or very severe ME/CFS and its impact include that interactions should be risk assessed in advance to ensure its benefits will outweigh the risks to the person.

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Stonebird	Guideline	035	001 - 002	This would need high-level empathy, that we have never yet come across.	Thank you for your comment and information.
Stonebird	Guideline	035	003 - 004	This is an extremely patronising statement, it implies an underlying attitude towards people with ME and their symptoms leading to denial of the true nature of their disease. It really is offensive that severely ill people still have to endure this misdirection away from the physical truth of their illness.	Thank you for the comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Stonebird	Guideline	035	005 - 007	We cannot understand how someone physically ill can be expected to "improve their functioning" by thought. This again smacks of the denial of the physical reality of the disease and the incapacitating nature of the disease.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to

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					accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). The committee agreed that it was important that CBT should be available for all people with ME/CFS but that is was important to highlight the additional caution needed for people with severe or very severe ME/CFS. The recommendations on the awareness of severe or very severe ME/CFS and its impact include that interactions should be risk assessed in advance to ensure its benefits will outweigh the risks to the person.
Stonebird	Guideline	035	008 - 013	This is unrealistic for people with Severe ME, it shows no understanding of how the symptoms affect a person or their capacity to manage anything. A psychosocial misinterpretation of ME which has dogged proper treatment and the development of a biomedical service for decades ekes out of this document.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence

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					reviews G and H for the evidence and the committee discussion on these recommendations). The committee agreed that it was important that CBT should be available for all people with ME/CFS but that is was important to highlight the additional caution needed for people with severe or very severe ME/CFS. The recommendations on the awareness of severe or very severe ME/CFS and its impact include that interactions should be risk assessed in advance to ensure its benefits will outweigh the risks to the person.
Stonebird	Guideline	035	022 - 026	This paragraph demonstrates how little Severe and Very Severe ME are understood in the Document. The suggestions are completely impracticable given the complexity of the illness and severe to profound cognitive disability that makes it impossible to engage in CBT. How can someone with variable ability to think, speak, process, understand, find answers and retrieve information, possibly tolerate or engage with the CBT process, ever? We cannot comprehend how anyone would think it would be appropriate to offer Cognitive Behaviour Therapy (CBT) to a person diagnosed with Severe ME or Very Severe ME.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).

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					The committee agreed that it was important that CBT should be available for all people with ME/CFS but that is was important to highlight the additional caution needed for people with severe or very severe ME/CFS. The recommendations on the awareness of severe or very severe ME/CFS and its impact include that interactions should be risk assessed in advance to ensure its benefits will outweigh the risks to the person.
Stonebird	Guideline	039	005	An awareness that the more ill you are, the harder it is to see people and the greater the risk of harm from the simplest interaction must absolutely be emphasised here. To increase the number of reviews depending on severity, may simply be too much to tolerate and place an intolerable burden on the person.. It requires careful thought and understanding how to approach and gain vital information without harming the person for days weeks months or longer potentially especially if they have deteriorated further. A Risk Assessment must be a required component of any Assessment or involvement.	Thank you for your comment. The committee agree that the need for an annual review will depend on the person's circumstances. Some people may find an annual review difficult for various reasons, but the committee agreed it was important that people with ME/CFS were offered the opportunity to have care related to their ME/CFS reviewed at least once a year in line with other long term conditions. In the section on Awareness of severe and very severe ME/CFS and its impact the committee have recommended that each interaction with people with severe or very severe ME/CFS should be risk assessed to ensure the benefits will outweigh the risks. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The committee note that the review

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					here is based in primary care and this would reduce the need for travelling to specialist centres.
Stonebird	Guideline	043	003 - 008	It is a huge concern that the Specialist Team has so much power in influencing Social Care Assessments, especially given that the management plan consists of energy management, physical maintenance, physical activity, CBT and dietary management, most of which would be unsuitable, potentially inappropriate and even dangerous for people with Severe and Very Severe ME. CBT, in particular is completely unrealistic in Very Severe ME and once again shows a great lack of awareness in this document. If a Practitioner wrongly assesses you or misinterprets your reality they could potentially misinform Social Services as to your Care Needs. The "Specialist Teams" are presumably the up to now Psychosocial Clinics offering CBT and GET and promoting the ideology that there is no underlying pathology to ME. This is of immense concern.	Thank you for your comment and information.
Stonebird	Guideline	044	012 - 014	This does not appear to take into account touch, or pressure sensitivity. In Very Severe ME you may not even be able to tolerate anyone in the room, never mind "passively" moving your limbs. People with Very Severe ME might not even consider that they have an "Energy Envelope" because the slightest thing can worsen drastically their health, the slightest touch at the wrong moment can be a disaster and have a long term effect, lasting years even. YOU MUST NEVER ASSUME PEOPLE WITH VERY SEVERE ME CAN TOLERATE TOUCH.	Thank you for your comment. The section on awareness of severe or very severe ME/CFS raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. This includes hypersensitivity.
Stonebird	Guideline	044	008	You absolutely do not want exacerbate symptoms in a person with Very Severe ME, however this does not acknowledge the severe to profound level of multiple symptoms that are a constant in someone with Very Severe ME such that people	Thank you for your comment. The section on awareness of severe or very severe ME/CFS raises awareness about the symptoms that people with severe or

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				can not endure physical contact or presence.	very severe ME/CFS may have and how these may be managed. This includes hypersensitivity.
Stonebird	Guideline	044	021	Add "or longer". There is no recognition of Post Exertional Neuroimmune Exhaustion (PENE) which better recognises the physiological nature. We cannot recognise the terms "relapse" or "flare" as being relevant to people with Very Severe ME who can deteriorate permanently from wrong intervention and plunge to new levels of horrendous symptom experience, particularly if mismanaged by practitioner involvement.	Thank you for your comment and information. After considering the stakeholder comments this definition has been edited to,' Post-exertional malaise The worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated. Symptoms can typically worsen 12 to 48 hours after activity and last for days or even weeks, sometimes leading to a relapse. Post-exertional malaise may also be referred to as post-exertional symptom exacerbation'. The definitions of flare up and relapse give further detail about symptoms worsening over longer periods of time.
Stonebird	Guideline	045	008 - 010	We do not feel this description is adequate. It says nothing of the severity of individual symptoms that can be extreme such as profound light , noise sensitivity or paralysis, which in themselves, individually incapacitate totally. It says nothing about being in bed for very different reasons. It says nothing of the fact that they are physically very ill and great care needs to be taken in how to approach these people without harming them, unintentionally or inadvertently. It does not recognise that only about 2% of people will have a Very Severe ME diagnosis, nor does it it say that it is a long term, significantly worse and constant state than Severe ME.	Thank you for your comment. The section on awareness of severe or very severe ME/CFS sets out the symptoms people with severe or very severe ME/CFS experience and the impact of them.
Stonebird	Guideline	045	001 - 007	General Point : There is no apparent separation between Severe and Very Severe ME in the Guidance. The description here is minimal. People may not be able to use a wheelchair at all. They may need specially adapted wheelchairs. It is unlikely they will be able to tolerate alternative settings such as a clinic or hospital, because of hypersensitivities that are not accommodated.	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The committee note that definitions of severity are not clear cut.

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Stonebird	Guideline	045	011 - 016	A "Therapy Blueprint" we understand is found in CBT terminology? This does not sound appropriate for anyone with Severe or Very Severe ME, especially being goal-orientated. For someone with Very Severe ME we would expect any goal to be about practitioners doing no harm and understanding the ongoing experience and extreme physical suffering the person is experiencing. What does "supported by guidance by the therapist" mean ? There is a potential issue of power imbalance, covert influence and subtle pressure. We really feel this must not be recommended for people with Very Severe ME. It shows nothing of awareness of people with Very Severe ME at all.	Thank you for your comment. A therapy blueprint is CBT tool which summarises the work a therapist and patient have completed together. The definition describes examples of strategies that may have been useful for the purpose of explaining these would be included in the blueprint.
Stonebird	Guideline	045	017 - 020	The issues facing people around sleep are much more complex than this implies. For example people with Severe or Very Severe ME may experience sleep paralysis, inability to get to sleep, difficulty waking, shifting sleep patterns, difficulties lying down, extreme, untreatable pain, breathing issues, heart rate variability, oxygen depletion. This description really highlights the continual lack of recognition of the issues the most ill face. This document does nothing to reassure us there is any understanding, particularly of those who are the most ill and at great risk of deterioration. There are so many complex symptoms and underlying system dysfunction that are simply being diluted down and represented as fatigue that be managed or improved, with practitioner input.	Thank you for your comment and information.
Stonebird	Guideline	066	010 - 016	We welcome this long overdue recognition of drug sensitivity and more severe adverse reactions to drugs.	Thank you for your comment. To note after considering the range of stakeholder comments the committee agreed to delete more reference to more adverse effects.
Stonebird	Guidline	004	017	Remove "feel" and replace with "are" stigmatised by people who do not understand.	Thank you for your comment. The aim of the recommendation was to raise awareness that people with ME/CFS have experienced prejudice and stigma and is based on the evidence identified in the Evidence reviews A

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					and C and the committee's experience. The current wording addresses this and your suggestion does not add further clarification. For this reason the recommendation has not been edited.
The 25% ME Group	Evidence Review A	General	General	We note that the evidence reviewed in connection with developing guidance is heavily skewed towards publications by existing service providers and/or proponents of 'this illness is deconditioning' school of thought. This is a concern. The same can be said of Evidence Reviews B & C.	Thank you for your comment. The committee recognised the limitations of who publishes evidence in peer reviewed journals and as a result when developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The themes in the evidence discussed by the committee in reviews A,B and C were supported by the calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS.
The 25% ME Group	Evidence Review A	General	General	When reviewing pharmacological interventions a body of work has been excluded solely because recruitment did not include PEM as an essential criterion. When reviewing the evidence on diagnosed (or suspected) patients pertaining to this review question it would appear that no cognisance has been taken of the criteria used to diagnose or suspect. This is inconsistent.	Thank you for your comment. No study was excluded because recruitment did not include PEM as an essential criterion. The evidence was considered indirect and this was accounted for in the quality assessment of the evidence (See the Methods chapter for information on GRADE). *ME/CFS population evaluation in the evidence* When considering the stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed the requirement of PEM was particularly important in the studies evaluating interventions. The committee considered that the

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					response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. Whereas in the evidence reviews exploring the experience of people about services and information and support needs the presence of PEM is less likely to have an impact on the findings. For this reason the relevance of the evidence has been as assessed by considering how the diagnosis was established. For example, in Devendorf 2018 concerns about applicability are recorded due to self-identification as ME/CFS (Appendix D). Relevance is then considered in the body of evidence taking the individual studies into account (Appendix E). *The experience of interventions qualitative review and measurement of applicability and relevance* After considering the stakeholder comments the committee agreed to revisit the qualitative evidence for the experience of interventions further scrutinising the information on PEM reported in the trials and the application of relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) In summary the same requirement for PEM has been applied to the experience of interventions in line with the clinical and cost effectiveness review of interventions.
The 25% ME Group	Evidence Review A	General	General	Five of the 15 studies included in the review [18, 22, 26, 61 and 13] include an author who describes 'CFS/ME' as follows: "CFS/ME is defined as generalised fatigue, causing disruption of daily life, persisting after routine tests and investigations have failed to identify an obvious underlying 'cause' ", citing CG53	Thank you for your comment and information.

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				[2007] in support of this description. [SOURCE: Protocol for the 'FITNET' Trial] Three further papers [15, 32 and 58] include an author who has published on graded exercise, advising: "No systematic therapeutic attempt was made to change patients' beliefs about their illness or exercise … Drop outs from the trial may have been reduced and adherence to exercise improved if patients were given more specific psychological treatment such as cognitive-behavioural therapy." She speculates that "The high number of non-completers" is among factors which "may have resulted in an underestimate of the effects of graded exercise on fatigue and health perception." [pub. British Journal of Psychiatry; see Ref 101, Ev Rev G]	
The 25% ME Group	Evidence Review A	046 - 047	20 of 46 to 33 of 47	There is a lot of good practical info & guidance re what to do and what not to do in this section. We fear this risks being 'lost' unless placed in the full guideline. One additional point that should be stressed is that pupils with 'ME/CFS' should on no account be taking part in 'physical education'.	Thank you for your comment. There is a judgment as to the amount of information that is included in the recommendations. Too much information results in the guideline becoming unwieldy and unusable and for this reason your suggestion has not been added. There are links in the guideline to the evidence reviews and as you note these include more information in the discussion sections and are a valuable source for readers. The committee note that care for people with ME/CFS is personalised and any activity is tailored to their circumstances with the support of ME/CFS specialist care.
The 25% ME Group	Evidence Review A	043 - 044	27 of 43 to 49 of 44 Support Needs of Families and carers	It's not clear if paid carers come into this or if their needs are to be covered in Evidence Review B? There is a danger of paid carer need falling through a crack between the two. Much of what is said here would also apply to paid carers, including the need for support due to the demands of the caring role, particularly when caring for the most severely affected patients, which takes great skill and knowledge of their specific needs. We have heard the need expressed by paid carer need for some form of support and counselling to be provided to paid carer	Thank you for your comment. Paid carers are considered in health and social care professionals and would be included in Evidence review B. The committee note no evidence was identified for social care professionals. The training for health and social care professionals section of the guideline recommends that all staff that deliver care to people with ME/CFS should have training in ME/CFS relevant to their role so that they provide care in line with this guideline.

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				because exposure to the reality of how severely the cared for person's life is affected by illness become hard to cope with at a personal level.	To note the training recommendations have been edited.
The 25% ME Group	Evidence Review A	006	3	Study 131 is among those listed as included in the review, study 132 is not. However, Table 3 summarising review findings [P17] lists study number 132 but not 131. We have gone on the assumption that it is study 131 that is correct, based on the description in Table 2 [P15].	Thank you for your comment. This has been corrected.
The 25% ME Group	Evidence Review A	017	4 (Table 3)	We have not reviewed the evidence in respect of all the 'Main Findings' derived. However such work as we have carried out tends to reveal that the function of specialist services in providing information, education and support to patients and their families and carers is somewhat overplayed. For example, 'Main Finding': "those who ultimately were [referred to specialist services], had benefitted in ways including diagnosis, validation and information provision." Of the four papers cited only one provides any evidence at all in support of this assertion - and that is thin: REF 25 - Adult patients' experiences of NHS specialist services for chronic fatigue syndrome (CFS/ME): a qualitative study in England https://bmchealthservres.biomedcentral.com/articles/10.1186/s12913-017-2337-6 Reports feedback from 16 patients who had completed 'a course of treatment' at a particular service. (Course of treatment: "CBT and GET are the two main evidence-based therapies which (or components of which) are used in conjunction with techniques aimed at managing activity, sleep hygiene and relaxation". It's far from clear that this is a representative sample, as it does not report (i) response rate; (ii) proportion who had dropped out of the course before completion; (iii) proportion who had declined to undertake the course at all. Also the research does	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresentedunderrepresented in the literature. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed).

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				not advise the criteria used to establish diagnosis and the authors appear to include staff from the service in question. Patients in this study advised that GP can play a valuable role - however this isn't reported in the Evidence Review Regarding the other three REF 15 - Did not consider patients' experiences of specialist services at all REF 87- Concerns the hopes and expectations of patient who had not yet attended the specialist service to which they had been referred REF 131 - A US study which examined the experiences of 47 adults 'with CFS' participating in a research project to evaluate a "participant-designed rehabilitation program"; we can find nothing about specialist services being important providers of info here. The paper does however advise on a key point that is not reflected in this or any other evidence review presented to the GDC: *These experiences are consistent with findings from other research indicating that persons with CFS seeking medical services face disbelief, misunderstanding, misinformation, and an overemphasis on psychological explanations [5 refs provided]* and *Despite evidence against the hypothesis that depression is responsible for CFS [3 refs], many medical practitioners, as well as friends and families of persons with CFS, continue to believe that the illness is related to psychological dysfunction, and that the symptoms can be attenuated, relieved, or eliminated with psychotropic medications or if the individual would only learn to cope with them more effectively [Ref. Conant, 1990].*	Based on the evidence (Evidence reviews A.B,C,D and I) and the committee's experience referral to ME/CFS specialist care was recommended for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. ME/CFS specialist teams where seen as the most appropriate place for people with ME/CFS to access support with GPs providing ongoing support and review.
The 25% ME Group	Evidence Review A	043	1-3	This is excellent. Please consider emphasising the adverse impact of continuing to work due to financial constraints in the full guideline. Also give an explicit an indication for GPs and other health and care professionals that they can help their	Thank you for your comment. There is a judgment as to the amount of information that is included in the recommendations. Too much information results in the guideline becoming unwieldy and unusable and for this

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				patients by providing medical evidence / care needs evidence in this connection. This gives positive reinforcement to profs, that they can assist patients [Line 8 P15 of the draft guideline states' give advice about …' but does not advice that health and social care professionals can give vital evidence in support of benefits applications, without which an application is unlikely to succeed.]	reason your suggestion has not been added. There are links in the guideline to the evidence reviews and as you note these include more information in the discussion sections and are a valuable source for readers.
The 25% ME Group	Evidence Review A	043	23-25	Please note not all patients have a family or other informal carer. Some are entirely dependent on paid care. This is scanty coverage on social care support - issues include severe difficulty accessing appropriate care - or any at all, problems translating any funding provided to personal care and support to permit a tolerable existence etc. While the place for this may be in the full guideline, it does require the committee to discuss. Please see comments made in respect of full guideline in this regard.	Thank you for your comment. An additional sentence noting that not all people have family or an informal carer has been added to this section of the findings section. Social care support is further discussed by the committee in Evidence Review C -access to care.
The 25% ME Group	Evidence Review A	047	39-46 Access to care	This is about hospital care specifically, but it's unclear if it applies to inpatient or outpatient care. There are many practical considerations with respect to both, particularly concerning severely affected patients. These include, for example: (i) there may be a prohibition on home care workers accompanying patients to out patient appointments; this is one reason that severe ME patients may not obtain medical help for other illnesses - social services will not allow for this within the funded package and they have no one else to go with them; (ii) the patient's own costs benefits analysis all too often falls on the side of cost, in large part due to hospitals and hospital transport systems failing to take cognisance of their needs; in our experience this means that some people with severe ME have declined investigation and treatment for other disorders, including potentially serious and treatable illness. This can also result in very severely affected patients presenting late in the course of other illnesses.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The guideline about includes inpatient and outpatient care and makes specific recommendations for people with severe or very severe ME/CFS.

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				Please consider the relevance of these and other points made here for the guideline in full.	
The 25% ME Group	Evidence Review B	018 and 038	Table 3 and Table 7	The review of evidence in respect professionals' information, education & support needs revealed a need for 'increased training …to increase knowledge of ME/CFS and it's management'. [Table 3] In terms of barriers to this, a core issue listed is.: 'lack of training' [Table 7]. Unfortunately the problem is not simply an absence of training. It is the presence of *<u>the wrong sort of training</u>*. This misinformation then produces a faulty belief system that adversely influences health and social care professionals' approach to patients. University medical schools teach 'CFS' as a 'functional' disorder, if feedback from the five in Scotland is representative. The 25% ME Group is part of Taking ME Forward [TMEF], a federation of patients, carers and patient charity representatives. In 2014 TMEF lodged an FOI request. Summary of responses: - St Andrews describes ME as an alternative name for CFS, which is taught as a psychosomatic disorder. - Dundee describes ME as a 'Neurological Somatoform Disorder' under Medically Unexplained Symptoms (MUS), and queries the usefulness of the terms ME and Post Viral Fatigue Syndrome; course content equates 'CFS' with 'chronic fatigue'. - Aberdeen teaches CFS as 'Medically Unexplained Symptoms'; - Edinburgh teaches CFS as 'MUS/Functional Somatic Syndrome'; - Glasgow teaches CFS as 'Functional Somatic Syndrome' This is worse than a lack of education: misinformation is being purveyed via institutions of higher learning.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.

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				We are unclear how far a Clinical Guideline can go in attempting to address this. Certainly it presents a backdrop to the launch of guidance that is not propitious. Failings in medical education have led to the assumption this is a "non-disease". We suggest that this unfortunate circumstance is kept in mind when finalising the guideline, with a view to strengthening the information to the effect that this illness has a biomedical basis, which - while it may not be entirely clear - nonetheless is sufficient to undermine the assumption that patients have a 'functional' disorder or are physiologically deconditioned.	
The 25% ME Group	Evidence Review B	038	Table 7	Having established that there is an unmet need with regard to *Information, Education & Support for health and social care professionals* [Table 3 P18], the purpose of Table 7 is to summarise findings on '*the barriers and facilitators to providing information, education and support for health and social care professionals'* However it is dominated by reports of findings pertinent to giving information to and working with patients, with only 2 of the 12 'main findings' listed pertaining to barriers and facilitators in getting information, education or support to health and social care professionals themselves. Others concern perceived barriers to health professionals providing information to patients. The remainder are simply about meeting patients' need for information and support - i.e. the subject matter of Ev Rev A. This imbalance is reflected in the ensuing GDC discussion.	Thank you for your comment. The findings tables summarise the themes identified in the evidence and are applied to support health and social care professionals provide information with people with ME/CFS.
The 25% ME Group	Evidence Review B	038	Table 7	A tendency to assert a role for specialist services in a way that is not borne out by the evidence cited is evident in this summary (as with Ev Rev A). An example of both is: "Specialist services were seen as the best provider of information and support for people with ME/CFS, …" - linked to studies 15, 24, and 37. [NOTE: Consideration of Info and support for people belongs in Ev Rev A].	Thank you for your comment. The findings tables summarise the themes identified in the evidence and are applied to support health and social care professionals provide information with people with ME/CFS. The summary of Bayliss 2016 (ref 15) includes that GPs considered specialist services to be best placed at providing care for people with ME/CFS and found the online training materials

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				Ref 15 concerned a GP education programme - at no point were the GPs asked what they saw as the best source of info to give to patients; neither can we find anything to support this finding in Ref 37; ref 24 looked at patients' views, not profs; these patients was asked to reflect on their time with a specialist service and reported that service had helped by providing info (see comment on Ev Rev A study 25 for limitations - this is the same study).	useful (Appendix D). Both the other references directly support the statement that specialist services were seen as the best provider of information.
The 25% ME Group	Evidence Review B	038	Table 7	Another finding which does not relate to barriers and facilitators to providing information, education and support for health and social care professionals is: *HCPs can be hesitant to provide information and discuss psychological factors around ME/CFS due to concerns about patients' possible negative reactions*. Two pieces of evidence are cited in support of this. One study (19) concerned 15 health professionals in Canada. The other (13) is from the psychology dept. at Birkbeck College and concerns *patients'* views. Published in 1999, the paper refers to the patients concerned perceiving that their illness is not psychological, and treats this as a perverse viewpoint (without citing any evidence). This is in stark contrast to paper 130 - cited in connection with Barrier - [HCPs'] *limited knowledge of support groups,* a US paper which advises: *These experiences are consistent with findings from other research indicating that persons with CFS seeking medical services face disbelief, misunderstanding, misinformation, and an overemphasis on psychological explanations [5 refs provided]* and *Despite evidence against the hypothesis that depression is responsible for CFS [3 refs], many medical practitioners, as well as friends and families of persons with CFS, continue to believe that the illness is related to psychological dysfunction, and that the symptoms can be attenuated, relieved, or eliminated with*	Thank you for your comment. The findings tables summarise the themes identified in the evidence and are applied to support health and social care professionals provide information with people with ME/CFS. This finding refers to the negative interactions that can occur between people with ME/CFS and health and social care professionals and proposes this is a barrier to communication.

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				psychotropic medications or if the individual would only learn to cope with them more effectively [Ref. Conant, 1990].	
The 25% ME Group	Evidence Review B	051	32-48	The acknowledgement that lack of knowledge, lack of awareness and presence of misunderstanding can pose a hazard for patients is welcome. The ensuing recommendation - that *people with ME/CFS should have their care and treatment delivered by or as a minimum overseen by health and social care practitioners who have training and experience in ME/CFS relevant to their role* - may seem a statement of the obvious. However, our starting point is poor. Few have relevant training. Experience may well amount to experience of purveying the very interventions that have most potential for harm. Regarding training, may we suggest this CPD accredited on-line learning module is used: https://blog.diploma-msc.com/2020/05/13/new-cpd-myalgic-encephalomyelitis-chronic-fatigue-syndrome/ Existing services may be purveying the very interventions that have most potential to cause harm (graded exercise or activity, and CBT where the behavioural component is graded exercise or increasing activity). For this reason we would be very wary of existing services being given a role to educate GPs.	Thank you for your comment. The committee agree that training is an important issue and address this is in the 'training for health and social care professionals' section of the guideline. To note the training recommendations have been edited. . We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme
The 25% ME Group	Evidence Review B	051	26	Please delete "other". In her expert testimony, Dr Muirhead had advised: "Information from the Scottish freedom of information study shows that this is taught as a medically unexplained illness" [supporting documentation 3, page 18]. The issue is teaching as medically unexplained (i.e. 'functional'). Not the merging of this illness with "other medically unexplained symptoms".	Thank you for your comment. 'Other' has been deleted.
The 25% ME Group	Evidence Review B	052	13-18	Regarding discussion of 'symptom measurement scales' for 'diagnosis and recovery'. The 2003 Canadian Consensus Criteria and 2005 Overview contain the diagnostic protocol in checklist form, as well as several useful charts and scales that could help gauge progress or deterioration.	Thank you for your comment and information.

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				Other scales - of a generic nature - are useful for assessing overall function and/or impact of illness on quality of life. Published studies involving the use of generic scales are what reveal that this illness has a greater impact on quality of life and functioning than many other chronic diseases.	
The 25% ME Group	Evidence Review B	054	10-19	This paragraph discusses professionals' hesitance to discuss "psychological factors around ME/CFS" and the topic of "psychological symptoms". It is disappointing that the GDC seem to consider that all cases of 'ME/CFS' involve some 'psychological factors'. We expect that patients would be only too pleased to accept appropriate help with the psychological impact of having a long term illness that is not only life limiting but leaves them feeling very ill, often quite relentlessly, and with the impact of being disbelieved, including by profs who insist there *must* be 'psychological factors'. If the GCD is of the view that psychological factors are an intrinsic part of this illness then the guideline requires to be clear about this and about the evidence it rests on.	Thank you for your comment. This paragraph discusses the theme around the negative interactions that can occur between people with ME/CFS and health and social care professionals and the impact of this and how this can be addressed.
The 25% ME Group	Evidence Review B	054	10-19	The imputed professional hesitance rests on a paper from 1999 that looked at *patients'* perspectives [ref 13], and another [ref 19] which appears to be unpublished, so we cannot assess it. The 1999 paper states: "Satisfaction with medical support, it seems, is strongly associated with beliefs about CFS, attributions as to its origin, and ways of managing it. Most sufferers believed that CFS is a predominantly physical disease for which increased rest is the most appropriate treatment, but they judged such a belief incompatible with the views expressed by many physicians. This led to disagreements between the sufferers and their physicians and other health professionals, and to dissatisfaction with treatment and the medical establishment as a whole. … Clearly, the uncertainties about the aetiology or chronicity of CFS strongly encourage sufferers	Thank you for your comment. This paragraph discusses the theme around the negative interactions that can occur between people with ME/CFS and health and social care professionals and the impact of this and how this can be addressed.

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				to construct their own illness beliefs which may well lead to the adoption of inappropriate coping strategies. …Likewise, those same uncertainties create difficulties for clinicians not only in deciding which treatments and coping strategies to recommend but also in adopting a manner that enables the patient to accept them." It is most disappointing to find a 2020 draft guideline discussing how to overcome the 'barrier' that such a view on the part of patients is deemed to impose for professionals.	
The 25% ME Group	Evidence Review B	055	6-9	This paragraph aims to summarise findings as they relate to 'support from specialist services', advising that such support: "was identified from two perspectives in both reviews; access to services for people with ME/CFS and access to advice. The committee noted the need for access to specialist support was identified by both HCPs and people with ME/CFS and this theme was echoed throughout several of the guideline reviews." Unfortunately looking into the papers cited in support of findings put before the GDC reveals that the foundation for these assertions is shaky at best. However we cannot help but conclude that the GDC have not been well served by the conclusions drawn from the assessment of qualitative evidence with regard to the role of existing specialist services in the UK, as exemplified by our reference to the content of source papers cited.	Thank you for your comment. *ME/CFS specialist care* The committee agreed that access to ME/CFS specialist care was important for people with ME/CFS. Throughout the guideline there is reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support plan and supervision for the management of some symptoms This was based on the evidence across the reviews and their experience. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline and making the recommendations the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as

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					underrepresentedunderrepresented in the literature. As with all NICE guidelines the committee used its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee considered many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
The 25% ME Group	Evidence Review B	056	17-19	Regarding video resources, may we suggest this video educational project, funded by the Wellcome Public Engagement Fund: https://www.dialogues-mecfs.co.uk/about/	Thank you for your comment. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme
The 25% ME Group	Evidence Review B	057	37-40	We welcome the committee decision to dispel some of the common misconceptions, however the relevant recommendation in the draft guideline could be much stronger in emphasising that these are in fact "common misconceptions".	Thank you for your comment. The committee agreed your suggestion does not add any further clarity to the recommendation and your suggestion has not been added.
The 25% ME Group	Evidence Review B	057	48-50	We do not agree that the "profound fatigue after exertion" in ME/CFS means that such patients can have their condition "easily confused with fatigue in mental health conditions such as depression or in other diseases such as MS, cardiac failure and muscle disorders." Reasons: (i) even minor activity produces deterioration in ME/CFS patients; (ii) the nature of the deterioration is not confined to 'fatigue', in fact it may not involve fatigue at all; (iii) it is possible to ask a person how they feel, revealing that they are not lying in bed feeling tired (or lazy) but feel very unwell.	Thank you for your comment. As mentioned in the paragraph above in the discussion this is a common misconception.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management

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The 25% ME Group	Evidence Review B	057	42-43	We are alarmed to see apparent agreement among the GDC that the symptoms of ME/CFS "cannot be explained by current knowledge of organic pathology". We may not know all there is to know, however it is "current knowledge" among professionals charged with patient care that is the fundamental problem, not the absence of research studies on organic pathology. As long ago as 2003, the Clinical and Diagnostic Protocol by Carruthers *et al.* presented a detailed review of the clinical and biomedical evidence, linking symptoms to pathogenesis: "Our strategy was to group symptoms together which share a common region of pathogenesis, thus enhancing clarity and providing a focus to the clinical encounter. We hope that the clinical working case definition will encourage a consideration of the ongoing interrelationships of each patient's symptoms and their coherence into a syndrome of related symptoms sharing a complex pathogenesis rather than presenting a 'laundry list' of seemingly unrelated symptoms." Please note use of term 'complex' here, referring to the pathogenesis of symptoms in this context - the very terms in which the GDC apparently agree that 'symptom interaction' cannot be explained. Unless and until professionals gain some awareness of the organic pathology and the distinctive clinical picture, both adult and child patients will remain at risk of inappropriate 'safeguarding' and other legal procedures.	Thank you for your comment and information. The committee agreed that more research is need on this topic to improve the knowledge about organic pathology and support people with ME/CFS in the future.
The 25% ME Group	Evidence Review B	057	5	We welcome the recognition that families being disbelieved has led to a 'persistent feeling of a low level threat of accusation of making their child's illness up'. However, we are also aware of cases where this has gone much further, with families being accused of Fabricated or Induced Illness in their sick child, which in turn can lead to child protection proceedings, as well as 'Safeguarding'. Both acute experience and the longer-term	Thank you for your comment and information.

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				experience of 'low level threat' are very hard for families who are already living with the distress of seeing their child very ill, and chronically so.	
The 25% ME Group	Evidence Review B	057	17	We are also aware of instances where severely affected adults have been subject to inappropriate safeguarding due to lack of understanding by the health and social care professionals concerned. Threats of 'safeguarding' can also be used as a lever to 'encourage' the person do something that they do not wish to do (because it risks making their condition deteriorate). Again, this is grounded in misperception by professionals.	Thank you for your comment and information.
The 25% ME Group	Evidence Review C	016 - 017	Table 3	A range of barriers and facilitators to diagnosis emerge. We are acutely aware that present diagnostic practice in the UK is inadequate, and would hope that the guideline, when published, will provide a potent facilitator. Regarding facilitators:	Thank you for your comment. The committee agree and hope that the guideline, when published, will provide a potent facilitator.
The 25% ME Group	Evidence Review C	016 - 017	Table 3	Regarding barriers: why would 'focus on physical symptoms' present a 'barrier'?	Thank you for your comment. The later description of this theme notes that this could mean other symptoms might be missed. This could result in a mis or missed diagnosis. The committee recommend a holistic approach to any assessment.
The 25% ME Group	Evidence Review C	016 - 017	Table 3	Re 'complicated journey to specialist services' as a barrier - please see next comment. (Please note that Study 36, discussed there, is provided as a supporting reference in this regard.)	Thank you for your comment.
The 25% ME Group	Evidence Review C	016 - 017	Table 3	Regarding facilitators: once again we have a steer towards 'specialist services' in this regard. While this does reflect a lack of confidence on the part of GPs emerging from the evidence, one way to respond is to equip GPs and local paediatricians to make the diagnosis (rather than continuing to have patients referred to a 'specialist' service for diagnosis). The guideline in development has potential to play a key role in this regard. In any case, perusing some of the papers referenced does not bear out the findings listed. For example, paper 36 focuses on	Thank you for your comment. The committee agreed that access to ME/CFS specialist care was important for people with ME/CFS. Throughout the guideline there is reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support plan and supervision for the management of some symptoms This was based on the evidence across the reviews and their experience.

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				GP views. Main findings include: "the value of referral to secondary care was disputed, either in enabling a diagnosis to be made or offering support to the GP in supporting and managing the patient." The researchers conclude: The provision of services to support GPs develop confidence to make the diagnosis of CFS/ME and manage and support patients with this complex debilitating condition is necessary [REF: CMO's Wkng Grp Report 2002 and 2007 BMJ summary of CG53]. Incidentally, the authors refer to 'CFS/myalgic encephalitis'.	One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline and making the recommendations the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresentedunderrepresented in the literature. As with all NICE guidelines the committee used its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee considered many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). *Training* The committee agreed that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to

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					their role and in line with the guideline. To note the training recommendations have been edited.
The 25% ME Group	Evidence Review C	016 - 017	Table 3	Re 'heterogeneity' as a barrier. It is important to be clear about this. The diagnostic term 'CFS' is what has been used in practice in the UK for some time now. As defined in loose research definitions, notably 'Oxford' (though that definition was not intended to be used to loosely, as the relevant evidence review makes clear), and as applied to patients, this has indeed encompassed a heterogeneous group. The present guideline holds promise to identify a much more specific disorder, reflecting the distinctive core features of what the draft call 'ME/CFS'. Equipping GPs to make this diagnosis and to understand what is known about the nature of the disorder and what it means for safe and effective patient care is very much needed.	Thank you for your comment.
The 25% ME Group	Evidence Review C	041 - 042	Table 5	Reviewing the main findings emerging from the research studies reviewed on barriers and facilitators to care indicates that not all of these were focussed on ME or 'ME/CFS' as this draft guideline defines it.	Thank you for your comment.
The 25% ME Group	Evidence Review C	041 - 042	Table 5	Following on from the above, we respectfully submit that some of the issues identified here say more about professional and/or researcher mindset that about barriers inherent in patient attitude. For example Ref 35: 'Patients may experience difficulty implementing certain treatment models into their life.' relates to a trial of 'Pragmatic rehabilitation (PR)', defined as "a therapist facilitated self-management intervention for CFS/ME, which shares features in common with CBT and GET, but which does not require a specialist CBT or physiotherapist to deliver it." This paper is one of those published by the 'FINE' trial group. The 'FINE Trail failed (after which the PACE investigators	Thank you for your comment. Reflexivity is one of the factors taken into account by the committee when interpreting the evidence.

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				changed their proposed benchmarks of 'a positive outcome', as same benchmark had just been found to fail in FINE. The failure of the trial did not stop the investigators publishing further papers linked to their 'pragmatic rehabilitation' 'treatment'. Four papers are cited regarding 'personal attributes and motivation', advising that attributes such as "being proactive, determined and positive can facilitate treatment'. If only this were correct. It is not, and the mindset reflected here leads to the patient being blamed if they do not improve	
The 25% ME Group	Evidence Review C	052 - 053	Table 6	Similar points emerge in respect of barriers to the care of children and young people, as raised in commenting on Table 5.	Thank you for your comment.
The 25% ME Group	Evidence Review C	041	Table 5	Re 'Accessibility of treatment options in primary care': as far as we are aware, no treatments are available at all because there is no (recognised) treatment aimed at underlying cause. Indeed, one of the studies cited in support of this statement [REF 343] advises: There is no specific treatment, and those offered mostly focus on alleviating impairments and improving functionality.	Thank you for your comment. 'Treatment 'has been used as it is the term extracted from the study.
The 25% ME Group	Evidence Review C	068	4 onwards	Section: barriers and facilitators to accessing care. For the most part this considers healthcare only. The words "and social" seems to have been battened on routinely on after "health". There is virtually no consideration of barriers to accessing social care. Indeed, there are places where it is assumed that any care will come from family - as at P 73, line 7. The 25% ME Group have documented 'barriers to access', based on work supporting members in connection with social care.	Thank you for your comment. The evidence identified focused on access to health care services and as such the discussion focuses on this, where the committee were confident in generalising to social care they made additional recommendations.
The 25% ME Group	Evidence Review C	073	9-11	The acknowledgement that people with severe or very severe ME/CFS potentially receive care that is harmful due to lack of understanding is most welcome. We would also like to make the GDC aware that some members of the 25% ME Group were not severely affected until attempting graded exercise.	Thank you for your comment and information. See Evidence review G-non pharmacological management, for the evidence and committee discussion on physical activity and graded exercise therapy.

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				Unless and until there is genuine understanding on the part of medical and other health professionals, the prospects for appropriate care remain dim.	
The 25% ME Group	Evidence Review C	078	22-26	What is required most for people with ME/CFS to be reassured and supported to "engage in [health] services and to access the [health]care they require" is a revolution in professional mindset, so that only appropriate advice is given. No part of a 'management plan' should be counter productive for the patient. This has been the historical problem.	Thank you for your comment.
The 25% ME Group	Evidence Review D	146 -148	Table 13 Excluded studies, diagnostic tests	The approach to exclusion of studies discussed above has allowed at least a dozen to be disregarded, solely on the grounds that they looked at patients with confirmed CFS or ME when attempting to ascertain if a biomarker could be found. We note with concern that there has been no assessment of the potential value of the following research, which includes longitudinal and prospective studies: 1 (assessing the diagnostic value of microRNAs); 30 (evaluating four clinical laboratory parameters); 35 (specific blood biomarkers); 104; 106 (autonomic symptoms at baseline); 107 (orthostatic tolerance testing in a prospective cohort); 127 & 128 (again - these are prospective studies); 152; 155; 173 (pro- and anti-inflammatory cytokine production - longitudinal analysis); or 189 (two day cardi-pulmonary exercise testing)	Thank you for your comment. This systematic review aimed to identify the diagnostic accuracy of specific tests to identify ME/CFS. The protocol sets out the criteria for study inclusion and the excluded studies list you refer explains with reference to the protocol why the studies have been excluded.

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The 25% ME Group	Evidence Review D	064 - 065	37-2	In the absence of consideration of any studies in relation to identifying a possible diagnostic test throws doctors back on the requirement to make a diagnosis on clinical grounds only. We are baffled as to why a "psychological wellbeing" assessment should be routine element of a basic clinical diagnostic routine.	Thank you for your comment. The committee note the assessment recommended describes the routine examinations and assessments when a patient has an undiagnosed illness. To clarify this the recommendation has been edited from 'comprehensive clinical history' to 'medical assessment (including relevant symptoms and history, comorbidities, overall physical and mental health). In addition, psychological wellbeing has been edited to, 'an assessment of the impact of symptoms on psychological and social wellbeing' to clarify this assessment.
The 25% ME Group	Evidence Review D	060	Review Question on diagnostic tests	We note with concern the trajectory of the review question on diagnostic tests over the course of gestation of guideline development. The final scope proposed: *What tests are clinically and cost effective in diagnosing of ME/CFS?* (all questions in the final scope were referred to as a 'draft' questions.) However the question reviewed is: *What is the diagnostic accuracy of specific tests to identify ME/CFS in people with suspected ME/CFS?* We assumed that this implied that ME/CFS was 'suspected' in the absence of a definitive diagnostic test, which was being sought to facilitate confirmation. However we find that the review population is: *Adults, children and young people who are suspected of having ME/CFS by their primary clinician, but who are yet to be formally diagnosed.* [Table 5] It is almost perverse to look only at testing patients in whom the illness is merely suspected and then decide if the findings are fit to use to diagnose people, rather than permitting the findings of	Thank you for your comment. The process for developing the review questions is set out in Developing NICE guidelines: the manual, chapter 4. To summarise the review questions build on the draft questions in the scope. Review questions are drafted by the reviewing team, the questions and the protocols are then refined and agreed with the committee members. The aim of the question was to identify a test that could accurately diagnose ME/CFS. The approach for this question was a standard methodological approach for reviewing the evidence to identify the diagnostic accuracy of any tests that could be used in practice to diagnose people with ME/CFS. (see(see the methods chapter and Developing NICE guidelines: the manual).

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				biomarker studies on patients with confirmed diagnosis to be extrapolated for use at the diagnostic ('suspected') stage in future. The result of this peculiar delineation of the study population is that the review has failed to meet it's stated aim, *vis:* This review aims to identify up to date evidence in relation to tests which may help to identify ME/CFS, and to assess which of these may be useful to incorporate into clinical practice [lines 6-7]. We further note that the change in the framing of this question between the final scope and the conduct of the evidence review does not appear to be discussed or explained.	
The 25% ME Group	Evidence Review D	60	10 (Table 5)	In seeking to identify the diagnostic accuracy of specific tests in identify ME/CFS in people with suspected ME/CFS the evidence reviewers have taken a very narrow view of the relevant population when reviewing studies i.e. people who are suspected but have not yet been diagnosed. We respectfully suggest that conducting research on suspected patients as opposed to patients who have been diagnosed is not necessary - indeed, why would the patient be 'suspected' if not that they have the clinical features of ME/CFS - as the draft guideline itself proposes. It would almost be a contradiction in terms to look at research on tests conducted on suspected patients - given that suspected patients are not tested, specifically because no diagnostic test has yet been established. On the other hand, there are many studies indicating abnormalities in people who have been diagnosed and it is perfectly sensible to consider these in terms of do they have diagnostic validity.	Thank you for your comment. The aim of the question was to identify a test that could accurately diagnose ME/CFS. The approach for this question was a standard methodological approach for reviewing the evidence to identify the diagnostic accuracy of any tests that could be used in practice to diagnose people with ME/CFS. (see(see the methods chapter and Developing NICE guidelines: the manual).
The 25% ME Group	Evidence Review D	062	3	The predictable result of the approach taken is that precisely no relevant studies were identified. If this is allowed to stand, it eliminates any opportunity to make progress on the important issue of diagnostic testing - or indeed the identification of a biomarker pertinent to any stage of the illness.	Thank you for your comment. Unfortunately, this review confirmed the expertise in the ME/CFS patient and clinical community that there is not a diagnostic test for ME/CFS and this is why the committee made a research recommendation on this topic.

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The 25% ME Group	Evidence Review D	065	7-9	The GDC are of the view that consideration of tests that may show "differences in people diagnosed with ME/CFS compared to people without ME/CFS" is pertinent. This makes the approach taken by the evidence review to delineate the relevant study population all the more inexplicable.	Thank you for your comment. The aim of the question was to identify a test that could accurately diagnose ME/CFS. The approach for this question was a standard methodological approach for reviewing the evidence to identify the diagnostic accuracy of any tests that could be used in practice to diagnose people with ME/CFS. (see the methods chapter and Developing NICE guidelines: the manual).
The 25% ME Group	Evidence review F	006	13-15	We are unclear as to why evidence pertaining to "a wide range of non pharmacological management strategies" is considered relevant to a review of pharmacological evidence. This seems to stem from the tacking on a second review question *i.e. What are the experiences of people who have had interventions for ME/CFS?* to the question on pharmacology. While this may provide the 'how', it is hard to see the 'why' behind this procedure. We also don't find any reflection of this in the presentation of evidence and committee discussion.	Thank you for your comment. 'non-pharmacological' was written in error and should read 'pharmacological'. This sentence has now been corrected to 'The committee evaluated evidence from clinical effectiveness studies and patient experience from a wide range of pharmacological management strategies to inform the recommendation in these areas.' Note that interventions involving combinations of pharmacological and non-pharmacological interventions or comparing the pharmacological to non-pharmacological interventions were also considered relevant to this review. This was to ensure that all available evidence meeting the review protocol was reviewed and considered by the committee. The experiences of interventions review covered both pharmacological and non-pharmacological interventions. The majority of the evidence in this review pertained to non-pharmacological interventions, and therefore the full methods and results has been included in Evidence Review G. However relevant results pertaining to pharmacological interventions and the committee's discussion of the evidence is included in Section 1.2 of Evidence review F.

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The 25% ME Group	Evidence review F	006	16-18	Again, this refers to the evidence review on 'non pharmacological management'. We cannot see why this is considered relevant to pharmacological interventions.	Thank you for your comment. 'non-pharmacological' was written in error and should read 'pharmacological'. This sentence has now been corrected to 'The committee evaluated evidence from clinical effectiveness studies and patient experience from a wide range of pharmacological management strategies to inform the recommendation in these areas.'
The 25% ME Group	Evidence review F	006	6	We are disappointed at the generally negative tone, beginning with this first sentence. While no 'cure' has been identified, some patients have experienced remarkable improvement, even recovery, following prescription of pharmacological interventions aimed at underlying cause. For example: patients tested and found to have viral presence & the relevant anti viral administered (the work of Martin Lerner); patients treated for co-morbid cancer with B-cell depletion therapy. It is however possible that heterogeneous patient cohorts have resulted in some confused or mixed study findings in this regard. Meanwhile patients suffer.	Thank you for your comment. This is the introduction to the review and provides brief background information.
The 25% ME Group	Evidence review F	032	Table note 2	This refers to downgrading 'if confidence interval crossed one MID'. The term 'MID' is not spelt out, so it's hard to make sense of this.	Thank you for your comment. The minimally important difference (MID) is the smallest change in a treatment outcome that people with the condition would identify as important (either beneficial or harmful), and that would lead a person or their clinician to consider a change in treatment. These are determined in advance by the committee, prior to reviewing the evidence. A full explanation of the use and interpretation of the evidence relating to MIDs is found in the methods chapter of the guideline. The evidence reviews have now been amended so that 'minimally important difference' is written out in full, with reference to the methods chapter of the guideline.

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The 25% ME Group	Evidence review F	075	Table note 2	While identifying PEM as a compulsory feature represents a step forward for future work, it must be recognised that it has simply not been possible to publish research that selected participants on this basis. Researchers wishing to study people with ME - *i.e.* people who experience PEM - had no choice but to refer to 'CFS' and to use an existing set of research criteria - normally Fukada *et al.* 1994. These patients had nowhere else to 'go'. Patients are experiencing a most unpleasant illness and need relief. Downgrading the pharmacological research in this way is not helpful to this end and is likely to continue for the forseable future as we do not have accepted research criteria that include PEM as essential feature.	Thank you for your comment. The committee do not wish to downplay the illness experience of people with other chronic conditions, including those that cause chronic fatigue but are not ME/CFS; however it is possible that people with different conditions may respond differently to treatments. The committee consider PEM to be an essential feature for a diagnosis of ME/CFS, and this is supported by other diagnostic criteria such as the IOM 2015 criteria. This causes difficulty in interpreting the evidence from trials that do not use criteria that have PEM as an essential feature (and therefore a 100% ME/CFS population) or where the percentage of people with PEM are not reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported, and numbers of people with PEM are rarely reported. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendix G for the approach taken, the analysis and the impact on the results and interpretation of the evidence
The 25% ME Group	Evidence review F	075	Table note 2	To further downgrade a study of an anti-viral therapy [Montoya 2013] on the basis that the patients studied had had a suspected viral onset and confirmed elevated antibody titers would appear to be quite illogical.	Thank you for your comment. This study was downgraded for population indirectness, as the evidence was considered to apply to only a subset of participants with ME/CFS – those with a suspected viral onset and elevated specific viral antibody titres.

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					This limits to generalisability of this evidence and downgrading for indirectness captures this. Also note, after considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. They agreed that any evidence with a population ≥ 95% with PEM would be considered direct. As part of this a subgroup analysis has been performed, which examines results from trials where ≥ 95% of participants had PEM separately (including the GETSET trial) to trials where <95% of study participants had PEM or this was unclear. As more than 95% of study participants in Montoya 2013 had reported PEM, the study is no longer downgraded on the basis of PEM/diagnostic criteria. See evidence review H appendix G for full details on the approach taken, the analysis and the impact on the results and interpretation of the evidence.
The 25% ME Group	Evidence review F	091	10-18	We are disappointed to see such a negative appraisal of the findings of research studies on immunomodulatory drugs. In particular, there is promising evidence from studies of immunoglobulin. Can we ask please that the findings of studies on immunoglobulin are considered separately. Three studies have shown immunoglobulin to be beneficial, the results published in papers (46), (65), and (74 + 75). The latter study has been excluded from the review, on the grounds of having 'no relevant extractable outcomes'. (It was considered relevant in the 2005 York review for NICE). One study (99) failed to find a beneficial effect. No adverse effects were reported in any of the studies.	Thank you for your comment. Clinical benefit or harms for each outcome are determined based on the minimally important difference (MID) decided on by the committee prior to reviewing the evidence, not statistical significance or benefit/harms reported by study authors. Detailed information on this process can be found in the methods chapter. To clarify, different immunomodulatory treatments were considered separately from each other (IVIG, rituximab, and rintatolimod). The committee considered all available evidence meeting the review protocol for these immunomodulatory

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					treatments and determined that there was insufficient evidence to recommend any immunomodulatory treatments for use in people with ME/CFS. For IVIG specifically, 3 small studies were included. None of the outcomes could be pooled as all 3 studies reported different outcomes. Although there was clinically significant improvement in symptoms and return to work in one study of IVIG, this evidence was of very low quality, and no other clinically important benefits of IVIG were identified across the 3 studies. See evidence review F for full details of the interpretation of the evidence, and the committee's rationale for the recommendations. References 74 and 75 (Rowe 1997 and 1999) were excluded as no relevant outcome data was reported. In the 1997 paper results were only reported for 'functional score' which is not a validated outcome measure as defined in the review protocol. Results for relevant validated outcome measures were reported only for the study population as a whole, and there was no comparative data, Additionally, adverse events were reported but not in a format that could be used (percentage of infusions associated with 14 different symptoms). Likewise, there were no validated outcomes measures reported. Likewise, there was no relevant comparative outcome data for the 1999 follow-up study.
The 25% ME Group	Evidence review F	091	10-18	The research on immunoglobulin exemplifies the sad fact that it has been hard to gain traction - or funding - for studies of immunomodulatory therapies, as compared to behavioural interventions. The most recent of the immunoglobulin studies is	Thank you for your comment. Clinical benefit or harms for each outcome are determined based on the minimally important difference (MID) decided on by the committee prior to reviewing the evidence, not statistical significance or benefit/harms

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				from 1997. Unfortunately the benefits were considerably underplayed in the respective reporting of these studies in the 2002 CMO's Working Group Report and the 2005 York review for NICE. We are keen not to have this happen again.	reported by study authors. Detailed information on this process can be found in the methods chapter. The committee considered all available evidence meeting the review protocol for these immunomodulatory treatments and determined that there was insufficient evidence to recommend any immunomodulatory treatments for use in people with ME/CFS. For IVIG specifically, 3 small studies were included. None of the outcomes could be pooled as all 3 studies reported different outcomes. Although there was clinically significant improvement in symptoms and return to work in one study of IVIG, and fewer 'constitutional symptoms' in another study, this evidence was of very low quality, and no other clinically important benefits of IVIG were identified across the 3 studies. Due to the low quality of the evidence, including imprecision around the effect estimates, the committee were uncertain about the results from these studies. See evidence review F for full details of the interpretation of the evidence, and the committee's rationale for the recommendations.
The 25% ME Group	Evidence review F	093	33-41	This discussion of anti-viral therapy is very disappointing. The only one mentioned by name is acyclovir, which may be the anti viral for which there is the least evidence of benefit. Nonetheless, it is interesting to compare the coverage here with the published paper(s). "The committee noted that evidence for acyclovir came from two small studies and was of very low quality, and they could not be confident of the effects. Evidence of harm came from a single study on IV acyclovir with a short follow up of 37 days."	Thank you for your comment. Two small studies on antiviral medicines were included in this review, one of IV acyclovir and one of oral valganciclovir, not two studies of acyclovir which was incorrectly reported in the review. Thank you for pointing out this error which has now been corrected. Clinical benefit or harms for each outcome are determined based on the minimally important difference (MID) decided on by the

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				We assume that the reference to 'evidence of harm - listed as 'visible renal failure' [P 27] - concerns the Strauss study (REF 88), which reported that 3 participants had reversible renal failure during acyclovir infusions and were withdrawn from the study. Regarding treatment period: Following 7 days of IV acyclovir or placebo, acyclovir was given orally for 30 days (800 mg four times daily), with six-week observation periods before, between, and after the treatments. The authors conclude that "acyclovir, as used in this study, does not ameliorate the chronic fatigue syndrome. We believe that the clinical improvement observed in most patients reflected either spontaneous remission of the syndrome or a placebo effect." Reporting on this study in the 2005 York review for CG53, the reviewers state: A small RCT of acyclovir, reported a greater improvement in anxiety, depression and confusion in the control group compared to the treatment group, however, no differences in treatment effect were found for the other six outcomes investigated. We cannot find a 2nd acyclovir study listed among the references. The Montoya study concerned valgancyclovir, and concludes: VGCV may have clinical benefit in a subset of CFS patients independent of placebo effect, possibly mediated by immunomodulation and/or antiviral effect. VGCV was well-tolerated and was not discontinued due to hematologic or hepatic adverse events. Two patients were diagnosed with cancer during the study period (one in the study arm and one in placebo). These two serious adverse events were deemed unrelated to VGCV. While the work of Martin Lerner - who proceeded by identifying specific viruses in his patients and treating then with a matched anti viral, to good effect and without adverse events related to administration of the drug, has been discounted altogether.	committee prior to reviewing the evidence, not statistical significance or benefit/harms reported by study authors. Detailed information on this process can be found in the methods chapter. The committee considered all available evidence meeting the review protocol for antiviral treatments and determined that there was insufficient evidence to recommend any antiviral treatments for the purpose of curing ME/CFS. Specifically, there was very low-quality evidence of benefit for valganciclovir for fatigue from one small study. For IV acyclovir there was evidence of harm, both in terms of psychological outcomes, and reversible renal failure, which the committee considered to be a serious adverse effect. The committee acknowledged that antiviral medicines are used to treat certain viral infections, and as with all other NICE guidelines and recommendations, healthcare professionals should use their clinical judgement as to whether or not a specific treatment is indicated based the patient in front of them.

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				Given that "the committee recommended that antiviral drugs should not be used for purposes of treating or curing ME/CFS, however they acknowledged this recommendation should not stop antiviral drugs being used where a genuine indication exists, for example for the treatment of some viral infections." the setting aside of this evidence is remarkable. Perhaps the way forward is to follow the example of Dr Montoya and the late Martin Lerner, test patients for viral presence, and proceed to administer the relevant anti-viral drug.	
The 25% ME Group	Evidence Review G	General	General	It has been impossible for us to properly review the evidence and appraisal of evidence in this Evidence Review, because of anomalies in presentation. 110 studies / publications are listed among the references (starting page 348). Yet when details are presented of the various studies (Table 2, summary of studies included in the effectiveness evidence, starting on page 9) the reference numbers go up to 138. We haven't been able to resolve this by looking at lead author and comparing with reference list, because the particulars presented of studies don't necessarily match what was involved in the study. We noticed this when seeking coverage on the 'FINE' trial (referenced in Table 2 to publications 125, 126 and 128). This is described as entailing a 'step test'. This is not the intervention purveyed in the FINE trial. We don't know how many other studies may be mis-described. Given that this is an area where the reported findings of studies have been contentious it is particularly important to be able to scrutinise the review put before the GDC.	Thank you for pointing this out. There was an error with the formatting of the references for this review, and this has now been corrected.
The 25% ME Group	Evidence Review G	214	Table 70 Review Findings: CBT	We note that all but two of these review findings are based on one study. A further three studies are referenced, in respect of the other two findings. This is very shallow evidence on which to base a recommendation of CBT in this illness. It isn't as	Thank you for your comment. This is not the only evidence the committee has considered. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative

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				though some other source of evidence such as patient reports indicates additional support for these findings.	evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). After reviewing the evidence available, together with their clinical experience, the committee agree that although CBT is not curative for ME/CFS, it is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation has been made to offer CBT to ensure this will be the case. The discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in Evidence review G
The 25% ME Group	Evidence Review G	214	Table 70	We cannot appraise the original evidence by consulting the four studies referenced, because of the anomaly in use of study reference numbers. (ref numbers stop at 110 on the references list, don't relate to ref nos used in Table 2, for example -which has 138 as highest number).	Thank you for pointing this out. Reference numbers have been revisited and corrected.
The 25% ME Group	Evidence Review G	218	Table 74	We note that all but findings come from one or both of two studies. This is very shallow evidence on which to base a recommendation for rehab or condition management.	Thank you for your comment. This is not the only evidence the committee has considered. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative

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					evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). After reviewing the evidence available, together with their clinical experience, the committee agree that although CBT is not curative for ME/CFS, it is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation has been made to offer CBT to ensure this will be the case. The discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in Evidence review G.
The 25% ME Group	Evidence Review G	218	Table 74	We cannot appraise the original evidence by consulting the two studies referenced, because of the anomaly in use of study reference numbers. (ref numbers stop at 110 on the references list, don't relate to ref nos used in Table 2, for example - which has 138 as highest number).	Thank you for pointing this out. Reference numbers have been revisited and corrected.
The 25% ME Group	Evidence Review G	218	Table 77	This is a very narrow base on which to proceed to recommend CBT for children and young people	Thank you for your comment. This is not the only evidence the committee has considered. When developing this guideline the committee considered a wide range of evidence, including that

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					from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). After reviewing the evidence available, together with their clinical experience, the committee agree that although CBT is not curative for ME/CFS, it is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation has been made to offer CBT to ensure this will be the case. The discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in Evidence review G.
The 25% ME Group	Evidence Review G	218	Table 77 CBT in children	We cannot appraise the original evidence by consulting the three studies referenced, because of the anomaly in use of study reference numbers. (ref numbers stop at 110 on the references list, don't relate to ref nos used in Table 2, for example - which has 138 as highest number).	Thank you for pointing this out. Reference numbers have been revisited and corrected.
The 25% ME Group	Evidence Review G	218	Table 77	We note that the only evidence of effectiveness came from a single study, and that the participants also had depression.	Thank you for your comment. This is not the only evidence the committee has considered. When developing this guideline the

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			CBT in children		committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). After reviewing the evidence available, together with their clinical experience, the committee agree that although CBT is not curative for ME/CFS, it is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation has been made to offer CBT to ensure this will be the case. The discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in Evidence review G.
The 25% ME Group	Evidence Review I	026	10	May we suggest that the skills of a community based neurophysiotherapist will benefit some patients; likewise a specialist in enteral and parenteral feeding; these may not require to be part of every team, but there must be at minimum a well defined pathway to access such services when required.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee

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					recommended and described the expertise that should be available to a person with ME/CFS (see Evidence review I _Multidisciplinary care). In the section on Care for people with severe and very severe ME/CFS the committee have recommended access to a physiotherapist working within a ME/CFS specialist team and a dietician with a special interest in ME/CFS.
The 25% ME Group	Evidence Review J	009	27-31	We welcome the warning in this review that any contact with health and social care staff may affect people adversely so that services should be tailored to their needs and that adverse effects and patient satisfaction should be assessed.	Thank you for your comment.
The 25% ME Group	Evidence Review J	010	13-16	We welcome the attention brought to the needs of patients to have routine screening and preventative care. Risk assessment may be necessary.	Thank you for your comment.
The 25% ME Group	Evidence Review J	010	27-30	We welcome the importance attached to professionals providing documentation to help access disability support including for state benefits. Please reflect this in the guideline itself.	Thank you for your comment. The recommendations in the review section of the guideline include the minimum areas for assessment and documentation for all people with ME/CFS. This is not intended to be an exhaustive list and should be tailored according to the individual. As you comment these areas can be the basis for the accessing disability support where appropriate.
The 25% ME Group	Evidence Reviews	General	General	We make a number of comments with reference to the respective evidence reviews. For the most part we have not reiterated these in respect of the relevant part of the guideline. We anticipate that the GDC will assess the value of the comment and carry through the implications to the guideline itself. Similarly, where a point is made once - for example a request to clarify or change a term - we have not re-iterated this every time the term / issue appears.	Thank you for your comments.

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				We trust that this will be acceptable and note that in any case to do otherwise within the allocated timeframe would not have been possible.	
The 25% ME Group	Guideline	General	General	We welcome the steps taken to help ensure that the guideline considers the needs of the most severely affected ME patients, and of children and young people with ME. As these groups overlap, we would ask that the draft is reviewed to ensure that the needs of severely affected children and young people are adequately addressed.	Thank you for your comment. After considering the stakeholder comments the committee agreed to restructure the guideline and placed all the recommendations on the care of people with severe and very ME/CFS in one section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline. In NICE guidelines people refers to adults, children and young people where the committee thought it was appropriate they made separate recommendations for children and young people.
The 25% ME Group	Guideline	General	General	While there are many aspects of the guideline that we warmly welcome, we have identified some flaws which are likely to limit it's potential to improve patient care. We would ask the GDC to accept our thanks for their work and to consider this submission as providing some constructive criticism, mindful that the guideline is likely to have a substantial effect on professional practice for many years to come. We also offer some suggestions for alternative or additional wording which helps strengthen or clarify the issue being address / point being made in the draft. Please note too that we have not been able to appraise all parts thoroughly and some of the evidence reviews and other supporting documentation scarcely at all due to time constraints. There are over 2,500 pages of documents for review, and this had not been our only task over the last 6 weeks.	Thank you for your comment.
The 25% ME Group	Guideline	General	General	In a field that has been bedevilled by sloppy use of terms, to the detriment of patients, we would ask that careful consideration is given to the correct use of language throughout the final guideline. For example, the terms 'treatment' and 'recovery' are	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any

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				used widely in the draft documents, yet 'treatment' is usually referring to a management strategy and 'recovery' (adequately defined) is rare: published research bears out poor prognosis.	misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. Recover is used once in the recommendations and this is used to describe the range of long term outlook in people with ME/CFS noting that although a small proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS. Recovery is used once in reference to post exertional malaise.
The 25% ME Group	Guideline	General	General	In our comments we have (mostly) followed the draft in using the term 'ME/CFS'. This should not be construed as implying acceptance that this is the best term for this illness. We are aware that many stakeholders have raised the issue of the misleading nature of the term 'CFS' and requested change. At the scoping stage NICE repeatedly advised: "The use of the term ME/CFS in the scope does not pre-judge the terminology or title of the final guideline." Yet this remains unchanged and nomenclature does not appear to have been considered - despite the GDC moving away from a focus on 'fatigue' in the diagnostic advice provided and the two diagnostic protocols emphasised by the GDC [ICC 2011 and IoM 2015] both coming out firmly against 'CFS'.	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'* The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3)' has been added to the context.
The 25% ME Group	Guideline	General	General	We welcome the intention to include consideration of social care needs and to provide guidance to social care professionals. However care needs and the barriers and facilitators to social care receive relatively little attention in the draft, even though this area was identified in one of the pieces of evidence that led to the decision to replace CG53 *(Close to Collapse. An interim*	Thank you for your comment. This guideline is for both health and social care professionals and the recommendations unless stated apply to social care professionals. The guideline includes a section in the information and support section on social care and in the access care to section on maintaining independence with particular reference to

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				report on access to social care and advocacy for People with ME/CFS (AfME) 2015). We make comments about this at some specific points in the draft, but as it is an overarching theme and as time constraints have pressured ability to respond in detail at all relevant points, we are raising it here. If considered appropriate, might a sub-strand of continuing work to produce more specific evidence appraisal and development of guidance on social care needs be considered, if necessary as a separate guideline? Please see work by the 25% ME Group including: adult social care survey (https://25megroup.org/factsheets-and-leaflets, first item at 'Questionnaires & Surveys'); comments on: draft scope; consultation on scope and on draft Guideline on Intermediate Care, including Reablement [NG74].	social care needs assessment. In addition the guideline cross refers to the NICE guidelines on people's experience in adult social care services and on supporting adult carers. No further work specific to social care and ME/CFS is currently planned.
The 25% ME Group	Guideline	045 - 047	From line 21 on P45 to line 6 on page 47	Due to time constraints we have been unable to give this section the attention it deserves. However, we are disappointed at the absence of any research recommendations on following up on therapeutic medications that have shown some evidence of benefit in studies to date, or for which there is a rationale based on identified biomarkers. We do not wish to see further behavioural research. This includes research on 'self management strategies' and 'sleep management strategies'. Patients known what works for them and - importantly - what does not.	Thank you for your comment. *Medicines* The committee recognised the lack of research in medicines but did not identify any one medicine to prioritise for research and as such did not make any research recommendations on this topic. Based on the evidence the committee recognised that people with ME/CFS often want information and support on how to manage their ME/CFS symptoms and decided to make research recommendations in the areas where there was an absence of evidence (see evidence review A).
The 25% ME Group	Guideline	008 - 009	Box	Re 'Unrefreshing sleep'. We note that this criterion appears in the IoM but without explication. We commend the GDC effort to expand. The most basic manifestation is feeling completely	Thank you for your comment. After considering the stakeholder comments on the description of sleep symptoms the committee edited the bullet points to,

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				unrefreshed by sleep; patient may feel flu like on waking - however this is just as likely to occur at other times of day and/or throughout the day. Hypersomnia is very common, particularly in the early stages - however this is something different from unrefreshing sleep.	'unrefreshing sleep and /or sleep disturbance, which may include: • feeling exhausted, feeling flu-like and stiff on waking • broken or shallow sleep, altered sleep pattern or hypersomnia. The committee have also edited the definition in the terms used in the guideline section. The committee hope this has added some clarity for readers.
The 25% ME Group	Guideline	034 - 035	all	We welcome the instruction not to offer CBT as a treatment or cure for ME/CFS. We suggest that the section entitled 'cognitive behavioural therapy ' be deleted. We ground this request in the following points: (i) the thrust of CBT in general - this is what CBT involves: • "Dysfunctional behaviour is attributed to maladaptive learning. Re-learning more functional behaviours is the goal. • The therapist adopts an active and directive role throughout treatment. He can be didactic sometimes but his main role is to facilitate the definition and resolution of problems. • The principal therapeutic method is socratic questioning, which is to ask a series of questions aimed at bringing the patient to identify his underlying thought, to perceive alternative solutions, or to modify his opinions." Therefore, unless the person concerned has maladaptive 'learning' that is impacting adversely in the form of misguided behaviour choices, CBT is of no relevance. (ii) the absence of evidence of efficacy in ME/CFS (as acknowledged in Ev Rev H)	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.

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				(iii) we consider the case can be made in terms of either one of the above in themselves, however even if this were not so people with ME are well and truly disenchanted with CBT having had it foisted on them for so long, and from a completely wrong perspective. Neither the evidence nor patient feedback nor the rationale for CBT in general imply that this would be a suitable approach for people with ME.	After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). After considering the range stakeholder comments on this section the committee edited the title to remove psychological support recognising this section only referred to CBT.
The 25% ME Group	Guideline	027 - 028	11-21	We welcome the 'do not advise' and 'do not offer ' statements	Thank you for your comment.
The 25% ME Group	Guideline	022 - 023	14-16	Regarding the specific list of expertise required - not every patient will require an MDT	Thank you for your comment. People with ME/CFS often require the input of different professionals, the optimal approach is good communication between the different professionals and that care is coordinated to avoid duplication of assessments and appointments for the person with ME/CFS. See Evidence review I- multidisciplinary care for details of the committee discussion. The list does not propose that everyone with ME/CFS requires all the expertise listed but that they should have access to relevant expertise based on their need. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about

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					their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan.
The 25% ME Group	Guideline	051 - 052	27-3	The rationale provided for GP referring patient straight to 'specialist team' lies in "lack of knowledge of ME/CFS and evidence that non specialists are not confident about diagnosing and managing ME/CFS". One way to remedy this situation is to equip 'non specialists' with the any tools, information and education they may require in order to develop confidence - this guideline being a case in point. This would represent a more appropriate course of action than reinforcing the current abnegation of responsibility by GPs	Thank you for your comment The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. The committee recognised certain parts of the care and support plan should only be delivered or overseen a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. .
The 25% ME Group	Guideline	028 - 029	12 of 28 to 16 of 29	We reject this section as it is encouraging increases in activity and subsequent worsening can be permanent. We suggest that for patients who are struggling with basic functions i.e. to eat, drink and toilet and whose lives are limited to a survival mode that resources from health and social care be better focused on assisting these patients to obtain and manage help with activities of daily living, the tasks required to run a home and the advocacy required to do so	Thank you for your comment. This guideline aims to provide support for all people with ME/CFS and the different ranges of severity as such the committee agreed it was important to provide specialist information and support for people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or exercise programme into the managing their ME/CFS .

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The 25% ME Group	Guideline	001	box	NICE have repeatedly advised that this guideline will replace CG53.	Thank you for your comment. This has been edited to update and replace.
The 25% ME Group	Guideline	002	box	We are disappointed to see the references to 'fatigue' and nothing but 'fatigue' in this regard. ME is not about 'fatigue' - chronic or not. We are aware that this has been raised repeatedly, by many people and organisations and over a long time period. Yet it bears repeating, because it's proving stubbornly hard to change. There are some welcome signs of movement in the draft, notably the proposed diagnostic criteria. However this needs to be carried through more consistently and extended to other aspects of NICE work - notably the newly published long COVID guideline. Both ME patients and patients with continuing ill health having become ill on contracting SARS-CoV-2 virus will be well served once 'fatigue' as the core principle is consigned to history.	Thank you for your comment. The reference to fatigue has been removed here.
The 25% ME Group	Guideline	004	7-9	Please replace 'Can have' with 'Has' and refer to the impact being greater than in other chronic illness. "The quality of life (QOL) of ME/CFS patients shows marked diminution which is more severe than in many other chronic illnesses." REF Carruthers *et al*, 2003 *Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome: Clinical Working Case Definition, Diagnostic and Treatment Protocols* in the Journal of Chronic Fatigue Syndrome, Vol. 11 (1) 2003, pp7-115; summarising the findings of six published studies.	Thank you for your comment and information. The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes.. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS. The section on people with severe and very severe ME/CFS and report in Appendix 2_People with severe ME/CFS has further details on quality of life.

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The 25% ME Group	Guideline	004	10-12	(i) Rather than putting the emphasis on difference from patient to patient, it would be helpful to highlight key features - the distinctive and unique clinical pattern - thereby informing doctors from the start that, with the support of this guideline, they should be able to confidently diagnose. From draft Scottish GPS: "A positive diagnosis can be based on pattern recognition of recognised symptoms and features and on how they relate to activity. It can and should be an active diagnosis, and not simply a diagnosis of exclusion." (ii) No person is only ever 'mildly' affected by ME. Severity of impact is an under-recognised theme and needs to be emphasised. For example: US infectious diseases specialist Philip Peterson and team employed the 'Medical Outcome Study', comparing their CFS patients' scores with people suffering from myocardial infarction and rheumatoid arthritis [RA]. A score of one hundred was 'best health'. Victims of RA scored in the high 40s range; patients with myocardial infarction scored slightly lower. Patients in Peterson's clinic scored, on average, 16. As far as Peterson and colleagues knew, such low scores had never before been encountered. Presenting findings at a medical conference, Peterson said *"We really haven't seen anything like it with respect to the other medical illness,"* adding that he had needed to engage an artist to redesign the morbidity graph for the slide presented, since **no other category of patients had ever scored so low.** REF: Peterson PK, Schenck CH, Sherman R. *Chronic fatigue syndrome in Minnesota. Minnesota Med* 1991; 74: 21-26.	Thank you for your comment. (i)The committee agree that ME/CFS is a condition that affects people differently and also that is a fluctuating condition in which a person's symptoms can change unpredictably. The committee agreed it was important to raise awareness of the heterogeneity seen in ME/CFS and this has been reflected in the recommendation. The suspecting ME/CFS section highlights the key criteria for diagnosis and other symptoms that are commonly seen in people with ME/CFS. (ii) The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes.. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS. *Severity of impact* The severity of the impact of ME/CFS has been recognised throughout the development of this guideline. The scope included people with severe and very severe ME/FCS as a population for special consideration and each review highlighted any relevant evidence. In addition recognising the lack of evidence NICE commissioned a report to ensure the views of people with severe and very severe ME/CFS were include in the guideline (Appendix 2_People with severe ME/CFS) and this was considered alongside the other evidence by the committee.

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					When making the recommendations the committee considered people with severe and very severe ME/CFS separately and made additional recommendations where relevant. After considering the stakeholder comments the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline and had more emphasis.
The 25% ME Group	Guideline	004	13-15	(i) 'Fluctuating' is another term that requires explication; the fluctuation of symptoms from day to day and within a day - as described by Dr A Melvin Ramsay - tends to be conflated with the longer term picture, whereby *some* patients have periods of *relative* remission. In our experience professionals tend to assume that 'fluctuating' implies that most patients experience periods when they are more or less back to normal. (ii) The potential for symptoms to change is not entirely or even mostly random; symptom lulls and flares are strongly correlated with presence or absence of activity and exposure to stimulus (light, sound etc.) (iii) Only patients in relative remission will be able to carry out most 'normal' daily activities without paying a high price; most will be severely debilitated at some point. In our experience the most severely affected patients are least likely to experience either fluctuations or periods of relative remission: their experience of ill health is more likely to be consistent and intense.	Thank you for your comment and information. (i) In addition to this recommendation the section on information and support raises awareness about the fluctuating nature of ME/CFS and this is followed by information on the long-term outlook noting that many people will need to adapt to living with ME/CFS.
The 25% ME Group	Guideline	004	5-6	Getting these introductory points as strong as possible matters. *Please carry forward comments regarding section 1.1.1 to the counterpart section 'Information about ME/CFS' [for patients] on*	Thank you for your comment. The committee agree that these introductory points should be strong and consider this wording acknowledges the reality and seriousness of ME/CFS as a medical condition without putting

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				page 14 - notwithstanding the instruction not to cross refer, we do not have time to do this. (i) The statement that this is a medical condition is most welcome. In view of the prevailing misperception, might 'medical' be put in bold? (ii) 'affecting multiple body systems' is also good to see; this may render the term 'complex' redundant; however when used it is important to spell out what this term implies as in our experience it is routinely used and interpreted to imply that psychosocial factors are at work. (iii) 'pathophysiology is unclear' is not sufficient to dispel the myths - *"Researchers have demonstrated numerous abnormalities of the immune, muscular, cardiovascular, and central nervous systems in people with CFIDS. It is truly a multi-system disease with a strong component of immune dysfunction."* Congressional statement by DeFreitas, 1991 [CFIDS - Chronic Fatigue & Immune Dysfunction Syndrome, term in use in the USA]	medical in bold. Complex reinforces this is a condition that requires …… (iii)This bullet point has been edited to,' and its pathophysiology remains under investigation' to clarify that there is not enough evidence to make any conclusions about the pathophysiology of ME/CFS and this is an active area of research.
The 25% ME Group	Guideline	004	Before 1	It may be routine for a clinical guideline to begin with recommendations, however this one is entering a field that has been dominated by myth and misconception over a prolonged period. Launching the 'CFS/ME' Working Group report in January 2002, then CMO Sir Liam Donaldson made a statement to the effect that this is a genuine medical illness. Yet 18 years later many doctors and other health and care professionals still fail to accept the reality of ME/CFS as an organic entity. The likely reason for this unfortunate state of affairs is the persistence of the psychosocial hypothesis, whereby biomedical factors are deemed secondary to maladaptive behaviour, and the failure of medical education to discredit it despite considerable evidence to the contrary.	Thank you for your comment. The committee agree that it is important to have clear statements about the seriousness of ME/CFS at the beginning of the guideline. The recommendations in the principles for care section do this and the first recommendation states the reality and seriousness of ME/CFS as a medical condition. The second recommendation acknowledges that people with ME/CFS have experienced disbelief and stigma. To note the context section of the guideline has further information on ME/CFS.

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				Accordingly something more emphatic and explicit is surely justifiable this time round. While we welcome the clear advice in the draft that this illness is not due to de-conditioning, such is the extent of entrenched opinion on this point that to be effective this may require to be placed prominently, at the start of the guideline. Suggestion: "The (psychosocial hypothesis is not fit for purpose and should be discarded. It has played a central role in perpetuating disbelief in ME/CFS as an organic entity and is responsible for much of the neglect and mismanagement to which patients have been subjected over the years, as acknowledged in this guideline. Its basic tenet is that ME/CFS does not really exist, but is a non-disease caused by a combination of faulty illness beliefs on the part of the patient combined with physiological deconditioning consequent on inactivity. It totally fails to explain the range of symptoms and features, the well documented occurrence of epidemics, the relationship of symptoms to activity or stimulus, the physiological differences identified between these patients and sedentary controls, nor the research evidence showing that this is a multi-system disease with a strong component of immune dysfunction. Neither does it explain why interventions aimed at gradually increasing activity have failed to return patients to normal function." A firm statement along these lines is all the more vital because reviewing the research evidence on abnormalities was not part of the remit of the GDC. Unless something is said clearly the danger is that professionals will continue to assume that there is nothing wrong with patients that cannot be 'explained' by psychosocial factors.	
The 25% ME Group	Guideline	004	After 15	Suggest insert point about prognosis; this should reflect the existing research findings.	Thank you for your comment. In the 'information about ME/CFS' section of the guideline the variation in long-term outlook is highlighted.

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The 25% ME Group	Guideline	005	15-17	While this is an important principle, people with ME will be only too glad to accept a treatment or symptomatic relief that can ease their suffering and improve their function. The issue to date with declining or withdrawing is that the 'management' in question was counter productive. We anticipate that, once graded exercise or activity is no longer advised, 'declining' and 'withdrawing' will be far less common. NB: This applies to exercise / graded activity accompanied by a cognitive component challenging the patient's view that this is not right for them *i.e.* CBT, as practiced in various research trails. There is an implication that the professional continues to consider that any intervention which the patient has declined or withdrawn from is in fact suitable. Please note that the 25% ME Group - UK charity specifically supporting severely affected patients - has members who were not severely affected before trying to increase their activity in line with advice given by health professionals charged with their care. It is important for health professionals to be in a position to prescribe and provide relevant and safe care to people with M.E. While all health professionals should be aware of the law of negligence as it applies to ensuring informed consent - i.e. duty to take reasonable care to ensure that a patient is aware of material risks of injury that are inherent in treatment [Montgomery v Lanarkshire Health Board [2015] UKSC 11; heard 2014, Judgment given 11 March 2015 https://www.supremecourt.uk/cases/docs/uksc-2013-0136-judgment.pdf http://www.medicalprotection.org/uk/for-members/news/news/2015/03/20/new-judgment-on-patient-consent] unless the professional is aware of the potential harms of an intervention they are in no position to make patient aware of any material risk. This is particularly important as the contra	Thank you for your comment and information. This recommendation is supported by the evidence and the committee's experience. Some people with ME/CFS reported negative reactions from health and social care professionals when they did not want to follow the advice given (see Evidence review A, Appendices 1 and 2). The committee agreed it was important to make a recommendation supporting people's choices and involvement in their care.

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				indications for ME patients of undertaking physical activity, particularly exercise, are not well known.	
The 25% ME Group	Guideline	005	4 & 11	There is a tendency throughout the draft to refer to 'symptoms' as if these are entities in themselves rather than manifestations of a 'chronic medical condition affecting multiple body systems' [P4]. Language matters. It both generates and reflects mindset. Language particularly matters in this field, where misuse historically has brought about considerable adverse consequences for patients and undermined the ability of doctors and other health and care professionals to identify appropriate care. SYMPTOMS ARE RELATED TO PATHOGENESIS: "Our strategy was to group symptoms together which share a common region of pathogenesis, thus enhancing clarity and providing a focus to the clinical encounter. We hope that the clinical working case definition will encourage a consideration of the ongoing interrelationships of each patient's symptoms and their coherence into a syndrome of related symptoms sharing a complex pathogenesis rather than presenting a 'laundry list' of seemingly unrelated symptoms. We believe this will sharpen the distinction between ME/CFS and other medical conditions that may be confused with it in the absence of a definite laboratory test for ME/CFS." (Carruthers et al. 2003)	Thank you for your comment and information.
The 25% ME Group	Guideline	006	12-27	This focus on severe ME is most welcome. However (i) many of these features apply to all ME patients and (ii) this description of severe ME precedes the counterpart re ME in general.	Thank you for your comments. After taking into consideration the comments from stakeholders the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section after the description of the criteria and associated symptoms to suspect ME/CFS . The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not

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					hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS.
The 25% ME Group	Guideline	006	9-10	After "significantly affect their" please add "physical wellbeing, mobility, and ability to care for themselves and may".	Thank you for your comment. After considering the stakeholder comments the beginning of this recommendation has been edited to 'including activities of daily living, mobility, the ability to interact with others and care for themselves and emotional wellbeing' to match recommendation 1.1.1 describing the impact of ME/CFS.
The 25% ME Group	Guideline	006	8	The focus on severe ME is most welcome. As the charity specifically supporting severely affected patients we would like to make some constructive suggestions for strengthening. Please delete "may".	Thank you for your comment. Not all people with severe or very severe ME/CFS will have all of these symptoms and as such 'may' is appropriate.
The 25% ME Group	Guideline	006	15	Please delete 'smells' and replace with 'chemicals, including perfume and scented beauty products'.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
The 25% ME Group	Guideline	006	22	Please delete 'incontinence' here and refer to "constipation and diarrhoea. Please insert addition point: urinary incontinence - this is remarkably common, from our experience of supporting members with disability benefits applications; it may be underreported by patients, for obvious reasons.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
The 25% ME Group	Guideline	007	22-26	We very much welcome this stress on risk assessment and that this should be discussed with the patient when possible, and when this is not possible with a family member, carer, or advocate - though this should require the person's permission. Please note that many home care workers will be quite unable to assist with this, and will need to follow the outcome of risk assessment rather than being involved in it.	Thank you for your comment. 'if appropriate' has been added to the recommendation. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the

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					guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.
The 25% ME Group	Guideline	007	11-13	Again, very welcome. In interest of accuracy, please adjust to: "…easily or at all and will need support with …"	Thank you for your comment. Not all people with severe or very severe ME/CFS will have all of these symptoms all of the time and as such 'may' is appropriate.
The 25% ME Group	Guideline	007	6-7	This and other points have implications for social care delivery, but are mixed in with others which do not. We suggest presenting the points about social care delivery together and/or spelling out implications for home care staff. For example, lines 1-3 would translate to: "May require to have personal care delivered in conditions of low light and minimal sound."	Thank you for your comment. After considering the range of stakeholder comments bullet points 2 and 4 have been combined and edited to, 'are housebound or bed-bound and may need support with all activities of daily living, including aids and adaptions to assist mobility and independence in activities of daily living (for example wheelchairs)'.
The 25% ME Group	Guideline	007	8	Please add: 'profiling bed and pressure relieving mattresses'.	Thank you for your comment. After considering the range of stakeholder comments this has been edited to, 'are housebound or bed-bound and may need support with all activities of daily living, including aids and adaptions to assist mobility and independence in activities of daily living (for example wheelchairs)' The section on aids and adaptions provides further information.

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					These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
The 25% ME Group	Guideline	007	15	Please delete "headache" and state "migraine".	Thank you for your comment. Headache includes migraine and for this reason your suggestion has not been added.
The 25% ME Group	Guideline	007	After 16	Add point: "Social care staff and home care workers must be particularly careful to follow EPIC3 Infection Protection Guidance. "Social care staff and home care workers should not attend if they have an infection." This is covered in the 25% ME Group's Home Care Briefings: Full version https://25megroup.org/wp-content/uploads/2018/07/Home-Care-Briefing-Aug-2015.pdf Key messages https://25megroup.org/wp-content/uploads/2018/08/Home-Care-Worker-Key-Messages-May-2016.pdf	Thank you for your comment. This section highlights the symptoms that people with severe or very severe ME/CFS may have and how these may be managed and not about the processes for social care staff and home care workers. The committee agree that all staff delivering care to people with ME/CFS should have training in line with this guideline and this is included in the recommendations in the training health and social care professionals section of the guideline.
The 25% ME Group	Guideline	008	8	Patient could be asked about their state of mental health and offered an assessment if indicated / if they wish. However we query the value of conducting of a 'psychological wellbeing assessment' as a matter of routine.	Thank you for your comment. The committee agree at this stage the person has not been diagnosed with ME/CFS or any other condition and as you comment it is important to investigate the possibility of other diagnosis and co-existing conditions. The committee note the assessment recommended describes the routine examinations and assessments when a patient has an undiagnosed illness. To clarify this the recommendation has been edited from 'comprehensive clinical history' to 'medical assessment (including relevant symptoms and history, comorbidities, overall physical and mental health). In addition psychological wellbeing has been edited to, 'an assessment of the impact of symptoms on psychological and social wellbeing' to clarify this assessment.

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The 25% ME Group	Guideline	008	8	Please be aware that aspects of some assessment check lists will pick up features that are merely indicative of poor psychological wellbeing, not conclusive, and would also apply to ME e.g. abnormal sleep pattern.	Thank you for your comment and information.
The 25% ME Group	Guideline	008	16	Please remove "and had a specific onset". No set of criteria that we are aware of to date has suggested that the onset must be specific. On the contrary, it has long been recognised that onset may be sudden or more gradual - including in the IoM and ICC papers.	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the symptoms have developed and have not always been present covering that the symptoms are not lifelong. This now includes the cohort of people who develop symptoms gradually sometimes over months or even years.
The 25% ME Group	Guideline	034 - 025	all	Should the GDC decide to continue with a recommendation for CBT despite the above and in the absence of evidence of efficacy and presence of evidence of CBT not being helpful, it is vital to ensure informed consent. This is particularly relevant as patients have been harmed by undertaking behavioural interventions.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

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The 25% ME Group	Guideline	009	21-26	After exclude, please insert "or identify". It is important that health and social care professionals are aware that having 'ME/CFS' does not preclude the presence of any other illness (to imply otherwise would be to accord this disorder protective properties). Likewise, having another disorder does not preclude the presence of 'ME/CFS'. This is one reason why it is important to equip doctors to recognise the clinical profile of this illness, enabling a positive diagnosis based on pattern recognition of the signs and symptoms and on how they relate to activity.	Thank you for your comment. This has been added.
The 25% ME Group	Guideline	009	15	Myalgia merits a higher profile. We refer to ongoing muscle pain, experienced at rest *i.e.* even when the muscle is not being used. It is important that doctors are advised to expect of myalgia in ME/CFS; otherwise myalgia in these patients may well be confused with fibromyalgia and the patient given the wrong diagnosis. (Fibromyalgia may also be present, of course, but is not the same disorder.)	Thank you for your comment. These are examples of types of pain that people may experience and the committee note that any list of examples is not intended to be exhaustive or is in order or priority.
The 25% ME Group	Guideline	009	After 15	There are rarer symptomatic manifestations which occur in some of the most severely affected patients. Due to rarity, most professionals are unaware of these and if the patient manifests them are prone either to deny that the patient has the problem or begin to question the diagnosis. To facilitate good patient care in respect of this group, we would like to see an addition paragraph about these less common manifestations (references available, on request: • paralysis • atypical seizures severe gastrointestinal difficulties including vomiting and pain after eating (some very severely affected patients have been found to have gastroparesis)	Thank you for your comment. The committee discussed the other symptoms you suggested should be on the list and they agreed to add gastrointestinal symptoms. Based on the evidence reviewed in evidence review D and on their experience the committee did not agree that paralysis and atypical seizures should be included in the list of associated symptoms.

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The 25% ME Group	Guideline	010	15-21	"give people personalised advice about managing their symptoms" is vague, providing the doctor with no idea how to go about identifying suitable 'personalised' advice. Might it be better to cite the bullet points first (which are excellent) and advise the doctor to assist the patient to make a reality of this advice in their own lives.	Thank you for your comment. The committee have reinforced the importance of personalised care throughout the guideline and they agreed it was important in this section to highlight this as the diagnosis of the person is not clear and any advice should be tailored to the person's symptoms.
The 25% ME Group	Guideline	010	17-21	Welcome. In particular, the importance of resting as much as required and not pushing is vital; getting this one piece of advice across to doctors and their patients could do a great deal to help ensure that fewer cases become lasting and severe.	Thank you for your comment.
The 25% ME Group	Guideline	011	general	We can find no place for consultant led healthcare in these proposals.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.

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The 25% ME Group	Guideline	011	general	As this illness affects multiple body systems the patient may require to be referred to the most appropriate consultant for their particular presentation.	Thank you for your comment. The committee agree that expertise may needed from other specialists. In the assessment and review sections of the guideline the committee have recommend that advice should be sought from an 1 appropriate specialist if there is uncertainty about interpreting signs and symptoms and whether a referral is needed.
The 25% ME Group	Guideline	011	general	We are concerned that the setting up of (often inadequate) regional specialist centres following CG53 has led to District General Hospital consultants and GPs abdicating responsibility for ME patients. There is a risk that the present proposals see this continue. Therefore we would like to see the guideline include see some sort of statement to the effect that • the ability to *diagnose* ME should be part of the core competence of all doctors (requires the ability to take a good history and basic knowledge about the classical symptoms) • the ability to *manage* all but the most severe forms of ME should be within the competencies of all GPs and DGH consultants • That local services are best placed to provide practical support and care to the vast majority of ME patients ➢ they are the ones who should be doing home visits for the very severely affected patients ➢ they are also the ones to be doing the review appointments ➢ they (either the GP or the local consultant) is the best placed to provide continuity of care ➢ the local paediatrician is the best person to relate to schools and social workers ➢ even the best regional specialist services cannot meet the needs of the large number of	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee highlight where access to a ME/CFS specialist services is required. They have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care

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				patients, in addition to the problem of geographical remoteness Otherwise the existence of specialist services tends to disempower them.	and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
The 25% ME Group	Guideline	011	General	Joint care between any specialist service and the GP / local paediatrician should be the ideal. Please consider this view on the service / skills / attributes required from medically led specialist service. This service should be staffed by: · Doctors who understand and believe in ME as a genuine (if poorly understood) organic/physical illness; · Doctors who remember the principles of respect for patient autonomy and the need for informed consent; · Doctors who will act as patient advocates and help patients with sickness and disability benefits, car badges, wheelchairs, and in children support for Home Tuition, protection from the pressures inherent in the educational system and most importantly from being inappropriately diagnosed as Munchausen Syndrome by Proxy or Fabricated or Induced Illness and threatened with Care Proceedings; · Doctors who can tolerate the severity of some cases and their own feelings of impotence when confronted	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee highlight where access to a ME/CFS specialist services is required. They have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies.

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				with them, and not feel duty bound to "cure" their patients somehow; · Doctors who are open to new ideas	After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. The committee discuss further access to ME/CFS specialist teams in Evidence review I-Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.
The 25% ME Group	Guideline	011	9-12	We are not convinced of the wisdom of always and immediately referring on to 'a paediatric specialist team', with apparently little further role for local paediatrician. **Two reasons: (i) it undervalues the role a local paediatrician can play in on-going monitoring, review and palliative response to symptoms; (ii) it assumes that an appropriate 'specialist team' exists, and indeed that a team of health professionals is required as opposed to a single competent physician.**	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section).

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					The committee highlight where access to a ME/CFS specialist services is required. They have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. The committee discuss further access to ME/CFS specialist teams in Evidence review I-Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.
The 25% ME Group	Guideline	011	7-8	We are not convinced of the wisdom of this proposed pathway, whereby on diagnosing ME/CFS GPs always and immediately "refer directly to a specialist team" Two reasons: (i) it undervalues the valuable role a GP can play in on-going monitoring, review and palliative response to symptoms - we would like to see this guideline enhance confidence and GP abilities; (ii) it assumes that an appropriate 'specialist team' exists, and indeed that a team of health professionals is required as opposed to a single competent physician.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.

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					Based on the evidence (Evidence reviews A.B,C,D and I) and the committee's experience referral to ME/CFS specialist care was recommended for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. ME/CFS specialist teams where seen as the most appropriate place for people with ME/CFS to access support. In the guideline primary care has a role in ongoing care and review once a personalised care and support plan has been agreed and developed.
The 25% ME Group	Guideline	011	7-8	A major concern is that no definition is provided of this 'specialist team'. It could be comprised of psychologist, physiotherapist for graded activity, CBT nurse to encourage graded activity. It need not be medically led.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). A definition of a ME/CFS specialist term has been added to the terms used in this guideline.
The 25% ME Group	Guideline	011	7-8	We note that the team is to be "Experienced in managing ME/CFS". We would prefer to see a recommendation for teams with appropriate skills and knowledge, whether for assessment or care planning. Existing teams may have experience in approaching ME as physiological deconditioning or as some form of 'functional' or conversion disorder. The presence of misunderstanding about the fundamental nature of 'ME/CFS' - i.e. "a chronic medical condition affecting multiple body systems" - tends to hinder the possibility of suitable assessment and care. We would like to see a fresh start in many areas.	Thank you for your comment and information. The committee agree that teams should have the appropriate skills and knowledge and the multidisciplinary section of the guideline sets out the minimum expertise that people with ME/CFS should have access to. In addition, the training for health and social care professionals section of the guideline recommends that staff providing care for people with ME/CFS should be trained in line with this guideline according to their role.

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				To illustrate why were are concerned about this, and that that graded activity remains on the agenda, please see this recent position paper from existing MDT professionals: https://www.bacme.info/sites/bacme.info/files/BACME%20Position%20Paper%20on%20the%20Management%20of%20ME-CFS%20October%202020.pdf	
The 25% ME Group	Guideline	011	7-8	A major concern is that no definition is provided of this 'specialist team'. It could be comprised of psychologist, physiotherapist for graded activity, CBT nurse.	Thank you for your comment. A description of a ME/CFS specialist team has been added to the terms used in the guideline and additional text added in the committee discussion of Evidence review I- multidisciplinary care.
The 25% ME Group	Guideline	011	7	Any team of health professionals addressing the needs of this patient group should be medically led: after "directly to a" please insert "medically led".	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.

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The 25% ME Group	Guideline	011	11	We note that the team is to be "Experienced in managing ME/CFS". We would prefer to see a recommendation for teams with appropriate skills and knowledge, whether for assessment or care planning. Existing paediatric specialist teams may have experience in approaching ME as physiological deconditioning or as some form of 'functional' or conversion disorder. We would like to see a fresh start in many areas. In the absence of medical understanding, the prospects for robust assessment are poor.	Thank you for your comment. **The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.**
The 25% ME Group	Guideline	011	13 onwards	There appears to be an assumption that an 'MDT' is best service structure to aim for. We are not convinced. We are not against knowledgeable, sympathetic and supportive OTs, dieticians and physiotherapists where appropriate, but they should not be seen as a substitute for doctors, and the need for them in every case is open to question.	The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.
The 25% ME Group	Guideline	011	15	'Holistic assessment' - Sadly, 'holistic' is interpreted by professionals as code for 'psychosocial'. Clearly patients should have all aspects of their needs assessed - however we are acutely aware that psychological factors have been very much overplayed in respect of this illness, with any	Thank you for your comment. A holistic assessment is an assessment that looks at the whole person not just a person's condition. This approach supports personalised care and support planning where a plan is developed after an initial holistic assessment

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				psychological impact of living with a long term illness conflated with the illness itself. The details of the assessment itself include mental health history, emotional stress (patients cannot cope with the aftermath of adrenal surges, this could be misinterpreted) and impact of symptoms [symptoms, not illness] on psychosocial wellbeing. All NHS services are stretched at present, none more so than mental health services. It would be wrong to routinely divert input from a psychologist, psychiatrist, or cognitive behavioural therapist to a person who does not have a psychological or behavioural problem.	(https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.
The 25% ME Group	Guideline	012	10 onwards	In order for a health professional to be able to develop a suitable 'personalised management plan' in the round, they must have some awareness of the underlying cause of symptoms that is emerging from a range of published biomedical research, and respect this.	Thank you for your comment.
The 25% ME Group	Guideline	012	10 onwards	Aspects of the proposed plan are welcome e.g. mobility aids and adaptations However the production of detailed written management plan for all, to include management of activity, is an area of concern: could be cumbersome and oppressive; time consuming for the professional to put together; a not altogether helpful attempt to micro manage the patient's activity. Producing the plan - or elements of it - may be a burden rather than a help and a waste of the patient and professional's time and energy.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
The 25% ME Group	Guideline	012	25	Please insert "Medically led" before "Symptom management" and add "by health professionals who are commissioned to prescribe medication and to refer on to other medical specialities"	Thank you for your comment. This recommendation reflects the different areas of the care and support plan, to address your point, 'including medicines management' has been added.

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The 25% ME Group	Guideline	013	12-13	The points we have raised re the MDT and management plan apply to severely affected patients. Please accept that we simply do not have time to review and reiterate. In addition, a palliative care approach would not be out of place, given the intensity and prolonged course of suffering and the absence of a cure. The most severe cases warrant the input of a palliative care consultant. It is disappointing to find the only occurrence of the tem in the drafts for consultation occurring in a paper referenced in the <u>non</u>-pharmacological appendix [H] In general terms we greatly welcome the move towards home visits for severely affected patients. However we have concerns regarding the 'holistic assessment' and 'management plan'	Thank you for your comment and information. The areas listed for inclusion in the personalised care and support plan and not meant to be exhaustive. The plan would be dependent on the individual and their specific needs.
The 25% ME Group	Guideline	013	16-17	We welcome the 'variety of formats' for communication.	Thank you for your comment.
The 25% ME Group	Guideline	013	10	Please add 'if consent is given by the patient to do so'.	Thank you for your comment. committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

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The 25% ME Group	Guideline	014	30	We are unclear as to what "may be self managed" implies - all patients have no choice but to manage their illness as best. Also this illness can simply get out of hand, despite the patient's best efforts at energy management.	Thank you for your comment. Evidence reviews G and H and the section on managing ME/CFS and symptom management of ME/CFS has further information on self- management strategies. After considering the stakeholder comments the committee edited the bullet point on flare ups to reflect that flare ups and releases can occur even if symptoms are well managed.
The 25% ME Group	Guideline	015	12-15	We are unsure why the issue of social care is to be approached with kid gloves. People with severe ME living alone will be well aware that they require assistance. The difficulty lies in convincing social services that care is required and then overcoming the barriers to the person securing appropriate - or even any - care in the current market economy. Unfortunately the situation is dire. People may do without care because the mode of delivery simply exacerbates their already poor state of health. Enhanced understanding among home care workers is very much needed. Anything a health professional can do to facilitate would be welcome. We also unsure why this section is divorced from the 'support for daily living' aspect of the 'management plan' - which the draft relates to 1.8.7 'Maintaining independence' [P20] but not this section.	Thank you for your comment and information. The first recommendation in this section refers to the NICE guideline on people's experience in adult social care services and provides detailed information on social care A link to the section on maintaining independence has been added.
The 25% ME Group	Guideline	016	8	This is welcome. Please add: advice about NHS Continuing Healthcare; advice about independent advocates. Severely affected patients need to know about both of these early on and not many years down the line (as tends to happen)	Thank you for your comment. Support with communication and advocacy is addressed throughout the guideline and is included in the section of people with severe or very severe ME/CFS.
The 25% ME Group	Guideline	016	11	Delete "symptoms" replace with "condition".	Thank you for your comment. This recommendation raises awareness that some of the symptoms people experience with ME/CFS (for example, very

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					limited mobility) may be mistaken for abuse or neglect. The correct term here is symptoms not condition.
The 25% ME Group	Guideline	016	11	Please delete "abuse or".	Thank you for your comment. This recommendation raises awareness about the difficulties that some people with ME/CFS have experienced where safeguarding concerns have been raised and for this reason abuse has not been deleted.
The 25% ME Group	Guideline	016	11	Please add: In the absence of understanding about how severely ME can affect a person, people who are too ill to care for themselves and lack sufficient - or even any - family or paid care support are vulnerable to inappropriate safeguarding proceedings. This risk is all the greater as protection from self neglect is (rightly) part of the 2014 Statutory Care and Support Guidance issued by the Dept of Health under the Care Act.	Thank you for your comment. The committee agreed that your additions do not add further clarity to the recommendation that people with severe or very severe ME/CFS are at risk of their symptoms being mistaken for abuse or neglect and for this reason your suggestion has not been added.
The 25% ME Group	Guideline	017	11-12	The problem is that the core features and symptomatic manifestations are not commonly recognised. This is a failure of medical and other professional education. Get the education right and the "illness pattern" ceases to be "not commonly recognised".	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. This applies to this section on safeguarding.
The 25% ME Group	Guideline	017	8	Please reword "are not necessarily" to read "are unlikely to be" or similar. This really does need to be strong given the extent of misperception, and given that some features e.g. reduced or non-attendance at school will be the norm rather than the exception for a schoolchild with ME.	Thank you for your comment. The committee agreed that your suggestion did not add further clarity to the recommendation and this has not been added.
The 25% ME Group	Guideline	017	18	Section is inadequate in terms of access to social care. There are a number of issues here. These include - 'provide help for self funders in obtaining home care'	Thank you for your comment. The employment of care workers is not in the remit of NICE and your suggestion has not been added.
The 25% ME Group	Guideline	018	20-24	We welcome the detail about the accommodations those very severely affected need to help them to access health and social	Thank you for your comment.

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				care, in particular the provision of home visits, online consultations and flexibility being built in to service provision.	
The 25% ME Group	Guideline	019	all	This page concerns hospital in-patient care and is most welcome. We suggest it may be helpful to have a care plan in place in advance, in case of emergency admission to hospital. See: https://www.coordinatemycare.co.uk (coordinatemycare@nhs.net) "Once completed the plan is approved and is immediately visible to all the urgent care services including 111, out of hours GPs, the ambulance (in their vehicles) and the emergency departments. This way everyone is in the loop with the patient in the middle."	Thank you for your comment and information.
The 25% ME Group	Guideline	019	16	Add 'limit the number of hospital attendances required for minor surgery and investigations'	Thank you for your comment These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
The 25% ME Group	Guideline	020	22	Add 'include self-funders of social care '	Thank you for your comment. These recommendations refer to the social care needs assessment and the aids and adaptions identified as part of that assessment. This has been made clearer in the recommendations
The 25% ME Group	Guideline	020	22	Add 'medically-led' before 'symptom management' Please also add 'neurophysiotherapy'	Thank you for your comment. After considering the stakeholder comments the committee agreed to edit this bullet point and include 'including prescribing and medicines management'. IN addition after considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care

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					and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a change in symptoms are investigated. As with the assessments above this would typically require access to medical expertise but would not exclude highly trained advanced practitioners. These are examples in the recommendation and as with any list of examples these cannot be exhaustive for this reason your suggestion of neurophysiotherapy has not been added.
The 25% ME Group	Guideline	025	29	We welcome the use of a phone heart- rate monitor for some patients	Thank you for your comment.
The 25% ME Group	Guideline	026	1-7	We suggest that this section is deleted as it is encouraging patients to do more physical and mental activity and doing so is likely to lead to a worsening in the health, including further deterioration of severely affected patients. Patients do not require encouragement to do more.	Thank you for your comment. Based on the quantitative and qualitative evidence(evidence reviews A, G and H and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into

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					managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
The 25% ME Group	Guideline	026	12-15	We reject the encouragement of Severely and Very Severely affected patients to increase their activity levels. The suggested energy management plan could be a burden to severe patients rather than a help, some patients may find it intrusive and wasteful of their efforts so should risk access themselves. We suggest that for patients who are struggling with basic functions i.e. to eat, drink and toilet and whose lives are limited to a survival basis that resources from health and social care be better focused on assisting these patients to obtain and manage help with activities of daily living, the tasks required to run a home and the advocacy required to do so. Please review these lines with this in mind.	Thank you for your comment. Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that all people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. The additional recommendations on people with severe to very severe ME/CFS are to ensure that additional caution is taken. The committee included (if possible) to emphasise that any increases may not be possible and the plan should be developed by a physiotherapist or occupational therapist working in a ME/CFS specialist team.
The 25% ME Group	Guideline	026	22	Please delete 'muscle strength and endurance'	Thank you for your comment. This has been edited to, 'muscle function'.

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The 25% ME Group	Guideline	027	4-7	We support the assessment of patients for pressure sores, risk of thrombosis and contracture risk	Thank you for your comment.
The 25% ME Group	Guideline	027	After 2	Please add: 'help with resting positions from a neurophysiotherapist'	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
The 25% ME Group	Guideline	027	17	We welcome the acknowledgement of the severity of disability that occurs in ME/CFS	Thank you for your comment and this information.
The 25% ME Group	Guideline	028	12 onwards	It is imperative that health and social care professionals are aware of the risks and warn patients of the potential of physical harm and long term consequences from undertaking structured physical activity.	Thank you for your comment. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agree it is important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
The 25% ME Group	Guideline	031	5	In the absence of depth of research evidence on the use of medicines in ME/CFS, a pragmatic approach to prescribing drugs that may not be licensed for this condition is justifiable, based on pharmacological principles and the judicious use of therapeutic trials. Medications may have a logic as to why they may help certain symptoms, on the basis of the pharmacology of the drug and with an understanding of what underlying pathophysiology may be contributing/causing the symptoms that the physician is attempting to treat. Clearly this would imply that medication introduced on a 'trial' basis for a period in respect of the patient concerned, so that the patient is not left on the medication if it proves ineffective.	Thank you for your comment. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.' The committee note the following subsection in the guideline is 'medicines for symptom management' and provides advice for prescribers. The discussion section of Evidence review F: Pharmacological management recognises some people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and this should be discussed on an individual basis.

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				The absence of 'gold standard' evidence should not preclude doctors attempting to help their patients - they should be encouraged to do so. Often medical advices are made through good clinical practice. To do otherwise is to condemn patients to what may be quite unnecessary suffering.	
The 25% ME Group	Guideline	032	8-9	Currently there is no relevant specialist training and dieticians with specialist knowledge of ME are scarce. Training is required. Nutrition support team will be required where there are significant gastrointestinal problems and/ or reduced ability or inability to eat and drink.	Thank you for your comment. The committee agree there is a lack of dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The recommendation has been reworded to describe dietician as a 'dietician who has a special interest in ME/CFS', the committee recognised that currently dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better. The recommendations on screening for malnutrition, indications for nutrition support, and education and training of staff and carers related to nutrition, in the NICE guideline on nutrition support for adults is cross referred to. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.

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The 25% ME Group	Guideline	032	10	Please be aware that restrictive diet may be due to severe allergy or food intolerance. In such cases social care provision to include shopping for and the preparation of fresh food 'cooking from scratch'.	Thank you for your comment and information.
The 25% ME Group	Guideline	032	22	Currently there is no relevant specialist training and paediatric dieticians with a specialist knowledge of ME exceedingly rare. We suggest, pending the roll out of a suitable training programme, refer to a paediatrician or paediatric nutrition support team.	Thank you for your comment. The committee agree there is a lack of paediatric dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The recommendation has been reworded to describe paediatric dietician as a 'paediatric dietician who has a special interest in ME/CFS', the committee recognised that currently paediatric dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are paediatric dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better.
The 25% ME Group	Guideline	033	12-14	As well as reference to guidance, please insert: Consider intervention via enteral feeding in these patients before the problem becomes acute. We are aware of cases where this has become a life threatening problem. We are also aware of instances where the patient has been permitted to enter such a nutrition deprived state that they were at risk of refeeding syndrome on the reintroduction of nutrition. We suggest an early warning protocol for alerting to problems obtaining sufficient nutrition and hydration.	Thank you for your comment. The committee did not review the evidence for enteral feeding and are unable to add any further recommendations. The committee hope that the recommendation to monitor people with severe or very severe ME/CFS who are at risk of malnutrition or unintentional weight loss will prevent people deteriorating.
The 25% ME Group	Guideline	033	4	Rather than a blanket recommendation for this group, refer in appropriate circumstances. Physical difficulties around intake of adequate hydration and nutrition may be due to difficulty swallowing or sheer debility.	Thank you for your comment. The committee do not agree and consider the complex needs of people with severe and very severe ME/CFS require an assessment by a dietician with a special interest in ME/CFS.

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The 25% ME Group	Guideline	033	10	The need to avoid allergens and intolerances mean that ready meals are not necessarily a viable option; this should be acknowledged and addressed in community care packages	Thank you for your comment.
The 25% ME Group	Guideline	033	11	This should be split into two points: (i) nausea (ii) difficulty chewing and swallowing	Thank you for your comment. These bullet points have been separated.
The 25% ME Group	Guideline	033	After 11	Please add further points: (i) gastrointestinal pain after eating; (ii) difficulty with or inability to open the mouth sufficiently	Thank you for your comment. This list includes examples of risk of malnutrition and unintentional weight loss identified by the committee and is not intended to be an exhaustive list.
The 25% ME Group	Guideline	033	After 11	Please stress that weight loss can be due to gastrointestinal problems	Thank you for your comment. This list includes examples of risk of malnutrition and unintentional weight loss identified by the committee and is not intended to be an exhaustive list.
The 25% ME Group	Guideline	033	12	Suggested additions: BAPEN Decision Tress: https://www.bapen.org.uk/media-centre/press-releases/293-bapen-unveils-its-decision-trees Assess using MUST. Patient may be completely unable to stand to be weighed, or may exert to do so and suffer afterwards. Therefore obtain a weight by measuring mid upper arm circumference (MUAC) or by using skin callipers.	Thank you for your comment and information. Wording for NICE guidance only refer to NICE guidelines
The 25% ME Group	Guideline	033	13	Please expand and clarify, to read: "training of hospital and community-based staff, family carers and homecare workers"	Thank you for your comment. This text refers to the NICE guideline on nutrition support for adults. The guideline is for all healthcare workers in hospital and the community who are directly involved in patient care and people who are malnourished or at risk of malnutrition in hospital or in their own home or a care home and their families and carers.
The 25% ME Group	Guideline	033	23	Please note that enteral feeding may be required by: Nasogastric Tube (NG); NasoJejunal (NJ); Percutaneous Endoscopic Gastrostomy (PEG); Percutaneous Endoscopic Jejuneostomy (PEJ), including total parenteral nutrition (TPN)	Thank you for your comment. The committee considered that reference to enteral feeding was sufficient information for this guideline. Further information was more relevant in guidelines focused on this level of care.

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The 25% ME Group	Guideline	034	5	We are surprised to find that the section on 'Psychological Support' is confined to CBT. There is no mention of supportive person-centred counselling. This could be very helpful for people who are struggling with the long term impact of pain, discomfort, and a severely restricted daily life.	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). After considering the range stakeholder comments about the title not being representative of this section the committee edited the title of this section to remove psychological support recognising this only referred to CBT.
The 25% ME Group	Guideline	036	5	We welcome the best practice statement on coexisting conditions	Thank you for your comment.
The 25% ME Group	Guideline	039	23-25	We welcome the instruction to refer patients on to other medical specialists.' Training on ME is required for all medical specialisms so that a health care professional seeing an ME patient for a different condition understands the impact of their ME.	Thank you for your comment.
The 25% ME Group	Guideline	039	After 7	Please add: The review should be medically led and performed by staff trained to notice and act on 'red flags'.	Thank you for the comment. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and

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					multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a change in symptoms are investigated. As with the assessments above this would typically require access to medical expertise but would not exclude highly trained advanced practitioners.
The 25% ME Group	Guideline	043	4-8	We are very concerned at the prospect of a single management plan that will form the basis of all assessments, including social care. If flawed, this 'all eggs in one basket' approach will undermine the patient's provision of and access to all services. Given existing misperceptions on the part of professionals we do not think this is an unlikely scenario.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
The 25% ME Group	Guideline	048	15	Late diagnosis is to be avoided, of course. However early diagnosis is helpful only in so far as the patient receives the correct advice. If diagnosed early and told to stay active - or obliged to continue active by default because the doctor will not support sickness absence the diagnosis has not helped the patient at all.	Thank you for your comment. The committee agree that a timely and accurate diagnosis is important and have edited recommendation 1.1.4 to reflect this. The committee agrees that advice when ME/CFS is suspected is important and included this in the guideline.
The 25% ME Group	Guideline	049	24-26	The relationship to activity and stimulus is what is critical.	Thank you for your comment.
The 25% ME Group	Guideline	049	22-23	It is important to be clear that ME is not a botched convalescence.	Thank you for your comment.
The 25% ME Group	Guideline	049	19	Please delete "symptoms" and insert "features"	Thank you for your comment. The committee agreed these are symptoms or ME/CFS and symptoms is commonly understood in this context and for this reason your suggestion has not been included.

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The 25% ME Group	Guideline	067	1-18	Recognise some severely affected ME patients experience difficulty obtaining sufficient nutrition and hydration and will need tube feeding.	Thank you for your comment. In the section on dietary management and strategies for people with severe or very severe ME/CFS oral nutrition support and enteral feeding is included.
The 25% ME Group	Guideline	067	2	Remove "who specialise in ME"	Thank you for your comment. After considering the range of stakeholder comments this has been edited to, 'a dietitian with a special interest in specialises in ME/CFS.'
The 25% ME Group	Guideline	067	6	Remove "who specialise in ME"	Thank you for your comment. After considering the range of stakeholder comments this has been edited to, 'a dietitian with a special interest in specialises in ME/CFS.'
The Centre for Welfare Reform	General	General		We also wish to note our concern that the amount of time given to comment on this draft was too little considering the quantity of documents released, the complexity of the changes being proposed, and the ever-changing demands of the C-19 pandemic.	Thank you for your comment.
The Centre for Welfare Reform	Guideline	General	General	We'd like to start by acknowledging the difficult task the committee had in trying to address current problems surrounding ME/CFS while also planning for what will hopefully be a more positive future. The advice that "if I were you, I wouldn't start from here" kept coming to mind. The proposed guidelines represent an improvement on the previous version and we welcome the efforts made to move towards a more cautious and patient-led approach to ME/CFS. We would still like to see further moves in that direction, and greater clarity in areas where we felt phrasing could be interpreted in different ways. No guidelines alone would be able to fully address the serious problems with the way ME/CFS has been viewed and treated in the UK, but we hope	Thank you for your comments. The committee have taken into account the comments from stakeholders and have made changes to the structure and wording in the guideline and hope these add further clarity for the reader. To note we have addressed your comments individually.

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				that some further changes might help NICE to more effectively address the problems the committee identified, and more.	
The Centre for Welfare Reform	Guideline	General	General	**Question 1: Which areas will have the biggest impact on practice and be challenging to implement?** The recognition of the prejudice and stigma that have been allowed to surround ME/CFS is a vital step, and one that we hope will help lessen some of the social problems that patients face not just within the NHS, but in the media, social security system, employment, and elsewhere. However no-one will expect these problems to fade away overnight, and their ongoing influence is likely to make the implementation of these guidelines more of a challenge. For some of those whose careers have been built upon strong claims about their ability to effectively treat ME/CFS and help patients recover, these guidelines will require a radical change in both how they treat patients and how they think of themselves. We suspect that this will lead to some challenges with implementation. Some senior figures with a history of making exaggerated claims have already spoken out against the draft guidelines. We would also expect some institutional and professional push-back to occur. For example, people promoting Liaison Psychiatry have used CFS as a case-study to illustrate the value of their profession and expertise, and to argue for greater funding. Accepting that we should adopt a more modest approach will necessarily undermine the interests of a number of influential groups.	Thank you for your comment and your suggestion. *Implementation of the guideline* The guideline recommends that people with ME/CFS once diagnosed should be referred to ME/CFS specialist services for confirmation of the diagnosis and a care and support plan and receive care in line with the guideline. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS. It is beyond the remit of this guideline to advise how and where ME/CFS services should be offered within in Trusts. *Training* The committee agree that training should be designed with the input of people with ME/CFS. This is reflected in the discussion section of evidence review B.

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				Another challenge we see with implementation is related to changes occurring outside of these guidelines. There is a drive by some to manage patients with a wide range of conditions within Persistent Physical Symptoms/Medically Unexplained Symptoms clinics. Unfortunately, it seems that this approach is commonly tied to some of the more troubling aspects of the way ME/CFS has been treated, and having care for ME/CFS subsumed within the culture of these new clinics risks undermining attempts to bring about much needed improvements to care for ME/CFS patients. NICE should offer clear guidance against caring for ME/CFS within the MUS/PPS framework. Dr Nina Muirhead is reported explaining in Evidence Review B (page 51 line 23) that "her experience has been that the information, education and support provided by medical bodies is mostly outdated, misleading and not in line with patient experience. In particular, she expressed concerns that ME/CFS training and education is not mandatory, is often merged with other medically unexplained symptoms and is based on theories of deconditioning and fear avoidance of exercise." In order to ensure that these guidelines lead to real change much of the training surrounding ME/CFS will need to be substantially rethought, and it is important that future training is designed with the guidance of patients. The MRC linked CFS/M.E. Research Collaborative includes representatives of the major UK patient groups and the committee should consider recommending that they be involved in the development of improved training so that patient concerns about training being affected by misinformation or prejudice can be raised before it is too late.	

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The Centre for Welfare Reform	Guideline	004	16	The recognition of the prejudice and stigma that has been allowed to surround this condition at the start of the new guidelines is extremely welcome. Hopefully just acknowledging these problems will be helpful in itself. We would request that some additional information in included here. A later section of the guidelines on the prejudices some children and young people face (page 5, lines 19-26) goes into more detail and we recommend adding in further information here too, for example: *1.1.2 Recognise that people with ME/CFS may have experienced prejudice and disbelief and feel stigmatised by people who do not understand their illness (family, friends, health and social care professionals, employers and colleagues, and those working within the social security system or for private insurance companies). Try to take into account:* *•that information previously provided about ME/CFS may have been shaped by the prejudices surrounding the condition* *•that your own views and interpretations of ME/CFS patients may have been influenced by misleading claims or prejudice,* *•how this could affect the person with ME/CFS* *•that they may have lost trust in health and social services and be hesitant about involving them.*	Thank you for your comment. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. As you note there is further information on prejudices people face in the guideline and for this reason your suggestion has not been added to the recommendation.
The Centre for Welfare Reform	Guideline	005 & General	1-8	There are parts of the guidelines that, to us, sound unrealistically idealistic. For example, how consistently will staff be able to take the time to "build supportive, trusting and empathetic relationships" in a genuine sense? Such guidance could even risk making room for a continuation of some of the problematic parts of past care for ME/CFS that left some	Thank you for your comment. The recommendations you comment on are strongly supported by the evidence. The damaging impact of lack of understanding and empathy, including people not believing ME/CFS was real, was reported by people with ME/CFS in Evidence review A, Appendices 1 and 2 and supported by the committee's

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				patients feeling manipulated and unable to trust medical staff. For example: if health and social care professionals feel that they need to encourage the pretence of a supportive, trusting and empathetic relationship with a patient they do not particularly like or understand then this may do more harm than good. The guidance to "acknowledge to the person the reality of living with ME/CFS" could also lead to empty tick-boxing interactions lacking in substance, particularly considering the history surrounding ME/CFS in which 'acknowledging the reality of ME/CFS' has been used as a way of implying more than is said. We feel it would be better to emphasise the importance of professionals being aware that they will often not have the time to truly understand the patients' situation and concerns, or develop a genuinely trusting and empathetic relationship, and that this is why the guidelines place such importance in taking a patient-led approach. We recommend including as guidance: "-recognise the importance of maintaining a trusting relationship by always being honest and clear about our limited current knowledge of ME/CFS. - try to take time to understand the patient's concerns and priorities, while recognising that our ability to understand another person's situation is limited and the patient themselves will be the best judge of what care suits them."	experience. Validity and understanding are fundamental in the care of all people and these recommendations reinforce it for people with ME/CFS. The aim of NICE guidance is to provide advice to improve health and social care and to reduce inequity in the access and provision of services and not to accept where services are suboptimal.
The Centre for Welfare Reform	Guideline	005	19-26	It is a valuable part of the new guidelines that professionals are asked to be aware that many children with ME/CFS will have faced prejudices from others, and to think about some of the ways this may have affected them. It is also useful that this time it is noted that health and social care workers are	Thank you for your comment.

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				responsible for some of the prejudices coming from those who do not understand the illness.	
The Centre for Welfare Reform	Guideline	005 & General	9-14	Changing language from "Recognise that people with ME/CFS need" to "Recognise that people with ME/CFS should be able to choose to have" would sound less prescriptive. Some patients' knowledge of their own situations may lead them to decide that they would not benefit from regular monitoring and review, and at the moment we have no good evidence to indicate that they would be wrong. There may also be some patients who judge that an early and accurate diagnosis may not be in their interests. The guidance (line 17, page 9) not to delay making a provisional diagnosis should not trump patient preferences, and might be better phrased as offering to make a provisional diagnosis. It should be made clear throughout the guidelines that any form of care offered to patients is for them to consider and take up or reject as they see fit.	Thank you for your comment. The recommendation has been edited to 'should have access to'. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
The Centre for Welfare Reform	Guideline	008 - 10 & General		Given the paucity of clear and solid evidence showing how to best diagnose and manage ME/CFS, particularly for patients who had only been suffering from symptoms for a short period of time, we felt that some patients could find it useful if medical staff were encouraged to make clear from the start that patients themselves would be best placed to decide what worked for them and any advice they give was unlikely to be useful to all. It would be useful if the guidance in section 1.3 (page 10) began by emphasising that patient preferences should shape any advice given. For example, line 5 could be altered to: "When ME/CFS is suspected make clear that you will attempt	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.

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				to support the patient in how they choose to manage their health, and then offer to give people personalised advice about managing their symptoms. Also advise them:"	
The Centre for Welfare Reform	Guideline	008	1, Section 1.2	Given the high rates of misdiagnosis reported amongst ME/CFS patients, particularly in primary care, we would suggest that a greater emphasis be placed on examining patients for alternative diagnoses. A list of testing and alternative conditions to be considered could be included so that patients have a better understanding of what they should be able to expect.	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
The Centre for Welfare Reform	Guideline	011	3, Section 1.4	Given the high rates of misdiagnosis reported amongst ME/CFS patients, particularly in primary care, we would suggest that a greater emphasis be placed on examining patients for alternative diagnoses. A list of testing and alternative conditions to be considered could be included so that patients have a better understanding of what they should be able to expect.	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. The discussion section of Evidence review D- Diagnosis includes a list of differential and co-existing conditions that commonly occur in people with ME/CFS.
The Centre for Welfare Reform	Guideline	011	15	Considering some of the problems we saw occur under the previous guidelines, recommending a "holistic assessment" could be unhelpful. The use of the term 'holistic' could be seen as inviting clinicians to believe that they have greater insight into a patients situation than they do.	Thank you for your comment. A holistic assessment is an assessment that looks at the whole person not just a person's condition. The committee does not agree that this could be inviting clinicians to believe that they have greater insight into a patient's situation than they do. This

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				Emphasising to patients and staff that any assessment will necessarily be of limited value considering inevitable time constraints and our lack of knowledge of ME/CFS might help reduce potential problems with some medical staff being overly confident in their own views on how patients should manage their health.	approach support personalised care and support planning where a plan is developed after an initial holistic assessment (https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/. The aim of NICE guidance is to provide advice to improve health and social care and to reduce inequity in the access and provision of services and not to accept where services are suboptimal.
The Centre for Welfare Reform	Guideline	012	10-12	It should also be made clear that some patients may have already developed an approach to managing their illness that works for them, and then it may largely be a case of discussing and recording what techniques they choose to use. It may also be that some patients value the generalised advice given, but prefer to develop a more detailed plan over time with their own support network. Any assessment of a patient will be partial and attempting to explain the specifics of ones own life, and how ones' health problems affect it, is a potentially gruelling task that may not be considered worthwhile by some patients.	Thank you for your comment. This approach support personalised care and support planning where a plan is developed after an initial holistic assessment (https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan.
The Centre for Welfare Reform	Guideline	012	4	The addition of the term 'psychosocial wellbeing' seems to add nothing of value beyond 'wellbeing', but brings some unfortunate connotations. In the context of ME/CFS, approaches described as 'psychosocial' have often avoided real engagement with the sorts of social problems that often impact patients' well being. Patients have reported concerns that a 'psychosocial' view of the illness led to some CFS clinics refusing to provide letters to the Department of Work and	Thank you for your comment. After considering stakeholder comments this bullet point has been edited to, 'the impact of symptoms on psychological, emotional and social wellbeing' to highlight that the assessment

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				Pensions, though these types of letters are a common part of disability social security applications. Social security assessors have stated that they are using the biopsychosocial model for examinations and went on to make claims that, for example, an ME/CFS patients' condition was "60 per cent psychosocial", in a way that led to a loss of financial support. Minutes from a meeting on ME/CFS at the British social security ministry record a Minister being informed that benefits can often make patients worse by a researcher who went on to build their career on bold claim of expertise about the 'psychosocial' aspects of ME/CFS. It seems that the 'psychosocial' term is associated with more psychosocial harm than benefit for ME/CFS.	is holistic and impact of symptoms on psychological wellbeing is not the only area of wellbeing to assess. This bullet point is not describing ME/CFS as psychosocial but noting the impact of symptoms on wellbeing should be assessed as with any long term illness.
The Centre for Welfare Reform	Guideline	013	1-2 & General	It is another positive point that the guidelines emphasise that the person with ME/CFS is in charge of the aims of their management plan. We felt this point should be strengthened further by stating that, as a part of assessment and care planning, patients should be informed that specialist knowledge about ME/CFS and how to help patients is still limited and that patients may find that the approaches they develop themselves are the most useful. The phrasing "mutually agreed" could be taken by some as indicating that staff held some veto over a patient's management plans, so we would recommend removing this phrase. The guidelines' important and valuable recognition of the limited evidence base and lack of effective treatments could be missed by people only reading, or being shown, small sections of language like this that seem to carry a different implication.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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				A term like 'care plan' would avoid the connotations of patients being 'managed' that 'management plan' could bring. That could also be preferable considering the recognised limits in our knowledge about how to best manage ME/CFS.	
The Centre for Welfare Reform	Guideline	014	22-24	The cautious and realistic information on prognosis provided here is to be welcomed, and is particularly important considering the problems caused by a culture which encouraged some professionals to confidently give unduly 'optimistic' information on prognosis and recovery, and the role this has played in some of the breakdown in patient trust. These past problems were likely to have played a role in the evidence the committee described of patient desire for realistic information.	Thank you for your comment. After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS. See evidence review A for the committee discussion on information about the long term outlook for people with ME/CFS
The Centre for Welfare Reform	Guideline	015	8	It is good to see it recognised that patients should be able to receive advice on financial support. This can be a difficult and complicated topic, and it could be that specialist clinics would require a specific member of staff to take a lead on this issue, or that the clinic would need to connect with other sources of advice and support.	Thank you for your comment.
The Centre for Welfare Reform	Guideline	021	11-14	Recommending that staff offer to liaise with employers, education providers and support services is likely to be able to bring real benefits to patients. We would request that this offer also be made with regards to the Department of Work and Pensions and also insurance companies. Patients with ME/CFS have been unusually likely to have been forced to go through a lengthy process of appeals before being found eligible for financial support, and this appears to be partly as a result of the prejudice recognised by the committee. It could be that these hardships would be greatly reduced with support from specialist services.	Thank you for your comment. The aim of the recommendation is to support employers, education providers and support services in understanding ME/CFS to provide reasonable adjustments and adaptions. The remit of NICE does not extend to providing guidance for the Department for Work and Pensions (DWP) and insurance companies, the committee are not able to make recommendations about providing information for them.

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The Centre for Welfare Reform	Guideline	024	4-5	**Question 1: Which areas will have the biggest impact on practice and be challenging to implement?** The poor quality of research that had led to exaggerated claims about our ability to treat ME/CFS has been a central cause of the problems surrounding ME/CFS in the UK, and we hope that the new guidelines stating that there is no current treatment or cure for ME/CFS will contribute to overcoming some of the cultural problems that have interfered with patients' ability to receive appropriate care. While we expect that most staff will be keen to focus on a more modest and genuinely patient-led approach, we also fear that some staff and professional bodies may find it difficult to accept that their own expertise is of less value in guiding patients than they had believed, and be resistant to changes that could be seen as lessening their prestige and status over patients. We expect this is most likely to be the case amongst those whose own research is increasingly recognised as generating only poor quality evidence. One reason why so many parties at the scoping meeting requested that NICE make room for more professionals unconnected to ME/CFS on the committee was due to a view that this was an area of medicine where people were too often able to build careers and influence from bold claims based on flimsy evidence rather than careful and rigorous medicine. It is important to ensure that the more cautious and patient-led ethos that these guidelines move towards is actually followed through, even if there is inertia from entrenched professionals and institutions that have an interest in downplaying the	Thank you for your comment.

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				problems of the past and may have views shaped by the prejudices that surround this condition. Much is likely to depend upon the future training of staff. We hope that guidelines can be produced in a way that will help make it clear that the need for change cannot be ignored if patients are to receive appropriate care.	
The Centre for Welfare Reform	Guideline	024	11-12 & General	While there is reason to be wary of offering guidance to ME/CFS patients, considering our lack of knowledge and the variety to be found amongst patients, the history surrounding this condition means that it is useful for these guidelines to emphasise that any approach taken should be led by the person themselves. We would recommend changing to "is a self-management strategy led by the person themselves, who may choose to make use of support from a healthcare professional" as the patient may choose to not make much use of support from a healthcare professional, particularly as they develop their own understanding of what works best for them. We believe that if these guidelines successfully reduce problems with unhelpful advice and management from professionals then there could be less need for active advice on things like rest and activity than the committee currently assumes. It could be that many patients will be better able to work out how to best manage their symptoms themselves, particularly if they now feel that they will be supported in their own decisions rather than judged on the assumption that 'every patient who wishes to be helped should be willing to try' CBT or GET as a treatment, and thus that those who do not want to try these treatments may not really want to be helped to recover from their health problems.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.

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				These guidelines already represent a useful step in the right direction, but we would still encourage going further.	
The Centre for Welfare Reform	Guideline	025	18-22 & General	Even with these guidelines' move towards a more cautious and patient-led approach we still had concern that parts of the guidelines might leave room for over-management from well-meaning staff that assume they know more about how patients should respond to their condition than they do. As an illustration, in lines 18-22 of page 25 the example of an activity plan could be seen as implying that patients should adopt a relatively regimented plan for activity and rest as a part of their approach to activity, with alternating between different types of activity, even though many patients might prefer to follow as spontaneous and fluid an approach as their symptoms allow. While recognising that not every potential approach patients may choose to follow can be explained here we would recommend a line making clear that 'energy management' need not require a plan like this be followed, but can simply be a way of thinking through and examining the options available to those with ME/CFS.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
The Centre for Welfare Reform	Guideline	025	1-2 & General	We recommend deleting these lines. Asserting that this is a long-term approach could discourage patients from finding their own ways to improve upon their own management. It could be that patients find it useful in the short-term, when they are adjusting to their health problems, but over the longer-term are more able to find their own approaches. It may be that for some people this approach does not help with either stabilisation or increasing tolerance or activity.	Thank you for your comment. Comment on not deleting the lines The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that

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					they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. This applies to the energy management plan. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits.
The Centre for Welfare Reform	Guideline	026	9	This could be changed to 'Offer to refer people'. Informing patients that we do not currently know who might, or might not, benefit from physio or OT input would also help make clear that this is a service being offered to patients who may decide for themselves if they were likely to find it useful.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. In line with this someone could decline a referral to a specialist ME/CFS physiotherapy or occupational therapy service.

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The Centre for Welfare Reform	Guideline	028	19-21	An acknowledgement of how little we can confidently inform patients about the risks and benefits of a physical activity programme is valuable and we would recommend underlining that point to try to minimise the risks of individual professionals making claims that go beyond the evidence as they promote their own particular views.	Thank you for your comment. The committee agree it is important that people with ME/CFS are fully informed about the risks and benefits of any part of their care and this is emphasised throughout the guideline. In addition to this, the rationale and impact sections of the guideline and the committee discussion sections of the evidence review provide further detail on the committee's decision making and reinforce their points.
The Centre for Welfare Reform	Guideline	028	1-2	It is valuable for the guidelines to note that any assistance given around activity or exercise should not be presented as a treatment that patients should engage with, and this should help lessen the problems currently surrounding ME/CFS in the UK.	Thank you for your comment. *Treatment or cure* After considering the range of stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
The Centre for Welfare Reform	Guideline	028	10-11	The guidelines making it clear that the Lightning Process should not be offered to patients with ME/CFS is also welcome. If an intervention designed by someone who has claimed to have developed "powerful and magical" healing techniques is recommended to patients then that in itself can damage trust in medical staff. The problems surrounding the SMILE trial, which falsely claimed to have been prospectively registered in its ISRCTN entry (despite registration occurring after the trial was running and the primary outcomes had been swapped) and then downplayed null results for the trial's prespecified primary outcome, instead presenting the trial as a primarily positive outcome for LP, further illustrates further reasons for distrust amongst ME/CFS patients.	Thank you for your comment.

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The Centre for Welfare Reform	Guideline	034	9-20	The description of CBT provided here is quite different to what many have experienced in the past, to what has been described in many of the papers used to promote the use of CBT for ME/CFS patients, and what important trainers in CBT for ME/CFS have previously claimed. It is difficult to know what systems will be in place to ensure patients are not receiving inappropriate CBT and it has long been a concern that there is no equivalent to the yellow card system for psychological and behavioural interventions. As NICE appear to be encouraging the use of a more non-directional form of psychological support than traditional forms of CBT, focussing on 'CBT' may do more harm than good. We would again encourage the committee to consider re-framing the recommendations on psychological support in a way that was less likely to be entangled with the past problems that have been allowed to surround CBT for ME/CFS.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). The committee also recommend that CBT should be only delivered by a healthcare professional with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS to ensure that CBT is delivered in line with this guideline. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).

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The Centre for Welfare Reform	Guideline	034	6-8	The guidelines state that "CBT should be only delivered by a healthcare professional with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS" and we have concern that this may encourage an unduly optimistic view of the value of the UK's training in CBT for ME/CFS that fails to account for the problems with the culture and training surrounding CBT for ME/CFS in the UK. The PACE trial researcher who most publicly made the misleading "back to normal" claim is regularly running training sessions for CBT for CFS. Who is to decide what training is 'appropriate'? The systems currently in place do not seem fit for purpose. We would recommend changing the guidelines to recognise that psychological support should only be provided cautiously, and with an awareness that there is a lack of appropriate training and expertise in this area.	**Thank you for your comment.** The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
The Centre for Welfare Reform	Guideline	034	13-15	Besides noting what this form of CBT may be designed to do, the guidelines should also make clear that ME/CFS patients should also be informed that currently we do not have good evidence showing the CBT is likely to succeed in those aims, eg "improve functioning".	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).

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The Centre for Welfare Reform	Guideline	034	17-18	To say that CBT "recognises that thoughts, feelings, behaviours and physiology interact with each other" seems redundant (who thinks that any of these things are entirely independent of the others?), but also recalls a worrying history in which more manipulative approaches to ME/CFS have been presented as being justified by the observation that thoughts and physiology interact with each other.	Thank you for your comment. The committee specifically rejected the assumption that people with ME/CFS have 'abnormal' illness beliefs and behaviours as an underlying cause of their ME/CFS. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT as described in the guideline could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
The Centre for Welfare Reform	Guideline	034	5 & General	Being clear that CBT should not be presented to patients as a treatment or cure should help lessen some of the problems surrounding its use with patients, but considering those problems we believe that when patients request psychological support then other forms, like non-directive counselling, might be a preferable initial recommendation. In some ways, the PACE trial's claims about CBT (described as being founded on "the fear avoidance theory of chronic fatigue syndrome") have become emblematic of the problems surrounding CBT for ME/CFS. Following publication of the PACE trial's initial paper, the BMJ's All You Need to Read in the Other General Journals section claimed that PACE showed CBT led to 30% of patients being "cured" (https://www.bmj.com/content/342/bmj.d1168). This claim was founded on a post-hoc outcome measure for participant's	Thank you for your comment. After considering the range of stakeholder comments the first recommendation in this section has been edited to remove the word treatment. The committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. The recommendation now starts with, 'explain to people with ME/CFS that cognitive behavioural therapy (CBT) may help them to manage their symptoms but it is not curative' After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that

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				SF36-PF and Chalder Fatigue Scores that used cut-offs overlapping with the PACE trial's own entry criteria. While this meant it could include patients who had declined on all outcomes from when they had entered the trial it was still described as a "strict criterion for recovery" in a Lancet commentary (https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)60172-4/fulltext), and presented as showing patients were "back to normal" by members of the PACE team speaking to the press and patients. This sort of misrepresentation is an important problem, and seems to be illustrative of the tolerance for manipulation surrounding approaches to ME/CFS that purport to be biopsychosocial. While this has received criticism from academics around the world, particularly after the release of data showing that CBT and GET failed to improve results for PACE's pre-specified recovery criteria (https://www.tandfonline.com/doi/abs/10.1080/21641846.2017.1259724?journalCode=rftg20), we are not aware of any ME/CFS CBT therapists working within the UK having spoken out against problems like this. That does not reflect well on the culture surrounding CBT for ME/CFS in the UK. Indeed, we have seen those responsible for these problems go on to take leadership roles in organisations like BABCP, and train future staff on CBT for ME/CFS patients. Until there is evidence that this culture has changed, alternative forms of psychological support are likely to pose less of a risk of undermining the new guidelines' attempt to shift the culture surrounding ME/CFS. The guidelines later state that the "committee also made recommendations based on their experience to explain the principles of CBT for people with ME/CFS and what people	although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.

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				should expect if they decide to consider CBT". For the sake of informed consent, patients should at least be provided with information about the problematic history surrounding CBT from ME/CFS before being asked if this is something that they wish to pursue. While the guidelines largely present CBT as just a type of supportive therapy, with cautious and limited aims (though with some ambiguity about what "managing their symptoms" means in line 3), this appears to be a very different form of CBT for CFS/ME from that which many CBT therapists have been trained in, and that many patients have complained about. Some of those still training CBT therapists have themselves been responsible for the form of CBT that has led to problems for patients. Describing radically different forms of therapy using the same label seems likely to lead to problems for patients and staff. In the later rationale contrast was drawn between inappropriately delivered CBT associated with harm and CBT delivered "by a therapist who understands ME/CFS". It seems risky to recommend CBT in the hope that it will be consistently delivered by therapists who understand their patient's illness, particularly when considering our lack of knowledge about ME/CFS and the culture surrounding CBT for ME/CFS in the UK.	
The Centre for Welfare Reform	Guideline	040	11 & General	Updating training on ME/CFS is an important issue that we are glad to see addressed in these guidelines. However we are concerned that this section is overly vague, and would leave considerable room for training to continue to reflect the sorts of prejudices that can surround ME/CFS.	Thank you for your comment. The committee discussed the level of detail that should be included in training programmes and agreed on a general description to avoid a prescriptive interpretation of the content

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				A deputy Medical Director at the Joint Royal Colleges of Physicians Training Board was recently speaking on Long Covid and repeated the misleading claims about 'recovery' and the PACE trial by claiming that the results seen with CBT and GET in ME/CFS clinics are in line with PACE: about one third of patients making a complete recovery and going back to a pre-morbid existence. For decades misinformation and prejudice about ME/CFS has been allowed to spread throughout British medical institutions and this means that we can be less confident in judgements made about what is 'evidence-based' training on ME/CFS. Stating just that training should be "developed and supported by specialist services with input from people with ME/CFS" is insufficient, particularly when there are still senior figures at specialist ME/CFS services with a record of promoting misleading claims about the value of the treatments that they have been providing. It is important that training does not just "represent the experiences of people with ME/CFS, using video and other resources", particularly when those devising the training can just select patient anecdotes that serve their preferred narrative. Instead, patient organisations must be fundamentally involved with the way training on ME/CFS is devised and presented. We would recommend that the guidelines make clear that in order to reduce the harm done to patients the training on ME/CFS provided in the UK needs to be fundamentally reconsidered, with a central role for patient groups so that concerns about training being affected by misinformation or prejudice can be raised before it is too late. The MRC linked CFS/M.E. Research Collaborative includes representatives of the major UK patient groups and the committee should	allowing the recommendations to remain relevant as research in the area develops. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. It is beyond the remit of NICE to stipulate exactly how training materials should be developed but the committee discuss this further in the committee discussion in evidence review B.

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				consider recommending that they be involved in the development of improved training. The problems surrounding training on ME/CFS also affect most of the rest of the guidelines considering the repeated references to ensuring patients have access to those "who have training and experience in ME/CFS". We appreciate that the committee recognises the need to try to improve training on ME/CFS and hopefully in time training will improve, but the current problems underline the need to take an even more cautious and patient-led approach than seen in the draft guidelines.	
The Centre for Welfare Reform	Guideline	045	21	While 'Investigations into diagnostic criteria' would seem to be relatively safe, we worried that many of these recommendations seem shaped simply by a desire to find an answer to important questions, without accounting for the currently messy reality of the culture surrounding ME/CFS research in the UK. Considering the problems that still surround important areas of ME/CFS research, we believe that the priority needs to be to raise standards for researchers. Without that foundation there is a danger that the research recommendations given here will lead to work that causes more problems for patients. While the quality of evidence for supposedly effective treatments for ME/CFS was routinely rated as poor or very poor, we believe that this form of assessment underestimates to the problems with the quality of research in this area as much of the evidence indicating a research culture that tolerates false and misleading claims is outside of the criteria NICE uses to assess research (for example, false claims in	Thank you for your comment. All NICE research recommendations are reviewed by the NIHR to consider for their funding streams. Other research funders also consider NICE research recommendations. It is beyond the remit of the guideline to provide more detailed information on how research in these areas should be conducted.

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				witness statements, failure to correct inaccurate claims identified in papers, misleading presentation of results to the media, etc)	
The Chartered Society of Physiotherapy	Guideline	General	General	Dear NICE Guideline Committee, We would like to bring to your attention something that has been highlighted to us by our members through our consultation on the ME/CFS draft guideline, and unfortunately may have serious implications on the independence and impartiality of the draft ME / CFS guideline. A number of our members have contacted us to report intimidating and bullying behaviour from people who oppose the provision of supported physical activity to people with ME / CFS. This has included barrages of emails and tweets and aggressive behaviour. This has impacted on our members and physiotherapists at large as they feel they cannot enter online discussions or use social media for fear of engaging with people who oppose their views. They also report this has made them less likely to engage with the guideline process, for fear of recrimination. All members who have provided feedback to the CSP have requested that their input remains anonymous. Unfortunately, this level of harassment does not only extend to practicing physiotherapists, but to members of the public who have had ME / CFS and have tried to speak positively of their experiences with physiotherapy. Our members report that their patients are now unwilling to speak out to support the role of physiotherapy and the benefits they have had, for fear of recrimination.	Thank you for your comment. We are very sorry to hear that your members experienced intimidation and bullying behaviour. We are grateful to all of your members that submitted comments on the guideline.
The Young ME Sufferers (TYMES) Trust	Guideline	General	General	We have also contributed to the submission by Forward ME, of which we are a member.	Thank you for your comment.

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The Young ME Sufferers (TYMES) Trust	Guideline	004	2	Our view is that ME and CFS should be separated and CFS should exist within a separate section	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'*
The Young ME Sufferers (TYMES) Trust	Guideline	004	After 15	It should not be confused with medically unexplained symptoms (MUS) or with functional neurological disorder (FND).	Thank you for your comment. This section of the guideline raises awareness about what ME/CFS is and not what it isn't. The section on 'suspecting ME/CFS' has further details on how to diagnose ME/CFS and emphasises is the importance of excluding other diagnoses. For this reason your suggestion has not been added to the recommendation.
The Young ME Sufferers (TYMES) Trust	Guideline	005	After 8	Shared Decision Making principles should be adhered to, put people at the centre of decisions about their own treatment and care. People with ME, their parents and their carers, should be made aware of potential benefits and/or side effects of any treatment.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that

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					they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
The Young ME Sufferers (TYMES) Trust	Guideline	005	After 8	Social Workers should be advised to approach those families who have been referred to them with an open mind and a willingness to speak to all involved in their care. **It is imperative** that social services are informed that ME is a serious disease, for which there is no cure.	Thank you for your comment. The guideline applies to all health and social care professionals that are involved in the care of people with ME/CFS.
The Young ME Sufferers (TYMES) Trust	Guideline	005	7&8	Health & Social Care professionals should be aware that cognitive difficulties may mean that children and young people will need their parents/carers, at times, to speak for them. This is not indicative of abuse.	Thank you for your comment. Safeguarding is addressed in detail in the safeguarding section of the guideline and includes the points you make.
The Young ME Sufferers (TYMES) Trust	Guideline	005	19	We believe there should be a separate 'Education for Children & Young People' section. Our experience is that the majority of families experience extremely stressful education issues, often resulting in education professionals referring families to social services under child protection procedures. Educational mismanagement undermines these children's health. Therefore it is vital for NICE to include clear points eg "Children with ME/CFS may require extensive periods learning at home rather than at school.	Thank you for your comment. Section 1.9 address supporting people with ME/CFS in work, education and training and includes the points you have made.
The Young ME Sufferers (TYMES) Trust	Guideline	006	8	Mild to moderate cases can also experience some of these symptoms, not just severe cases.	Thank you for your comment. The committee agree that this section is important. Taking into account the range of stakeholder comments on the descriptions of severity in the guideline the committee have moved the recommendations on people with severe and very severe ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS.

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					The following section on suspecting ME/CFS includes the symptoms that all people with ME/CFS experience and those symptoms that are commonly associated with ME/CFS and now precedes this section. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations.
The Young ME Sufferers (TYMES) Trust	Guideline	006	28	Very important that this is not information is not restricted to solely severe cases- this is also required in mild to moderate cases to ensure they don't worsen.	Thank you for your comment. This section highlights the difficulties that people with severe or very severe ME/CFS may have and is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these difficulties and the support that may be needed to manage their symptoms. In the assessment and care and support planning section of the guideline the committee have made a recommendation that a personalised care and support plan should be agreed and developed, this includes the management and support of the person's symptoms.
The Young ME Sufferers (TYMES) Trust	Guideline	010	1	There are a significant number of "specialist" centres who, we have been told, push GET. It is reported to us that children who do not recover using GET are then accused of not trying hard enough or re-diagnosed with a psychiatric condition.	Thank you for your comment and information. Please see evidence review G- non pharmacological management for the evidence and committee discussion on physical activity and graded exercise therapy.
The Young ME Sufferers (TYMES) Trust	Guideline	010	9	This must be in consultation with the child and their parent/carer. Healthcare and Education professionals should not assume a child or young person is capable of hours at school, or in education, without full consultation with the family. Education professionals should be fully informed of the recurrent, fluctuating, nature of the disease.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the

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				Department of Education statutory guidance and advice on children with medical needs should be followed. Education professionals should be informed that CYP with ME might have SEN. SENCOs should always be involved with C&YP in education.	guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan. The committee agree early communication with schools and colleges is very important. This recommendation refers to children and young people with suspected ME/CFS and the assumption should not be final diagnosis is ME/CFS. This recommendation is to raise awareness in the short term and allows for further communication when the diagnosis is confirmed. Further advice is addressed in the recommendations in section 1.9 supporting people with ME/CFS in work ,education and training. Also see the committee discussion in Evidence review A:Information for people with ME/CFS.
The Young ME Sufferers (TYMES) Trust	Guideline	011	5	Whilst waiting for a diagnosis, families will need support from healthcare processionals to obtain support from education professionals. It should be acceptable for a GP to communicate with education professionals.	Thank you for your comment. Communication with educational services for children and young people with suspected ME/CFS is addressed in recommendation 1.2.8
The Young ME Sufferers (TYMES) Trust	Guideline	011	9	Families report to us: 1. they struggle with long travel times to specialist centres 2. families report symptoms to specialist centres who prescribe GET/management programs that exacerbate their symptoms; families then stop following the management plan and their children improve; by the time of their next appointment with the specialist centre their health has improved and they're again put on the problematic GET/management plan Specialist centres need to ensure that Graded Exercise Therapy is not prescribed and that GET is not offered under the guise of something else.	Thank you for your comment and information.

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The Young ME Sufferers (TYMES) Trust	Guideline	011	17	Pain relief should also be part of any conversation about symptoms. Pain is often reported to us as a primary symptom	Thank you for your comment. These are the minimum areas to be considered in the assessment the list is not meant to be exhaustive and does not exclude the areas you have mentioned.
The Young ME Sufferers (TYMES) Trust	Guideline	014	After 7	Bearing in mind cognitive difficulties/brain fog, written information should be made available to parent/carers	Thank you for your comment. The points you raise about cognitive difficulties are addressed in the access to care section of the guideline. Recommendation 1.6.7 recommends that information should be given to families and carers.
The Young ME Sufferers (TYMES) Trust	Guideline	014	28	Families report to us that children's symptoms have been exacerbated by puberty	Thank you for your comment. There were several stakeholder comments about the examples of triggers that worsen ME/CFS. Some of the examples were considered potentially misleading information and not always a trigger and as you have commented there are other examples that could be added. After considering the stakeholder comments the committee agreed to delete the examples and not provide any examples in the recommendation recognising the variation in triggers in people with ME/CFS.
The Young ME Sufferers (TYMES) Trust	Guideline	015	3	Where is the evidence for this?	Thank you for your comment. This recommendation was based on the qualitative reviews exploring the experiences of people with ME/CFS and the committee's experience. See evidence review A for the committee discussion on further information about the long-term outlook for people with ME/CFS.
The Young ME Sufferers (TYMES) Trust	Guideline	015	After 8	Include national charities including Tymes Trust (the only dedicated charity for children and young people with ME)	Thank you for your comment. The committee agreed on a broad recommendation on where to access information and not to add examples of organisations. As with any list of examples these cannot be exhaustive and there is the risk these are taken as the only options available.

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The Young ME Sufferers (TYMES) Trust	Guideline	016	21	Peer reviewed paper False Allegations of Child Abuse in Cases of Childhood Myalgic Encephalomyelitis (ME) (https://www.tymestrust.org/pdfs/falseallegations.pdf) should be linked to within this section	Thank you for your comment and information. Published papers are not linked to in NICE guidelines.
The Young ME Sufferers (TYMES) Trust	Guideline	027	21	Children and young people with ME should be advised to avoid PE lessons whilst at school. Schools should be advised that their students with ME are not to attend PE lessons.	Thank you for your comment. The section on supporting people with ME/CFS in work, education and training (and evidence review C) addresses the importance of working with schools and making sure there are appropriate adaptions for children and young people with ME/CFS.
The Young ME Sufferers (TYMES) Trust	Guideline	032	8	Children and/or young people who experience weight loss as part of ME should not automatically be referred to social services as a possible neglect/abuse case.	Thank you for your comment. The committee discussion section of Evidence review G- non pharmacological management includes the rationale for ensuring children and young people are referred to a paediatric dietitian who understands the impact of ME/CFS in weight.
The Young ME Sufferers (TYMES) Trust	Guideline	035	23	Process and pace of CBT should be adapted for all cases of ME- Mild-very severe. Cognitive difficulties/"brain fog" requires this. CBT should not be used as form of GET.	Thank you for your comment. The committee agree that flexibility in accessing to services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments or focusing for periods of time can be difficult, and particularly so for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The committee agreed that it was important to highlight the additional caution needed for people with severe or very severe ME/CFS.

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The Young ME Sufferers (TYMES) Trust	Guideline	043	1	'Flares' can occur up to 72 hours following the exertion; to say flares will typically resolve within 1-3 days is misleading, as they may not have shown in this time.	Thank you for your comment. After considering the range of stakeholder comments the reference to 1-3 days has been removed and 'after a few days' included.' A relapse lasts longer than a flare up' has been added to this definition.
University of Plymouth	Guideline	General	general	Having been previously involved in primary care consultation guidance for MUS and recently developed a linking lecture for 'mind, brain, body syndromes/conditions' for year two medical students I am concerned that currently the guidance does not sufficiently portray the complexity of underlying pathophysiology and relative weakness of the evidence base for aetiology and management. There is, especially with increasing understanding of the role of both ACEs and viral assault (eg'long covid') on fatigue, pain and distress, an opportunity to bring together protagonists of the viral and psychological models of CFS in a unified model (albeit with lots of uncertainty). While I saw some good bits in the draft I was also concerned about too many definitive statements based on qualitative evidence and consensus. Instead the range of experiences portrayed in the qualitative literature and the small effect sizes in trials points to heterogeneity of prognosis (without treatment) and a need to allow n=1 (individual patient experiences) be used to guide next steps in management. Acknowledging the limitations of our knowledge about what individuals should do seems an appropriate ethical way forward. Providing definitive statements about 'not doing' based on qualitative evidence given that some individuals may benefit and other do less well is problematic.	Thank you for your comment and information. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee included members with clinical and personal experience of children and young people with ME/CFS. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). The committee agree that the approach to care should be individualised and the guideline has an emphasis upon being

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					centred on the person's needs and wishes and adopting a holistic approach. The personalised care and support plan supports the person's aims and the management of their health and well-being within the context of their whole life and family situation. However, based on the evidence and the committee's experience there are some approaches to physical activity and exercise as outlined in the recommendations that are not appropriate for people with ME/CFS (see evidence review G).
University of Plymouth	Guideline	004	5	Why call ME/CFS a 'medical' condition? (1.1.1), as if there is a strong binary of ill or well, when symptoms are on several spectra. While we have created a set of symptoms etc to define ME/CFS as a syndrome (nosologically) we should be much clearer that syndromes are imperfect models aiming to give some understanding of underlying dysregulation rather than being immutable entities which need detecting and diagnosing. Instead there is good evidence that social and biological causes contribute (likely interacting as per mental health problems), but that we can't make diagnoses based on biological tests (yet) - because the underlying pathophysiology - while we have some evidence as to what's happening (1,2,3) - is still contested; and rather than individuals being either diseased or not (as with HIV, cancer etc where there is a binary condition or no condition situation), for ME/CFS (and Fibromyalgia and other MUSs) both the symptoms and the underlying pathophysiological processes are in flux, interacting and overlapping. 1. Danese, A., J Lewis, S. Psychoneuroimmunology of Early-Life Stress: The Hidden Wounds of Childhood Trauma?. *Neuropsychopharmacol* **42,** 99–114 (2017). https://doi.org/10.1038/npp.2016.198 2. Rasa, S., Nora-Krukle, Z., Henning, N. *et al.* Chronic viral infections in myalgic encephalomyelitis/chronic	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change the terms used.

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				fatigue syndrome (ME/CFS). *J Transl Med* **16,** 268 (2018). https://doi.org/10.1186/s12967-018-1644-y 3. Anda RF, Felitti VJ, Bremner JD, et al. The enduring effects of abuse and related adverse experiences in childhood. A convergence of evidence from neurobiology and epidemiology. *Eur Arch Psychiatry Clin Neurosci*. 2006;256(3):174-186. doi:10.1007/s00406-005-0624-4	
University of Plymouth	Guideline	005	10	1.1.4 While agreed importance of review of symptoms, the need for early diagnosis is not proven as beneficial. We don't know how many people meet criteria and recover without diagnosis. While some people feel benefit from diagnosis others can be harmed by a diagnosis for which treatments are very ineffective. Suggest change to 'People with CFS are likely to benefit from early recognition of symptoms'	Thank you for your comment. After considering the stakeholder comments the committee have replaced 'early' with 'timely' and hopes this adds clarity.
University of Plymouth	Guideline	006	26	Why mention POTS specifically (1.1.8) when CFS/ME is one syndrome out of many overlapping syndromes (including other general ones like Fibromyalgia and organ specific like IBS, chronic pelvic pain, as well as POTS). More helpful to be clear these are overlapping syndromes and that individuals presentation may change such that they stop meeting criteria for one and may have none or another syndrome at a later time.	Thank you for your comment. Orthostatic intolerance and autonomic dysfunction have been added to clarify postural orthostatic tachycardia syndrome (POTS) and postural hypotension are examples of orthostatic intolerance.
University of Plymouth	Guideline	008	8	1.2.2 - why separate out a *psychological wellbeing* assessment. Surely better to do a full physical and mental health assessment to establish the range of physical, emotional and cognitive issues. And then also to carry out a	Thank you for your comment. The committee note the assessment recommended describes the routine examinations and assessments when a patient has an undiagnosed illness. To clarify this the recommendation has been edited from 'comprehensive clinical history' to 'medical

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				social and functional assessment, including establishing personal goals for the future.	assessment (including relevant symptoms and history, comorbidities, overall physical and mental health). In addition psychological wellbeing has been edited to, 'an assessment of the impact of symptoms on psychological and social wellbeing' to clarify this assessment.
University of Plymouth	Guideline	008	17	Re suspecting and diagnosing: This section would benefit from more clarity. Agree good to flag possibility early at six weeks. But not that the diagnosis is strongly suspected at only six weeks. Many individuals have fatigue and concentration problems but then recover in general practice. Such individuals recovering well have not been well studied in contrast to those who were diagnosed late. Box 1 is helpful for core symptoms but confusing as unclear if used to flag possibility and suspect or for diagnosis. The 'and' after each bullet being required as could be interpreted as needing all to suspect. Suggest revising heading to: Core symptoms required for diagnosis and useful for suspecting ME/CFS While we know is that for some/many there may not be obvious or clear immediate precipitants of increasing fatigue, it is important to allow that fatigability can be made worse by these stresses for some people. I think there is no evidence that we can be so definitive. Also for some rest may be helpful in relief sometimes. Perhaps add at end: These symptoms are required for diagnosis at three months, but for some people stresses can precipitate worsening and for some rest can partially alleviate symptoms.	*Suspecting and diagnosing ME/CFS* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the evidence review D. *Suspecting ME/CFS* The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. The committee note the evidence on advice was lacking but that the advice recommended in the guideline at this stage would not be detrimental to people who are then not diagnosed with ME/CFS. Rest is included in the section on advice for people with suspected ME/CFS. *Clarifications* After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your point and added some clarity for readers. In summary the edits to the point you make are: • 'Provisional' diagnosis has been deleted. As you note the symptoms should be investigated for other causes and the committee agree the term 'provisional diagnosis' was

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					confusing while waiting for the results of any assessments to exclude other conditions. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. - It is clear in the diagnosis section that diagnosis is dependent on the criteria persisting for 3 months and other conditions have been excluded. *Triggers* The committee discussed the inclusion of triggering events but decided not to include reference to this as it is not clear what causes ME/CFS and the inclusion of any examples of triggers may be taken as an absolute list.
University of Plymouth	Guideline	009	17	1.2.5 - I am not happy about 'not delaying' - I don't believe its proven that early specific CFS/ME diagnosis helps. I would say I talk early about 'disrupted physiological systems' and perhaps possibility of long term fatigue, but would not want to have to justify not giving an early diagnosis (especially when 1.2.3 says suspect as early as 6 weeks). In the absence of longitudinal studies of fatigue at six weeks, and on basis of anecdotal evidence from primary care that many individuals make good recovery by three months, it is important that we do not induce hopelessness and pessimism. Generating optimism about good recovery and advice about slowly increasing activity can be combined with a review at 3 months and investigation to rule out other pathology. The committee mentions qualitative evidence for harms of delaying diagnosis. But we have no access to those who may have benefits from delaying - no one has asked them in qualitative or epidemiological studies because they did well. Qualitative evidence should not be used to make definitive statements like this.	Thank you for your comment. This recommendation was to ensure that clinicians were alerted to the possibility of ME/CFS as soon as possible. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. See Evidence review D- for the evidence and committee discussion. However after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: - 'Provisional' diagnosis has been deleted for the following reasons: o The committee agreed the term 'provisional diagnosis' was confusing while waiting for the

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					results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for advice for people with suspected ME/CFS. In reference to your comment they agree there is a lack of evidence on the advice to give people with suspected ME/CFS, but they agreed the advice they have recommended in section 1.3 would not be harmful in the short term. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and it would not cause harm to anyone.
University of Plymouth	Guideline	010	5	1.2.8 - I am not convinced we have evidence that referring all under 18s with 6 weeks of symptoms (i.e. when they define need to suspect) to paediatricians is a good idea. I'm sure wecould put together an equally anecdote based strategy for why we should 'listen and validate symptoms and explain range of possible underlying brain body issues, and emphasise recovery for most, while committing to stay along side them and provide continuity while things still bad'. Important we look at natural course literature - how many with fatigue for 6 weeks get better? This is not referenced.	Thank you for your comment. The committee added referral at the 4 week point to a paediatrician in the first instance for further assessment and investigation and then to a ME/CFS specialist for confirmation of a ME/CFS diagnosis to ensure children and young people will have a timely accurate diagnosis of ME/CFS. In addition, the referral to community paediatricians for further investigations before ME/CFS specialist teams is the experience of committee members of working with children and young people.

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					See Evidence review D- for the evidence and committee discussion
University of Plymouth	Guideline	011	7	1.4. Agree diagnosis at 3 months with tightened criteria. But not if improving and still meeting criteria, or if following major stressor. Evidence for benefit of referral is poor. So I suggest 'offer referral' or if declined support a person centred plan in primary care, with support from specialist though liaison if required.	Thank you for your comment. Based on the evidence (Evidence reviews A.B,C,D and I) and the committee's experience referral to ME/CFS specialist care was recommended for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. ME/CFS specialist teams where seen as the most appropriate place for people with ME/CFS to access support with GPs providing ongoing support and review. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning.
University of Plymouth	Guideline	027	21	1.11.15 - not advising any unstructured unsupervised exercise - this seems extreme - while evidence that for some too much exercise causes problems ruling out any unstructured unsupervised exercise rule out most of what we do as humans and is over medicalizing and unrealistic. Better to advise people not to engage in abrupt significant increases in exercise, and to note responses to any gradual increases (we don't know at an individual level if sustained gradual increases will help or not. Many of us in primary care have provided such	Thank you for your comment. The committee agree there is little dispute amongst clinicians working with people with ME/CFS that they should not undertake exercise that is not part of a programme overseen by a ME/CFS specialist team, such as telling them to go to the gym or exercise more.

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				advise successfully for years – such individuals don't get in CFs ME stidies.	It is commonly agreed that people with ME/CFS experience post exertional malaise (PEM) after activity. PEM is a worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated. It is in this context, and recognising the evidence from people with ME/CFS indicating that misunderstanding of the impact of PEM and inappropriate advice on how to incorporate physical activity (and exercise) into their lives has resulted for some in a deterioration of their condition, that this guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS.
University of Plymouth	Guideline	027	24	1.11.16 - no graded exercise -. The quant evidence is I appreciate mixed and highly contested - it seems clear that the mean effects are small (neg or positive??) but this probably hides great heterogeneity in response – some may be harmed but some may benefit – the best evidence for individuals will be on basis of their personal response - to actively advise against graded exercise on basis of selected (biased in not involving those who benefited) qualitative data seems v	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence and other sources of evidence, in addition to this guideline committees are formed to reflect as far as

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				problematic and is probably the aspect of this guidance most likely to cause population harm (guidelines can harm too).	practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS.

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					This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy 'based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this

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					option. Where this is the case the committee agreed it was important people are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *Data excluded* No study was excluded that met the review protocols. We think your point refers to the decision by the committee to downgrade evidence that did not use a diagnostic criteria that includes post exertional malaise (PEM) as essential. PEM is widely acknowledged in ME/CFS specialist practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just do not know how many if the information is not reported. Where this is the case, the trial population could include people that do not have ME/CFS and this makes it difficult for the committee to be confident of the benefits and risks of the interventions on people with ME/CFS. Using GRADE and CERQual the committee agreed that evidence without this information would be 'indirect' (relevance in CERQual) acknowledging this uncertainty about the population. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and CERQual.

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					After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative and qualitative evidence and the application of indirectness and relevance. As part of this they agreed that any evidence with a population > 95% with PEM would be considered direct. (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) *Underrepresentation of people who have benefited from GET.* The committee membership had a broad range of professional and personal knowledge about the different experiences of people with ME/CFS and this was discussed and considered at all stages of the decision making. There is little representation in the qualitative literature of people who have benefited from GET and the committee hope that where this can be published it will be as this can only further inform the care and support of people with ME/CFS.
University of Plymouth	Guideline	028	16	1.1.18 what definitive evidence is there for only physio or OT with expertise being involved? While they may have been shown to be helpful for a select population effect sizes are likely small and hide heterogeneity of response – better identify active ingredients and share.	Thank you for your comment. Based on the quantitative and qualitative evidence * and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to

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					explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
University of Plymouth	Guideline	029	6	1.1.21 - if flares should always be followed by advice to reduce exercise then specialist OT/physios need to be involved for every return to previous norm – this will be unworkable. It suggest readjustment to a new lower baseline. This is a recipe for supporting people to become more disabled. Please clarify.	Thank you for your comment. The recommendation is for a reduction to stabilise symptoms. The new physical activity baseline is in reference to the current level. As you note this is a personalised collaborative physical activity or exercise programme and would be agreed with the person and reviewed regularly. The personalised collaborative physical activity or exercise programme includes the recognition and management of flare ups and relapses. This recommendation is about access this is not necessarily that involvement will be always be required. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas

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					that may need support and investment, such as training costs, to implement some recommendations in the guideline.
University of Plymouth	Guideline	030	15	1.11.27 - pain. Why refer to neuropathic pain guidance? (1.1.8 in that guidance: Offer a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment for neuropathic pain……..). We now know much more about potential harms of these drugs. They have not been tested in RCTs for those with pain and CFS/ME. There is a major danger of adding drugs which further dysregulate body systems. It cannot be justified to advocate practice which could result in law suits in future.	Thank you for your comments. *Neuropathic pain guidance* The committee disagree, people with ME/CFS report many different types of pain, neuropathic pain is one of them. These are examples of NICE guidelines on pain and is not intended to be an exhaustive list of the types of pain people with ME/CFS may experience. The committee linked to NICE guidance that was relevant to people with ME/CFS, the committee acknowledged that this does not address all the type of pain that people with ME/CFS may experience. The committee agree that care for people with ME/CFS should be personalised and recommend a personalised care and support plan in the assessment and care planning section of the guideline. Management of pain should be part of the personalised plan. The committee have noted at the beginning of the managing ME/CFS section and 'managing coexisting conditions that the recommendations in the section on principles of care for people with ME/CFS and section on access to care and energy management should be taken into account when managing symptoms and coexisting conditions in people with ME/CFS. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and

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					should be investigated and managed in accordance with best practice and referred to pain services if appropriate. The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS.
Voices of Recovery	Evidence review G	005	8	The members of our group, most of which have recovered from long term CFS/ME using the Lightning Process, find this decision to actively discourage the Lightning Process very alarming. All of them had official diagnoses, some from well-known professionals such as Professor Pinching, Dr. Geoffrey Smith, and Dr. Perrin. (The latter saying our member was the second worst case he'd ever seen). All these people made full and sustained recoveries, without relapses, and some have been well for over 16 years now. This is all due to the Lightning Process. We encourage the committee not to write off our experience and the positive findings reported in Reme (2013), where 7/9 participants improved or recovered; and Crawley *et al*. (2018) where the majority achieved statistically significant improvements (when undertaking the Lightning Process in conjunction with treatment vs the control group). To say there is no hope of recovery (as this guidance does) has a severe psychological impact on sufferers and their families. They should be allowed to investigate and choose their own self-funded treatment path if they wish and this guidance discourages that avenue. If there is not sufficient evidence to actively recommend the Lightning Process (or other therapies) yet, then further research should be undertaken, while remaining neutral.	Thank you for your comment and for reporting your experience. This however does not discount the negative experiences other people have had emerging from the qualitative evidence reviewed for the present guideline and concerns raised by the committee based on the evidence and their experience. The committee noted the clinical evidence emerging from the quantitative evidence (Crawley 2018) was limited to one study and was of very low to low quality which impacted the committee's confidence in those findings. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', Peer support', 'Goal setting', 'Practice and application' highlight aspects of the interventions that people had found helpful and the 'Relationship with the therapist' where as you state descriptions of staff as positive and encouraging have been included together with accounts of people who had a less positive experience. However, this was not representative of the experience of all people included in the evidence for the

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					Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding the Lightning Process. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns.The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on

					the principles of energy management and this therapy is at odds with these principles. *PEM reanalysis* Also, after considering stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of the findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance as the committee agreed that evidence based on populations not experiencing PEM, may not accurately represent the ME/CFS population and raises concerns about the generalisability of the findings. After revisiting all the studies, the Reme study upon which the majority of findings for the Lightning Process were base, was downgraded for moderate concerns over applicability as, study participants were reported to meet the Oxford (Sharpe 1991) criteria prior to undergoing the Lightning Process, where PEM is not a compulsory feature for the diagnosis of ME/CFS and there were no further details on the population to suggest they experienced PEM. This resulted in the overall confidence in the findings being downgraded from low to very low. The Beasant 2014 study also contributing to findings for the Lightning Process, included adolescents taking part in the SMILE trial and was not downgraded for concerns over relevance of the population, since the NICE 2007 criteria that include PEM were used for diagnosis in the SMILE trial. However, the aim of the study was to understand the experiences of accessing and using a specialist service (some had not yet used the service) and it was unclear to which

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					intervention arm the findings related to and findings seemed to be more relevant to the specialist service in general rather than the Lightning Process . This limited the extent to which conclusions about the Lightning Process could be drawn from this study. The committee did not dismiss any findings but the level confidence of the findings, which was compromised in the case of the Lightning Process, impacts the weight placed on those findings during decision making.
Voices of Recovery	Evidence Review G	220	table	This table includes some generalised negative statements about the Lightning Process, which appear to be drawn from the comments of the 2/9 participants in Reme (2013) who were dissatisfied with some aspects of the Lighting Process. This does not fit with the numerous experiences of Lighting Process participants within our group, who add weight to the 7/9 with positive experiences. Crawley *et al*. (2018) is a strong study compared to Reme (2013) in several respects: • More recent study (which captures some of the improvements to the running of the programme) • More robust sampling method (with less selection bias) • Larger sample number of n=81 (at 6 months) vs n=9 in Reme (2013) We are surprised that findings of Crawley *et al*. (2018) are not given more weight in conjunction with Reme (2013). Relationship with therapist – The negative feedback from 1-2 participants in the Reme (2013) does not reflect the experiences of the adults and young people represented in our	Thank you for your comment. As with all NICE guidelines, recommendations were developed using a range of evidence and other sources of evidence. When developing this guideline the committee considered evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The committee took great care to ensure that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource

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				group. All our members had very positive comments about their trainers with key words like "compassionate", "caring", "supportive" being common responses along with "open for questioning" "she/he answered all my questions". Dishonesty – Reme (2013) quotes one participant saying "I think the people that run it say they have 100% success rate", which is an unsubstantiated claim. In contrast, Reme (2013) points out that it is not what was stated on the official Lightning Process website in 2011 (i.e. 81.3%). All our members denied that a 100% success claim was made by their trainer. Instead, they were told they had a "good chance" of recovery or improvement but that "it doesn't always work". Members recall being asked to read the book first, discuss with a practitioner and fill in a questionnaire to see if it was a good match for them before signing up. Some also remember signing a form to the effect that success was not guaranteed. They all understood that the level and speed of success was down to several factors. One has course materials from 2007 explaining the importance of applying the techniques consistently. Secrecy – the Lightning Process is detailed in the books like 'Get the Life You Love Now' and 'An introduction to the Lightning Process'. They are not a secret. The thoughts of some Reme (2013) participants do not match our experience and we expect they are the minority. Members of Voices of Recovery (some of whom trained prior to or around the study dates) exclusively gave positive feedback about the structure, delivery and their subsequent understanding of theoretical elements. Comments frequently refer to it making "complete/absolute sense" being "clear" or "straightforward" and "easy to understand". This comment is characteristic: "You	impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee noted the clinical evidence you refer to (Crawley 2018) was limited to one study and was of very low to low quality which impacted the committee's confidence in those findings. Both positive and negative experiences of the intervention emerged from the qualitative evidence; these were synthesised into different review findings to capture the multiplicity of experiences people had and were equally considered by the committee. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the themes titled the 'Theory behind the Lightning Process', Peer support', 'Practice and application' highlighting aspects of the interventions that people had found helpful and the 'Relationship with the therapist' including descriptions of staff as positive and encouraging, have been included together with accounts of people who had a less positive experience. However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements from the Reme study reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical considerations. After considering all the evidence available and their clinical experience, the committee agreed that there is lack of transparency about aspects of the

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				could tell an incredible amount of thought had gone into absolutely every area of the course and everything around it. Far more than any other sort of therapy/treatments I've done. The theories made complete sense and the way they were delivered was also fantastic." Crawley *et al*. (2018) describe the structure of theory, followed by coaching through practical application, and the follow up to ensure that understanding and application of the process were still solid and participants had the best chance (P3 online). Conflict with pacing In respect to differences with the energy management strategy, our members reported that this strategy had limited positive results for them, didn't work at all or exacerbated symptoms. They found the different approach of the Lightning Process was the only method to generate real and lasting change. There is no conflict between the two because the Lightning Process does not tell people to 'push through' their symptoms but provides a way of eradicating them; healing the body so it can respond in a healthy way to stimuli that previously caused symptoms. Lightning Process trainees in our group have not reported relapses in the many years since their training. Some went back for reminders and coaching occasionally from their trainers when they hit some stressful times or a bad virus, others have never needed any further help.	research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. The aim of the experiences of interventions review was to examine people's subjective experiences of interventions. Thank you for reporting your experience. This however does not discount the negative experiences other people have had emerging from the qualitative evidence reviewed for the present guideline and concerns raised by the committee based on the evidence and their experience. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles
Voices of Recovery	Evidence Review G	250	10-13	The negative feedback from 1-2 participants in the Reme (2013) does not reflect the experiences of the adults and young people represented in our group. All our members had very positive comments about their trainers with key words like "compassionate", "caring", "supportive" being common	Thank you for your comment. Positive accounts of the Lightning Process emerging from the Reme study have been synthesised and contribute to different review findings that the committee has considered, however these were not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements

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				responses along with "open for questioning" "she/he answered all my questions".	reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case and did not find the intervention helpful. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical considerations. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles

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					Thank you for reporting your experience. This however does not discount the negative experiences other people have had emerging from the qualitative evidence reviewed for the present guideline and that the committee has been aware of from their encounters with people with ME/CFS and the concerns raised by the committee based on the evidence and their experience.
Voices of Recovery	Evidence Review G	250	13-16	A participant in Reme (2013) reported that "the Lightning Process placed the full responsibility of recovery on her; if she didn't do what she was taught at the seminar, it was her own fault" (p520). It may well be that this was her interpretation and not anything actually said by a practitioner. The Lightning Process principles (e.g. in Phil Parker's 'Du' book) specifically coach people away from blame of self or others. It seems unreasonable to extrapolate the interpretation of one person and ignore the written evidence to the contrary. Our members said that the Lightning Process gave them back control over their lives and that this was "liberating" or "empowering".	Thank you for your comment. Positive accounts of the Lightning Process emerging from the Reme study have been synthesised and contribute to different review findings that the committee has considered, however these were not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case and did not find the intervention helpful. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical considerations. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the

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					Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles Thank you for reporting your experience. This however does not discount the negative experiences other people have had emerging from the qualitative evidence reviewed for the present guideline and that the committee has been aware of from their encounters with people with ME/CFS and the concerns raised by the committee based on the evidence and their experience.
Voices of Recovery	Evidence review G	250	26-28	Reme (2013) quotes one participant saying "I think the people that run it say they have 100% success rate", which is an unsubstantiated claim. In contrast, Reme (2013) admit that is not what is stated on the official Lightning Process website (i.e. 81.3%). All our members denied that a 100% success claim was ever made by their trainer or in literature. Instead, they were told they had a "good chance" of recovery or improvement but that "it doesn't always work". Members recall being asked to read the book first, discuss with a practitioner and fill in a questionnaire to see if it was a good match for them before signing up. (These steps are also recorded in	Thank you for your comment. Positive accounts of the Lightning Process emerging from the Reme study have been synthesised and contribute to different review findings that the committee has considered, however these were not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Patient views are important as the aim of this report was to examine

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				Crawley *et al*. (2018).) Some also remember signing a form to the effect that success was not guaranteed. They all understood that the level and speed of success was down to several factors. One has course materials from 2007 (around the time of the Reme (2013) study), explaining the importance of applying the techniques consistently.	people's subjective experience rather than the information that can be found in official websites. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical considerations. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles Thank you for reporting the experience of your members. This has been considered by the committee who however cannot

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					discount the negative experiences other people have had or their concerns about the Lightning Process that have been supported by the qualitative evidence, their clinical judgment and awareness of what people with ME/CFS experience, developed through clinical practice.
Voices of Recovery	Evidence Review G	250	29-31	Reme (2013) admit to the selection bias, due to recruitment via Association of Young People with ME website (which is accepted in the guidance). They understood that and say "It may be speculated that the recruitment process favours those who have benefited less from the intervention" (p523) The small sample size (n=9) brings into question the weight this study is given in shaping the guidelines.	Thank you for your comment. Findings from the Reme study were only part of the multiple factors and sources of information the committee considered during decision making. All NICE guidelines follow the process for quality assessment of the evidence as set out in Developing NICE guidelines: the manual. Qualitative evidence is assesses using the GRADE CERQual approach This guideline was no exception. Limitations such as in the recruitment strategy of studies can vary, resulting in different levels of confidence in the evidence which influences the weight placed on findings during decision making. Limitations of the Reme study were taken into account in the assessment of confidence in the study findings which was judged to be low. After considering stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of the findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance as the committee agreed that evidence based on populations not experiencing PEM, may not accurately represent the ME/CFS population and raises concerns about the

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					generalisability of the findings (see Appendices on PEM reanalysis in Evidence review H for the committee's approach and the method followed). In addition to the limitations originally identified that had been accounted for in the assessment of methodological limitations of the study, also contributing to the overall assessment of confidence in the findings, after revisiting all the studies for the PEM reanalysis, the Reme study upon which the majority of findings for the Lightning Process were based, was also downgraded for moderate concerns over applicability as, study participants were reported to meet the Oxford (Sharpe 1991) criteria prior to undergoing the Lightning Process, where PEM is not a compulsory feature for the diagnosis of ME/CFS and there were no further details on the population to suggest they experienced PEM. This resulted in the overall confidence in the findings being downgraded from low to very low. As mentioned, the level confidence in the findings, which was compromised in the case of the Reme study and the Lightning Process, impacts the weight placed on those findings during decision making. Quantitative evidence was also limited to one RCT and the quality of the evidence also ranged from very low to low. As in all NICE guidelines, apart from the findings emerging from both the qualitative and the quantitative evidence, the committee utilised their clinical experience to inform decision making that has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). After considering all the above-mentioned factors, the committee agreed that there is lack of transparency about aspects of the

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					research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles
Voices of Recovery	Evidence Review G	250	42-43	There is solid scientific evidence for the 'brain-body connection' harnessed in the Lightning Process. Our members exclusively reported that the theoretical aspects were clearly and logically explained and they / their children understood them very well.	Thank you for providing the experiences of your members. Apart from the findings emerging from the qualitative evidence, as with all NICE guidelines the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). After reviewing the evidence available and considering aforementioned factors, the committee agreed there was a lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this

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					intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. The experiences you provide have been considered by the committee who however cannot discount the negative experiences other people have had or their concerns about the Lightning Process that have been supported by the qualitative evidence, their clinical judgment and awareness of what people with ME/CFS experience, developed through clinical practice. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Voices of Recovery	Evidence Review G	251	5-10	The thoughts of some Reme (2013) participants do not match our experience and we expect they are the minority. Members of Voices of Recovery (some of whom trained prior to or around the study dates) exclusively gave positive feedback about the structure, delivery and their subsequent understanding of theoretical elements. Comments frequently refer to it making "complete/absolute sense" being "clear" or "straightforward" and "easy to understand". This comment is characteristic: "You could tell an incredible amount of thought had gone into absolutely every area of the course and everything around it. Far more than any other sort of therapy/treatments I've done. The theories made complete sense and the way they were delivered was also fantastic." Crawley *et al*. (2018) describe the structure of theory, followed by coaching through practical application, and the follow up to ensure that understanding and application of the process were still solid and participants had the best chance (P3 online).	Thank you for providing the experience of your members. Views summarised here have been considered by the committee who however cannot discount the negative experiences other people have had or their concerns about the Lightning Process that have been supported by the qualitative evidence, their clinical judgment and awareness of what people with ME/CFS experience, developed through clinical practice. The committee recognises that experiences of people with different interventions can vary. They have taken this into account through the multiplicity of experiences both positive and negative emerging from the Reme study. As with all NICE guidelines, apart from the findings emerging from both the qualitative and the quantitative evidence, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review

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				In respect to differences with the energy management strategy, our members reported that this strategy had limited positive results for them, didn't work at all or exasperated symptoms. They found the different approach of the Lightning Process was the only method to generate real and lasting change. We didn't feel there was a major conflict between the two because the Lightning Process does not tell people to 'push through' their symptoms but provides a way of eradicating them; healing the body so it can respond in a healthy way to stimuli that previously caused symptoms. Lightning Process trainees in our group have not reported relapses in the many years since their training.	topic, and what recommendations can be made and the appropriate strength of the recommendation, considering multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles. In addition, evidence identified for interventions that encouraged self-management techniques such as energy management showed that people with ME/CFS appeared to value and benefit from this type of support. After considering the evidence identified for self-management, as well as the lack of information and support people with ME/CFS report in managing their symptoms emerging from Evidence review A and their clinical

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					experience, the committee agreed the evidence was unclear but recognised the benefits of self-management strategies including energy management for people with ME/CFS and the importance of having access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits (see Evidence review G for the committee discussion on self-management strategies and the rationale and impact section on energy management in the guideline). The committee recognised there is confusion over energy management stemming from the controversy around graded exercise and note that energy management is not a physical activity or exercise program but provides an important tool that people with ME/CFS can use to manage their activity levels. They agreed it was important to provide clarity around this and clear guidance on energy management, making specific recommendations and listing the components of energy management. The committee recognise people may benefit from different self-management strategies and that these should be discussed and agreed with the person with ME/CFS to support them in developing a care and support plan that is tailored to their individual needs as reflected in the recommendations
Voices of Recovery	Evidence Review G	252	45-48	The Lightning Process is detailed in the books like 'Get the Life You Love Now' and 'An introduction to the Lightning Process'. The techniques and theories behind them are not a secret. In general, our members said they were encouraged to talk about the Lightning Process with friends and family, where this would be helpful. A parent attending their child's sessions	Thank you for your comment. Positive accounts of the Lightning Process emerging from the Reme study have been synthesised and contribute to different review findings that the committee has considered, however these were not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to

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				specifically notes that discussion between parents and children was not discouraged in any way. However, she decided to wait for her child to share whatever they wanted. This would be the case with similar therapies that deal with some inner thoughts. It may not always be useful to share what was said between an individual and their therapist. Participants are welcome to bring family members and many choose to do so. Some members, especially those who trained in the earlier years (2006, 2007) remembered discussions around when it might not be helpful to discuss the Lightning Process: • It benefits from a scientific explanation as to why it works, which may be hard for people to convey in a very short conversation. Therefore, listeners may get the false impression that the Lightning Process suggests ME is 'all in the mind'. (This would be a gross misunderstanding and discourage people.) • Some trainees, while understanding the theory themselves, didn't feel confident enough explaining it to highly sceptical or hostile respondents. (Many members reported surprising hostility and antagonism when explaining their recovery to others and they needed to be in a strong place mentally to take this.) • An unqualified trainee trying to 'teach' someone else the process, for their own application, would likely be ineffective. It requires specialist training as for any therapy. These logical reasons are similar to that given by the one participant in the Reme (2013) study: "you're not really supposed to talk about it with other people, is what he said, *because it only confuses you and them*." This comment seems to have been unfairly extrapolated into generalised repeated	talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical considerations. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.

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				statements about the "Secrecy" of the Lightning Process, which we find to be gross misrepresentation. Furthermore, all these experiences date back over a decade and more recent respondents in our members' survey did not report any such sentiments. They were actively encouraged to speak of how they recovered, in order to share hope with others. These members felt confident sharing their stories in part, because they could point interested people towards the published works explaining the Lightning Process effectively.	Thank you for reporting the experience of your members. This has been considered by the committee who however cannot discount the negative experiences other people have had or their concerns about the Lightning Process that have been supported by the qualitative evidence of a number of people included in the evidence, their clinical judgment and awareness of what people with ME/CFS experience, developed through clinical practice.
Voices of Recovery	Evidence Review G	252	10-12	While some members of Voice of Recovery commented that the course was intense, they stressed that they felt this was necessary to effect the changes they made and that it wasn't too much. Some commented that they had thought they would struggle but due to the structure and delivery of the sessions, and the improvements they made on the first day, it was easy to manage.	Thank you for reporting the experience of your members. This has been considered by the committee who however cannot discount the negative experiences other people have had or their concerns about the Lightning Process that have been supported by the qualitative evidence of a number of people included in the evidence, their clinical judgment and awareness of what people with ME/CFS experience, developed through clinical practice.
Voices of Recovery	Evidence Review G	252	22	Members of Voice for Recovery have completed the Lightning Process over the last 16 years. More follow up is included now than in the earlier years when Reme (2013) participants were asked. All our respondents reported that the course and follow-up was sufficient or exceeded their needs. Several commented that they did not require much follow up but that support was always there. Different means of follow up (e.g. in person, phone, and video calls) were mentioned. It would be most fair, to assess the Lightning Process on what is offered now, rather than in 2007. Crawley *et al*. (2018) detail a more current programme (P3 online).	Thank you for your comment. Positive accounts of the Lightning Process emerging from the Reme study have been synthesised and contribute to different review findings that the committee has considered, however these were not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical considerations. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment.

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					Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles. Thank you for reporting the experience of your members. This has been considered by the committee who however cannot discount the negative experiences other people have had or their concerns about the Lightning Process that have been supported by the qualitative evidence of a number of people included in the evidence, their clinical judgment and awareness of what people with ME/CFS experience, developed through clinical practice.
Voices of Recovery	Evidence Review G	330	51-53	The extrapolation of a "theme of dishonesty" from one or two comments in Reme (2013) appears to demonstrate a bias against the Lightning Process. No other technique is so under attack with so little evidence.	Thank you for your comment. Guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by

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				As stated above: The Lightning Process is detailed in the books like 'Get the Life You Love Now' and 'An introduction to the Lightning Process'. The techniques and theories behind them are not a secret. In general, our members said they were encouraged to talk about the Lightning Process with friends and family, where this would be helpful. A parent attending their child's sessions specifically notes that discussion between parents and children was not discouraged in any way. However, she decided to wait for her child to share whatever they wanted. This would be the case with similar therapies that deal with some inner thoughts. It may not always be useful to share what was said between an individual and their therapist. Participants are welcome to bring family members and many choose to do so. Some members, especially those who trained in the earlier years (2006, 2007) remembered discussions around when it might not be helpful to discuss the Lightning Process: • It benefits from a scientific explanation as to why it works, which may be hard for people to convey in a very short conversation. Therefore, listeners may get the false impression that the Lightning Process suggests ME is 'all in the mind'. (This would be a gross misunderstanding and discourage people.) • Some trainees, while understanding the theory themselves, didn't feel confident enough explaining it to highly sceptical or hostile respondents. (Many members reported surprising hostility and antagonism when explaining their recovery to others and they needed to be in a strong place mentally to take this.)	the guideline. In addition to this, as with all NICE guidelines, recommendations were developed using a range of evidence and other sources of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. When making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). When reviewing qualitative evidence, we have carefully considered the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesised them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', Peer support', 'Goal setting', highlighting aspects of the interventions that people had found helpful. However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure

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				• An unqualified trainee trying to 'teach' someone else the process, for their own application, would likely be ineffective. It requires specialist training as for any therapy. These logical reasons are similar to that given by the one participant in the Reme (2013) study: "you're not really supposed to talk about it with other people, is what he said, *because it only confuses you and them*." This comment seems to have been unfairly extrapolated into generalised repeated statements about the "Secrecy" of the Lightning Process, which we find to be gross misrepresentation. Furthermore, all these experiences date back over a decade and more recent respondents in our members' survey did not report any such sentiments. They were actively encouraged to speak of how they recovered, in order to share hope with others. These members felt confident sharing their stories in part, because they could point interested people towards the published works explaining the Lightning Process effectively.	to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case and did not find the intervention helpful. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment in the consideration of the multiple factors mentioned above. The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles. Thank you for reporting the experience of your members. This has been considered by the committee who however cannot discount the negative experiences other people have had or their concerns about the Lightning Process that have been supported by the qualitative evidence, their clinical judgment and

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					awareness of what people with ME/CFS experience, developed through clinical
Voices of Recovery	Evidence Review G	332	3-6	The guidelines report mixed effectiveness of the Lighting Process from Reme (2013). This study includes those who made a gradual recovery and those who had what were termed in Reme (2013) as "Instant healings" or "Instant cure" from years of chronic illness. Many of these young people had previously tried other methods unsuccessfully. Crawley (2018) also reported statistically significant improvements across a range of measures (physical, mental, psychological). These results do not appear to arouse any interest and barely a mention in the guidelines, when no other treatments are mentioned as "healing" or "curing" the condition; only managing it. This suggests potential bias against the treatment within the committee, possibly due to recorded beliefs that "there is no known cure". Science should be open to re-evaluating 'facts' based on the evidence before them.	Thank you for your comment. Guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. In addition to this, as with all NICE guidelines, recommendations were developed using a range of evidence and other sources of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. When making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). When reviewing qualitative evidence, we have carefully considered the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesised them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been

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					synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', Peer support', 'Goal setting', highlighting aspects of the interventions that people had found helpful. However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case and did not find the intervention helpful. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical considerations surrounding the Lightning Process. The committee also noted the clinical evidence emerging from the quantitative evidence (Crawley 2018) showed mixed findings of a clinically important benefit and no clinically important difference for different outcomes, was limited to one study and was of very low to low quality which impacted the committee's confidence in those findings. Please note that statistical significance is not used in NICE guidelines, that instead review clinical importance (see NICE guidelines: the manual). Both positive and negative experiences have been reflected in the guideline and considered by the committee, who as with all NICE guidelines, used their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment in the consideration of the multiple factors mentioned above. The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the

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					Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles. Based on their clinical experience the committee agreed that there is currently a lack of cure for ME/CFS. They were aware of claims that have been made about cures and that there is often a financial cost to people with ME/CFS when they pursue these. Statements about instant healing raised the committee's concerns further.
Voices of Recovery	Evidence Review G	332	10-13	**As previously stated** The members of our group, most of which have recovered from long term CFS/MEusing the Lightning Process, find this decision to actively discourage the Lightning Process very alarming. All of them had official diagnoses, some from well-known Dr.s such as Professor Pinching Dr.Geoffrey Smith, and Dr. Perrin. (The latter saying our member was the second worst case he'd ever seen). All these people made full and sustained recoveries, without relapses, and some have been well for over 16 years now. This is All due to the Lightning Process. We encourage the committee not to write off our	Thank you for your comment and for reporting the experience of your members. While the committee acknowledge there are reports of recovery these cannot discount the negative experiences other people have had emerging from the qualitative evidence reviewed for the present guideline and concerns raised by the committee based on the evidence and their experience. The committee noted the clinical evidence emerging from the quantitative evidence (Crawley 2018) was limited to one study and was of very low to low quality which impacted the committee's confidence in those findings.

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				experience and the positive findings reported in Reme (2013), where 7/9 participants improved or recovered; and Crawley *et al*. (2018) where the majority achieved statistically significant improvements (when undertaking the Lightning Process in conjunction with treatment vs the control group). To say there is no hope of recovery (as this guidance does) has a severe psychological impact on sufferers and their families. They should be allowed to investigate and choose their own self-funded treatment path if they wish and this guidance discourages that avenue. If there is not sufficient evidence to actively recommend the Lightning Process (or other therapies) yet, then further research should be undertaken, while remaining neutral.	When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', Peer support', 'Goal setting', 'Practice and application' highlight aspects of the interventions that people had found helpful and the 'Relationship with the therapist' where as you state descriptions of staff as positive and encouraging have been included together with accounts of people who had a less positive experience. However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding the Lightning Process. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact,

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					clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles. *PEM reanalysis* Also, after considering stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of the findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns

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					over relevance as the committee agreed that evidence based on populations not experiencing PEM, may not accurately represent the ME/CFS population and raises concerns about the generalisability of the findings. After revisiting all the studies, the Reme study upon which the majority of findings for the Lightning Process were base, was downgraded for moderate concerns over applicability as, study participants were reported to meet the Oxford (Sharpe 1991) criteria prior to undergoing the Lightning Process, where PEM is not a compulsory feature for the diagnosis of ME/CFS and there were no further details on the population to suggest they experienced PEM. This resulted in the overall confidence in the findings being downgraded from low to very low. The committee did not dismiss any findings but the level confidence of the findings, which was compromised in the case of the Lightning Process, impacts the weight placed on those findings during decision making.
Voices of Recovery	Evidence Review G	332	4-6	Reme (2013) does not mention “harms” as stated here in the guidance. It suggests certain aspects may be “unhelpful”, but our members find these accusations do not match their personal experiences of the treatment. All members questioned reported that the Lightning Process was delivered in a way that carefully avoided any blame, guilt etc. and this is key to the principles of the Lightning Process, as documented in books by Phil Parker (e.g. Get the Life You Love Now and Du). As also mentioned in a previous point, our members found that the previous therapies they had tried (especially, the energy management strategy) *did* in fact lead to blame by practitioners and feelings of guilt and obsession about sticking within their energy windows. The Lightning Process gave them the tools to get back control.	Thank you for your comment. Please note that for qualitative evidence we refer to people's perceptions of harms. This statement has been removed from the discussion of findings from the Reme study. The committee recognises that experiences of people with different interventions can vary. They have taken this into account through the multiplicity of experiences both positive and negative emerging from the Reme study. As with all NICE guidelines, apart from the findings emerging from both the qualitative and the quantitative evidence, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See

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					Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles. The committee recognised there is confusion over energy management stemming from the controversy around graded exercise and note that energy management is not a physical activity or exercise program but provides an important tool that people with ME/CFS can use to manage their activity levels. They agreed it was important to provide clarity around this and clear guidance on energy management, making specific recommendations and listing the components of energy management. The committee recognise people may benefit from different self-management strategies and that these should be discussed and agreed with the person with ME/CFS to support them in developing a care and support plan that is tailored to their individual needs as reflected in the recommendations made.

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Voices of Recovery	Evidence Review G	344	4-11	Findings in Crawley *et al*. (2018) showed a significant improvement in participants, which was cost-effective, especially compared to long-term or lifelong treatments and therapies. They did not report "harms", in fact no serious adverse effects. The idea of "harms" again appears to have been taken from 2 out of 9 participants in the Reme (2013) study. Crawley *et al*. (2018) results from a larger, more recent study, specifically to address the issue of cost effectiveness, should be given more consideration here. Our members who undertook the Lightning Process on a private basis also said it was the best money they had ever spent and soon reclaimed their expenses in income generated by a return to work. (This positively affects the state in reduced benefits claims.)	Thank you for your comment. The committee noted the clinical evidence you refer to (Crawley 2018) showed mixed findings of a clinically important benefit and no clinically important difference for different outcomes, was limited to one study and was of very low to low quality which impacted the committee's confidence in those findings. Please note that statistical significance is not used in NICE guidelines, that instead review clinical importance (see NICE guidelines: the manual). Both positive and negative experiences of the intervention emerged from the qualitative evidence (Reme study); these were synthesised into different review findings to capture the multiplicity of experiences people had and were equally considered by the committee. Negative experiences including statements from the Reme study reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical considerations. After considering all the evidence available and their clinical experience, the committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push

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					through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Voices of Recovery	Evidence Review H	200 -203	General	Crawley *et al*. (2018) reported statistically significant positive results (of LP intervention vs control group) across a range of physical and mental health measures and did not report adverse effects from the LP intervention. The sample group was larger (than Reme, 2013) and the sampling adhered to a robust method; whereas the evidence review admits that the Reme (2013) participants were recruited from an ME charity, where people are unlikely to have recovered and that this constitutes a bias. Why is Crawley *et al*. (2018) not given more weight in the evidence and so much emphasis placed on comments of 2/9 participants in the Reme (2013) study?	Thank you for your comment. The committee noted the clinical evidence you refer to (Crawley 2018) showed mixed findings of a clinically important benefit and no clinically important difference for different outcomes, was limited to one study and was of very low to low quality which impacted the committee's confidence in those findings. Please note that statistical significance is not used in NICE guidelines, that instead review clinical importance (see NICE guidelines: the manual). As with all NICE guidelines, recommendations were developed using a range of evidence and other sources of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The committee took great care to ensure that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. When making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing

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					NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Both positive and negative experiences of the intervention emerged from the qualitative evidence; these were synthesised into different review findings to capture the multiplicity of experiences people had and were equally considered by the committee. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the themes titled the 'Theory behind the Lightning Process', Peer support', 'Practice and application' highlighting aspects of the interventions that people had found helpful and the 'Relationship with the therapist' including descriptions of staff as positive and encouraging, have been included together with accounts of people who had a less positive experience. However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements from the Reme study reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical considerations. After considering all the evidence available and their clinical experience, the committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation.

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					In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Voices of Recovery	Evidence Review H	541	e	**As previously stated** The negative feedback from 1-2 participants in the Reme (2013) does not reflect the experiences of the adults and young people represented in our group. All our members had very positive comments about their trainers with key words like "compassionate", "caring", "supportive" being common responses along with "open for questioning" "she/he answered all my questions".	Thank you for your comment. Both positive and negative experiences of the intervention emerged from the qualitative evidence; these were synthesised into different review findings to capture the multiplicity of experiences people had and were equally considered by the committee. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered. However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements from the Reme study reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical considerations. After considering all the evidence available and their clinical experience, the committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a

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					recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles. Thank you for reporting the experience of your members. These have been considered by the committee who however cannot discount the negative experiences other people have had emerging from the qualitative evidence reviewed for the present guideline and concerns raised by the committee based on the evidence and their experience.
Voices of Recovery	Evidence Review H	541	g	**As previously stated** The Lightning Process is detailed in the books like 'Get the Life You Love Now' and 'An introduction to the Lightning Process'. The techniques and theories behind them are not a secret. In general, our members said they were encouraged to talk about the Lightning Process with friends and family, where this would be helpful. A parent attending their child's sessions specifically notes that discussion between parents and children was not discouraged in any way. However, she decided to wait for her child to share whatever they wanted. This would be the case with similar therapies that deal with some inner thoughts. It may not always be useful to share what was said between an individual and their therapist. Participants are welcome to bring family members and many choose to do so.	Thank you for reporting the experience of your members. These have been considered by the committee who however cannot discount the negative experiences other people have had emerging from the qualitative evidence reviewed for the present guideline and concerns raised by the committee based on the evidence and their experience. In addition to the positive experiences emerging from the Reme study, negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts such as this on the secrecy surrounding the Lightning Process raised the committee's concerns about ethical considerations. After considering all the evidence available and their clinical experience, the committee agreed that there is lack of transparency about aspects of the research and the treatment

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				Some members, especially those who trained in the earlier years (2006, 2007) remembered discussions around when it might not be helpful to discuss the Lightning Process: • It benefits from a scientific explanation as to why it works, which may be hard for people to convey in a very short conversation. Therefore, listeners may get the false impression that the Lightning Process suggests ME is 'all in the mind'. (This would be a gross misunderstanding and discourage people.) • Some trainees, while understanding the theory themselves, didn't feel confident enough explaining it to highly sceptical or hostile respondents. (Many members reported surprising hostility and antagonism when explaining their recovery to others and they needed to be in a strong place mentally to take this.) • An unqualified trainee trying to 'teach' someone else the process, for their own application, would likely be ineffective. It requires specialist training as for any therapy. These logical reasons are similar to that given by the one participant in the Reme (2013) study: "you're not really supposed to talk about it with other people, is what he said, *because it only confuses you and them*." This comment seems to have been unfairly extrapolated into generalised repeated statements about the "Secrecy" of the Lightning Process, which we find to be gross misrepresentation. Furthermore, all these experiences date back over a decade and more recent respondents in our members' survey did not report any such sentiments. They were actively encouraged to speak of how they recovered, in order to share hope with others. These members felt confident sharing their stories in	protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.

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				part, because they could point interested people towards the published works explaining the Lightning Process effectively.	
Voices of Recovery	Evidence Review H	541	i	Our members had no criticism of the cost, even though some had to borrow money to do the course. They all said it was completely worth it to get their lives back. One noted that she earnt the money back within months by returning to work, which she was previously unable to do. By regaining full health, there is a net financial gain for participants and the state (who no longer need to pay benefits).	Thank you. For those patients who improve after the process, the cost would appear to be justified. The cost was seen as a negative aspect of the Lightning Process by some interviewees in the qualitative evidence. The committee considered all the costs, benefits and harms of the Lightning Process for all attendees in making their recommendations.
Voices of Recovery	Guideline	General	General	There is concern that the independence and impartiality of the guidance may be affected by those such as Dr Charles Shepherd, who does not believe recovery is possible and has expressed bias against some of the treatments examined, specifically The Lightning Process. Dr. Shepherd, is medical advisor for the ME Association, and refers to "members" who do not get results using the process. However, in our experience (as ex-sufferers), those who recover do not remain members of such associations and therefore he draws his opinions from a self-selecting 'unsuccessful' group, which constitute the minority. Dr Charles Shepherd, states on ME Association website: *"The Lightning Process is not a treatment that we endorse or recommend for people with ME/CFS.* *"Patient evidence, gathered from our members over many years, indicates that some people who have gone through the LP try to make rapid and unrealistic improvements in their physical and mental activity levels. However, this is followed by a relapse or significant worsening of symptoms.* *"Others who have gone through the LP programme, report that they have spent huge amounts of money with no obvious benefit.*	Thank you for your comment. The NICE Policy on declaring and managing interests for NICE advisory committees sets out the processes for : • what interests need to be declared and when • how declared interests should be recorded • when a declared interest could represent a conflict of interest and the action that should be taken to manage this. As with any other guideline this Policy has been applied to this guideline. The Interests Register for the committee is published on the NICE website (https://www.nice.org.uk/guidance/indevelopment/gid-ng10091/documents) . The register has been updated throughout the development of the guideline and includes the decisions and actions made on the interests declared. *Underrepresentation from patients who have recovered from ME/CFS* The committee membership had a broad range of professional and personal knowledge about the different experiences of people with ME/CFS and this was discussed and considered at all stages of the decision making. It is true that there is little representation in the literature of people who have recovered from ME/CFS and the committee

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				"It may well be that there are some people with a general fatigue state resulting from stress, emotional or psychological problems who could benefit from a 'mind over matter' retraining approach such as this. Such fatigue states are a separate entity and not to be confused with ME/CFS." Dr. Shepherd expresses the common view that those recovering from ME/CFS using the Lighting Process did not have true ME. However, members of our Voices of Recovery group have official diagnoses (including from Professor Pinching, another medical advisor to the ME Association before retirement) of severe and long term ME, which they would be happy to provide. These same members made full and sustained recovery with the Lightning Process and many have been well for over a decade, without relapse. We argue that at very least, the panel accepts that recovery is possible and does not exclude this hope for sufferers. We urge that further research be undertaken into the Lightning Process, given the positive results of the studies included. Even Reme (2013), which is often negatively presented in this guidance, reported 7/9 of participants had improvement or success. Crawley *et al*. (2018) reports statistically significant improvements across a range of measures (when compared to the control group). Why is the Lightning Process not among research recommendations? When asked about responses to their recovery, all respondents in Voices of Recovery had similar experiences with ME organisations, including denial of their illness, dismissal of their recovery and much hostility toward them trying to share that there is hope for others. It is of great concern that such organisations are not more open-minded	hope that where this can be published it will be as this can only further inform the care and support of people with ME/CFS.

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				and we fear their opinions may have affected their analysis of the evidence if they were present on the committee. It does not appear that efforts have been made to consult with recovered sufferers when compiling this guidance, which biases it further against the possibility of recovery. This is not only untrue, but damaging to mental health if people think there is no way out. E.g. members of our group felt they would be more suicidal if they had read this guidance when they were diagnosed. Furthermore, it has been proven in considerable numbers of studies that the belief you will not recover will hinder the chances of doing so (nocebo effect). Those who have recovered are a huge resource that could be utilised by the NHS and for further study and our members are happy to be contacted for testimonials.	
Voices of Recovery	Guideline	004	5	1.1.1 we think the use of the word 'chronic' is not helpful	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to delete 'chronic'.
Voices of Recovery	Guideline	007	1	1.1.9 We suspect that this needs very careful management as too much sensory deprivation could lead to decline to a more severe state.	Thank you for your comment. This section highlights the difficulties that people with severe or very severe ME/CFS may have and how these may be managed. As you note it is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these difficulties and the support that may be needed to manage their symptoms. The committee agreed that these recommendations could apply to children and young people with severe or very severe ME/CFS.

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					The level of support needed is individual to the person and agreed collaboratively as part of their personalised care and support plan with the health and social care professionals involved in their care. An assessment of benefits and harms would be part of this.
Voices of Recovery	Guideline	008	10	1.2.3 Early diagnosis is only useful if the information and interventions will increase chances of recovery. If given a diagnosis with no likely recovery ahead, this can increase anxiety, fear and depression and possibly set a course of illness for many years. Many of our group feel that if they had received the information and methods they learned on the LP course at the beginning, they would have never got into the spiral of illness.	Thank you for your comment. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. The committee discussion in Evidence review D and E set out the rationale for the committee's decision making on when to suspect ME/CFS and what advice to give people. In reference to your comment they agree there is a lack of evidence on the advice to give people with suspected ME/CFS, but they agreed the advice they have recommended in section 1.3 would not be harmful in the short term. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and it would not cause harm to anyone. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted for the following reasons: o The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This

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					section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis
Voices of Recovery	Guideline	010	17	Energy management can be helpful for some. However, several of our members who used this approach while ill, described increased anxiety, guilt, and exacerbated symptoms. Some became obsessed or fearful of doing 'too much' and over focused on their fatigue and pain; some felt guilty and 'to blame' if they 'overdid it'. One reports the therapist in a specialist CFS/ME centre, implying she was to blame for her symptoms by failing to stringently adhere to the 'pacing' programme. Therefore, the potential psychological effects of this approach are similar to the accusations made of the Lightning Process. We believe these accusations are founded on the interpreted comments of 2/9 participants, as 'feeling blamed' (Reme 2013). (However, the Lightning Process principles avoid blame of self or others (e.g.Dû , Phil Parker, 2011, Nipton Publishing.) By only recommending energy management, patients will continue to suffer and require long-term support, at cost to the NHS. This is unnecessary when there is an effective approach (for us it was a 'cure') with high success rates from our experiences (Members also report high success rates among friends and family to whom they recommended the process).	Thank you for your comment. After considering the stakeholder comments the committee agreed that this concept and energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on PEMPEM and energy limits* may not be helpful. At such keeping a diary at this stage may not be appropriate. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits.
Voices of Recovery	Guideline	012	14	1.5.1 psychosocial wellbeing also impacts on symptoms as well	Thank you for your comment. The first bullet point addresses your point, 'a medical assessment (including relevant symptoms and history, comorbidities, overall physical and mental health, *anything that is known to exacerbate or alleviate symptoms*, and sleep quality).

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Voices of Recovery	Guideline	014	1	1.6.2.When giving information to young people and their families, it is important to be very careful of what message they receive. To be aware of how important expectation of recovery is to them all and how the message can impact the direction of illness.	Thank you for your comment and information.
Voices of Recovery	Guideline	014	9	1.6.3 To be aware of how important expectation of recovery is to people and their families, and how the information they are given can impact the direction of illness.	Thank you for your comment and information. The following recommendation gives information about the long term outlook for people with ME/CFS. See evidence review A for the committee discussion on information about the long term outlook for people with ME/CFS
Voices of Recovery	Guideline	014	22	We wonder what the actual statistics are if recovered people were also included. Our experience and of others we know who have also done LP is that the majority recover. It may be true that not many people recover if they are given well intentioned, but in our opinion, poor advice on diagnosis, supported by negative opinions from support groups. One group member recalls her heart sinking and 'knowing, like it was a fact' that she would definitely be ill for years when she was told that people don't usually ever fully recover. And she was then ill for many years. We suggest that the prognosis would not be the same if given the more helpful and positive information at the start.	Thank you for your comment. After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS.
Voices of Recovery	Guideline	015	6	1.6.6.Information must be given, however information from self-help groups tends to offer only hope of management of illness, and again reinforces the negative prognosis. As some of our members found, some groups do not seem to allow a member to tell their stories of recovery if it is from the LP.	Thank you for your comment. The committee agreed on a broad recommendation on where to access information and not to add examples of organisations. As with any list of examples these cannot be exhaustive and there is the risk these are taken as the only options available.
Welsh Association of ME & CFS Support (WAMES)	Guideline	General		We welcome the additional information included in the guideline about severe ME/CFS as this continues to be a widely misunderstood issue.	Thank you for your comment.

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Welsh Association of ME & CFS Support (WAMES)	Guideline	General		We welcome the additional information included in the guideline about ME/CFS in children and young people, but feel the level of detail is lacking. While we understand that paediatricians have a large responsibility for managing the care of young people, other members of the health services will regularly come into contact with them, especially GPs, and they also need a greater understanding of the ways the illness affects young people.	Thank you for your comment. The committee agree that children are not the same as adults. Children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Welsh Association of ME & CFS Support (WAMES)	Guideline	General		The guideline will be used by the NHS and Social services in Wales. It is often not clear whether the documents on law and practice that are included or linked to, are also relevant in Wales. Alternative or additional documents are not routinely included. This is likely to make implementation of the guideline more challenging in Wales.	Thank you for your comment. All NICE guidelines and quality standards apply to Wales and are subject to Welsh legislation. See https://gov.wales/national-institute-health-and-care-excellence-nice-guidelines for Guidance for health boards, trusts and other stakeholders on how to follow NICE guidelines.
Welsh Association of ME & CFS Support (WAMES)	Guideline	024 - 026		We welcome the inclusion of the concept of the energy envelope, which patients tell us they have found to be a very helpful part of pacing / energy management. Some people with ME/CFS have struggled to put it into practice and would welcome advice and support, though professionals equipped to offer that are few and far between in Wales. There could be a significant challenge to locating, financing and training enough staff to meet the need! This could take many years. In the meantime there is a need for resources that the guideline could recommend for patients to educate themselves in this	Thank you for the comment. *Training* There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. A strong theme from the evidence was the lack of understanding about ME/CFS and training in health and social care professionals and the committee agreed it was important to make recommendations about training. Your

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				approach to energy management, or to use as the basis of a training programme for professionals.	comments will also be considered by NICE where relevant support activity is being planned.
Welsh Association of ME & CFS Support (WAMES)	Guideline	034 - 036		We welcome the acknowledgement that people with the life-changing, long term disabling illness of ME/CFS might need psychological support.	Thank you for your comment.
Welsh Association of ME & CFS Support (WAMES)	Guideline	008 - 009	Box	People with ME have queried the description of unrefreshing sleep as not being adequate. Exhausted is a word that healthy people believe they understand. Many people with ME/CFS instead talk about feeling "almost concussed", "my body is heavy ... it's as if something heavy is on top of me weighing me down", "I have pain, waking up feeling 'very ill' every day (for years)." "my body feels 'in shock' on waking, as if I have been badly shaken and need to lie for some time before I can safely attempt to get out of bed". These experiences can be repeated many times a night when sleep is interrupted. And are not confined to the severely affected. While sleep is certainly unrefreshing, maybe the term 'Sleep disturbance' is a better overall heading.	Thank you for your comment. After considering the stakeholder comments on the description of sleep symptoms the committee edited the bullet points to, 'unrefreshing sleep and /or sleep disturbance, which may include: • feeling exhausted, feeling flu-like and stiff on waking • broken or shallow sleep, altered sleep pattern or hypersomnia. The committee have also edited the definition in the terms used in the guideline section. The committee hope this has added some clarity for readers.
Welsh Association of ME & CFS Support (WAMES)	Guideline	026 - 027		Physical maintenance 1.11.11 We welcome the recommendations to advise patients and families how to recognise and prevent possible complications of long term immobility, but we would like to see a proviso added that any movement should be undertaken with as much care as physical activity.	Thank you for your comment. 'Strategies need to be carried out in small amounts and spread out throughout the day' has been added to the recommendation. To note after considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.

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Welsh Association of ME & CFS Support (WAMES)	Guideline	029 - 030		We welcome the inclusion of rest as a management tool, but wonder why the importance of 'sleep' isn't addressed, though mentioned in the title. People with ME/CFS are often told not to sleep during the day, but in the early stages of the illness and during relapses many people have found it essential to sleep when they can, often for long periods. To avoid stress and feelings of guilt at a time when people's lives have already been turned upside down, it is important that health professionals do not advise all people with ME/CFS to strictly follow standard sleep hygiene advice.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. The recommendations include that people should be given personalised sleep management advice.
Welsh Association of ME & CFS Support (WAMES)	Guideline	032 - 033		We welcome the acknowledgement that difficulties with tolerance of food, gastric symptoms and low energy levels can lead to nausea, weight loss and malnutrition in some people with ME/CFS.	Thank you for your comment.
Welsh Association of ME & CFS Support (WAMES)	Guideline	001		No explanation in this guideline has been given for the massive changes made to the 2007 CFS/ME guideline. We realise that there is a lot of information and explanation included in supporting documents but we believe that the high levels of disbelief, misunderstanding and disdain towards ME/CFS by health professionals require explanations be included early on in this document. We have met many doctors who are unaware that the previous guideline's management recommendations were based on poor quality research underpinned by the Biopsychosocial (BPS) Theory, which has played a major role in perpetuating disbelief in ME/CFS as an organic entity. There is little understanding that the 'Bio' part of this theory of ME/CFS refers to a one-time trigger, not the existence of ongoing dysfunction.	Thank you for your comment. The 2007 CFS/ME guideline was developed by the committee using the best available evidence and methods at the time. This guideline updated the 2007 CFS/ME guideline and the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). The rationale and impact sections of the guideline and the committee discussion sections of the evidence reports provide detail on the committee's decision making.

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				In addition, changing the minds of those doctors who have been persuaded that ME/CFS is a psychological condition requiring psychological and behavioural modification, will be a hard long process. More needs to be said about the emerging research so that doctors know physical dysfunction is being taken seriously in the scientific community. Comment needs to be made about why Graded Exercise Therapy and Cognitive Behavioural Therapy failed to be the intervention/ cure of the future and have been withdrawn. Comment also needs to be made about how CBT for CFS/ME was a different animal to the CBT used with other neurological conditions. The attitude we have heard expressed by doctors is that if CBT is good enough for conditions like MS, then it is good enough for ME. They do not realise that they are different forms of CBT and aim to achieve different outcomes.	
Welsh Association of ME & CFS Support (WAMES)	Guideline	004	10-12	i. We welcome the acknowledgement that ME/CFS '*affects each person differently and varies widely in severity – in its most severe form it can lead to substantial incapacity*' but we are aware that, like many serious neurological conditions, a small number of people have died, even with medical care. The role that ME/CFS has played in a person's demise is being added to the coroner's report more often in recent years. In addition to cases of suicide brought on by despair at the	Thank you for your comment. The severity of the impact of ME/CFS has been recognised throughout the development of this guideline. The scope included people with severe and very severe ME/FCS as a population for special consideration and each review highlighted any relevant evidence. In addition recognising the lack of evidence NICE commissioned a report to ensure the views of people with severe and very severe ME/CFS were include in the guideline (Appendix 2_People with severe ME/CFS) and this was considered alongside the other evidence by the committee. When making the recommendations the committee considered people with severe and very severe ME/CFS separately and made additional recommendations where relevant.

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				poor prognosis and lack of medical support, we know of 2 cases in Wales where ME/CFS has been considered to have contributed to the growing debility which led to death and more in the UK, many more around the world.	After considering the stakeholder comments the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline and had more emphasis.
Welsh Association of ME & CFS Support (WAMES)	Guideline	004	5-6	We welcome the acknowledgement of the impact of ME/CFS on multiple body systems and accept that there is much research needed to clarify the pathophysiology but we suggest that, in order to emphasise the biomedical underpinnings and key characteristic of the condition, it would be helpful to highlight the most promising line of research - namely dysfunction in cellular energy production. Ref:https://www.healthrising.org/blog/2020/12/07/energy-production-chronic-fatigue-syndrome-system-wide/ 1.1.1 Be aware that ME/CFS: is a complex, chronic medical condition affecting multiple body systems, notably dysfunction in cellular energy production, though the pathophysiology of the condition needs to be clarified	Thank you for your comment. This bullet point has been edited to,' and its pathophysiology remains under investigation' to clarify that there is not enough evidence to make any conclusions about the pathophysiology of ME/CFS and this is an active area of research.
Welsh Association of ME & CFS Support (WAMES)	Guideline	004	1	The box has a link to the 'Making decisions using NICE guidelines' page for information to include 'professional guidelines, standards and laws'. It is unclear whether this is for England only. No Welsh laws appear to be included.	Thank you for your comment. This is standard information included in all NICE guidelines. All NICE guidelines and quality standards apply to Wales and are subject to Welsh legislation. See https://gov.wales/national-institute-health-and-care-excellence-nice-guidelines for Guidance for health boards, trusts and other stakeholders on how to follow NICE guidelines.
Welsh Association of ME & CFS	Guideline	004	4	The link between ME/CFS and the post-viral experience is well known and although a combination of factors may lead to the development of full-blown ME/CFS, and not all patients can	Thank you for your comment. This bullet point has been edited to,' and its pathophysiology remains under investigation' to clarify that there is not enough

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Support (WAMES)				identify specific triggers we believe it is important that doctors are made aware of the link. Add an additional bullet point: 1.1.1 Be aware that ME/CFS: • Most often develops following a virus, but can also follow a variety of other events, such as vaccinations, chemical exposure…	evidence to make any conclusions about the pathophysiology of ME/CFS and this is an active area of research.
Welsh Association of ME & CFS Support (WAMES)	Guideline	004	4	1.1.1 Be aware that ME/CFS: We recommend including an additional awareness point here. It is not uncommon for more than one member of a family to be affected. In one family in Wales a mother and 2 of the 3 children have the condition. In another family a mother and daughter developed the condition while adults, and while living in different parts of the country. We are aware of many more families with 2 or more siblings or multiple generations affected, and are aware this phenomenon has been recorded elsewhere and that a possible genetic link has been suggested. Although this phenomenon has been mentioned later in the guideline, we believe it is important to emphasise this point early on as it can be difficult for health professionals to understand, and it can seriously affect the way they treat a family (sometimes resulting in accusations of FII) and can lead them to underestimate the added impact on their quality of life. Ref: https://www.meresearch.org.uk/mecfs-families/ https://academic.oup.com/hmg/article/29/R1/R117/5879704 Research recommendation: While the forthcoming DeCodeME and *Family Impact Survey* might add to the knowledge about this topic we recommend highlighting the need for more biomedical research looking at the familial incidence of ME/CFS.	Thank you for your comment. The committee agree this is important to note and as you comment have included this in the safeguarding section. The committee consider this to be the most appropriate section for this information. *Research recommendation* Research recommendations can only be made for where the evidence has been searched for within the guideline. Biomedical research was not included in the scope of this guideline as a topic to consider, and therefore we are unable to make research recommendations on this topic

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Welsh Association of ME & CFS Support (WAMES)	Guideline	004	4	*1.1.2 Be aware that ME/CFS:* ii. Attention is brought to the additional factors affecting the severely affected in 1.1.8 line 7+, but we believe that an additional point should be added here to highlight the fact that children can present slightly differently than adults: more stomach troubles etc. Early understanding of this could avoid GPs overlooking ME/CFS as a potential diagnosis in children.	Thank you for your comment. An additional recommendation has been added to the section on suspecting ME/CFS to highlight that children may describe symptoms differently to adults.
Welsh Association of ME & CFS Support (WAMES)	Guideline	004	9	We welcome the acknowledgement that *'ME/CFS can have a significant impact on people's (and their families and carers') quality of life*'. Please add 'finances' to the bullet point about the impact of ME/CFS - when a breadwinner has to give up work to care for a severely ill adult or child with ME/CFS this impacts on the family finances. This could mean moving down to one salary for a couple, or having to claim benefits for a single parent family. In the case of adults this could mean moving from a good salary to benefits, on resulting in a struggle to survive.	Thank you for your comment. The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes.. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS. The severity of the impact of ME/CFS has been recognised throughout the development of this guideline. The scope included people with severe and very severe ME/FCS as a population for special consideration and each review highlighted any relevant evidence. In addition recognising the lack of evidence NICE commissioned a report to ensure the views of people with severe and very severe ME/CFS were include in the

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					guideline (Appendix 2_People with severe ME/CFS) and this was considered alongside the other evidence by the committee. When making the recommendations the committee considered people with severe and very severe ME/CFS separately and made additional recommendations where relevant. After considering the stakeholder comments the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline and had more emphasis. *Finances* The impact on work has been noted in the recommendation and is further highlighted in the section on supporting people with ME/CFS in work, education and training. Finances are specifically highlighted in the recommendations on maintaining independence.
Welsh Association of ME & CFS Support (WAMES)	Guideline	005	26	We welcome the highlighting of the impact a poor experience of accessing services can have on a child or young person. False allegations made by professionals when a child/young person does not make their expected recovery impacts on all family members and continues to harm the relationship with professionals by all affected can continue for very many years and trust may never totally be regained by the patient and their carer and extended family. We recommend adding: *iii.* …which can continue into adulthood and affect the whole family.	Thank you for your comment. This recommendation focuses children and young people and for this reason your suggestion has not been added.

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Welsh Association of ME & CFS Support (WAMES)	Guideline	006	22-23	• *gastrointestinal difficulties such as nausea, incontinence, constipation and bloating* Add: stomach pain	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	006	26-27	Add: dysautonomia.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	006	7	1.1.8 We welcome the highlighting of severe and very severe ME early in the guideline. The widespread lack of understanding within the health & social care systems has caused carers many difficulties when trying to explain the severe limitations that their loved one's experience, and the harm that ignorance can cause. We welcome the listing of additional symptoms, but recommend the following additions:	Thank you for your comments, your suggestions have been answered individually.
Welsh Association of ME & CFS Support (WAMES)	Guideline	006	16	'extreme weakness, with severely reduced movement' Add: even paralysis or near paralysis.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	006	17	Add: resulting in mumbling or whispering	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	006	24	Add: loss of sight whether temporary or long term	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.

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Welsh Association of ME & CFS Support (WAMES)	Guideline	007	7	*'need careful physical contact when supported with activities of daily living, taking into account possible sensitivity to touch'* Add: the need to consistently speak softly, work in dimmed light, and to avoid perfumes, deodorants or other strong smells.	Thank you for your comment. Hypersensitivity and the examples you mention are included in the previous recommendations on symptoms people with ME/CFS may experience. These are examples in the recommendations and as with any examples these cannot be exhaustive for this reason your suggestions have not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	007	8	**'***need aids such as wheelchairs'* To illustrate the potential severity of the condition, add: mobility scooters, hoists, stair lifts, hospital beds and/or pressure-relieving mattresses, ramps, rails and specialist level access showers. Wheelchairs can be needed on occasion by the moderately affected so there is a need to show the added difficulties for the more severely affected.	Thank you for your comment. After considering the range of stakeholder comments this has been edited to, 'are housebound or bed-bound and may need support with all activities of daily living, including aids and adaptions to assist mobility and independence in activities of daily living (for example wheelchairs)' The section on aids and adaptions provides further information. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	007	17	It can be difficult to find care workers able to comprehend severe ME/CFS so they should be adequately trained or willing to undergo appropriate training. Add a bullet point: offered appropriate training	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training in line with this guideline and this is included in the recommendations in the training health and social care professionals section of the guideline.
Welsh Association of ME & CFS Support (WAMES)	Guideline	027 - 019		We welcome the acknowledgement of potential harm from graded exercise and the move to advise a more flexible approach to physical activity. We also welcome the explanation of the difference between physical activity and exercise.	Thank you for your comment.
Welsh Association of ME & CFS	Guideline	008	9	1.2.2 '*baseline investigations to exclude other diagnoses'*	Thank you for your comment.

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Support (WAMES)				Due to the high level of ignorance and misunderstanding surrounding ME/CFS in the medical profession it is crucial that further guidance is given on the range of helpful investigations.	Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
Welsh Association of ME & CFS Support (WAMES)	Guideline	008	16	1.2.3 '*symptoms are new and had a specific onset.'* While specific onset is common, there are also cases of gradual or delayed onset, where, e.g. initial recovery from a triggering incident (such as a virus) is followed by a gradual decline, maybe only becoming obvious weeks or months later. The ill person might find it difficult to identify the trigger (or might misidentify the trigger) until looking back much later. We recommend acknowledging this possibility to avoid potential cases of ME/CFS being overlooked.	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the symptoms have developed and have not always been present covering that the symptoms are not lifelong. This now includes the cohort of people who develop symptoms gradually sometimes over months or even years.
Welsh Association of ME & CFS Support (WAMES)	Guideline	008	17	Box 1 Symptoms for suspecting ME/CFS Fatigability - We welcome this alternative to the misunderstood term 'chronic fatigue' but question the spelling. Should it not be fatiguability?	Thank you for your comment. *Debilitating fatigability*. This has been edited to be more descriptive of the fatigue experienced by people with ME/CFS, 'Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.'
Welsh Association of ME & CFS Support (WAMES)	Guideline	008	17	We welcome the use of the term post-exertional symptom exacerbation rather than 'post-exertional malaise'. We have found that the term malaise (feeling ill all over) is not understood in the same way by all people and all health professionals. In addition, it is just one symptom and during	Thank you for your comment. After taking into consideration the range of comments made by stakeholders about the potential for misunderstanding the committee agreed to change *Post exertional symptom*

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

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				the post-exertional response all symptoms can potentially increase in severity. In the experience of many patients, especially more severely affected patients, the post-exertional exacerbation of symptoms is not necessarily delayed**.** The severity, disproportionate to the activity, and longevity of the response to activity, are however notable characteristics, as mentioned. An 'activity' can be anything physical or cognitive, and overdoing it will produce this exacerbation of symptoms. Some patients have wondered whether the cumulative effect of small activities can trigger a post-exertional response that can appear to be immediate. Learning to recognise the 'cost' of activities, especially apparently minor activities such as turning over in bed, listening to a set of instructions, reading an email etc. can take time. The patient may not be aware of a post-exertional response in the early days, weeks or months, if they feel very ill all the time and so it may not be able to tell the diagnosing physician about it. This may have to be uncovered over time.	*exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.
Welsh Association of ME & CFS Support (WAMES)	Guideline	009	21-22	Excluding other conditions – We ask for guidance to be given to doctors on which conditions to exclude and which may be co-existing. Many patients have spent years struggling to persuade doctors that one diagnosis does not adequately match their condition. Early MS, Ehlers Danlos Syndrome, Hypermobility, Mast Cell Activation Syndrome and Dysautonomia are among the conditions which patients and parents have been concerned about.	Thank you for comment. The committee agree it is important to exclude or identify other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have added examples of investigations to be done when suspecting ME/CFS. The discussion section of Evidence review D includes lists of common differential and co- existing diagnoses. The conditions you mention are included.

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Welsh Association of ME & CFS Support (WAMES)	Guideline	009	10	1.2.4 Add: tender glands 'across the body' It can be difficult to make doctors aware of this.	Thank you for your comment. These are examples of symptoms that people may experience under flu-like symptoms and the committee note that any list of examples is not intended to be exhaustive. For this reason your suggestion has not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	010	9	1.2.8 Referring children and young people with suspected ME/CFS**...** **"**Write to the child or young person's place of education or training to advise about flexible adjustments or adaptations We welcome this guidance and are told by parents that a knowledgeable advocate is very important. e.g. GP/paediatrician who can make direct contact with the school. Perhaps an OT who has visited the child at home can also support and intercede with the school regarding practical ways of supporting the child in maintaining their education and to provide training / awareness for staff. While putting the advice in writing is important, it may need more contact than that! Add: write, and make contact with…	Thank you for your comment. This recommendation has been edited to 'work with… to support'. The committee hopes this adds clarity to this recommendation.
Welsh Association of ME & CFS Support (WAMES)	Guideline	010	15	1.3.1 *When ME/CFS is suspected, give people personalised advice about managing their symptoms. Also advise them*: There is no mention of advising people to keep a symptom diary in the early stages to help both the patient and professional understand whether the post-exertional response is occurring. As many people are too ill to notice this phenomenon in the early days, we are unsure how the diagnostician aims to uncover the presence of PESE. We realise that keeping a diary uses energy and can be difficult, but could provide the doctor with vital insight to the way the condition affects the patient.	Thank you for your comment. After considering the stakeholder comments the committee agreed that this concept and energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on PEM and energy limits* may not be helpful. At such keeping a diary at this stage may not be appropriate. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits.

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Welsh Association of ME & CFS Support (WAMES)	Guideline	010	20	1.3.1 'to rest as they need to' We welcome this early advice to people with suspected ME/CFS but are aware that rest is not seen as proactive enough for many patients eager for a quick recovery, so we suggest elaborating: to rest as they need to, in order to give their bodies the best chance of healing and achieving the best function possible in the long term.	Thank you for your comment. The recommendation sets out the advice that people should be given. There is more detail in the hyperlinked rationale and impact that explains managing symptoms early may prevent people getting worse and this is further discussed the discussion section in Evidence review E. For this reason your suggestion has not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	011	4	1.4 Diagnosis We are concerned that there is not enough information to help doctors make an accurate diagnosis. There is a considerable lack of confidence amongst GPs as recorded in a number of surveys. And patients report experiencing a high level of ignorance or misunderstanding about the nature of the condition.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. The committee acknowledged that non- specialists may not feel confident in diagnosing ME/CFS and recommended that people with suspected ME/CFS are referred to a ME/CFS specialist service for confirmation of the diagnosis (Evidence review B). To note the training recommendations have been edited.
Welsh Association of ME & CFS Support (WAMES)	Guideline	011	6	**1.4.1** Add: 'after excluding other possible conditions Insert a list of exclusions and co-existing conditions (or link to a list), which could include (amongst others): • Anaemias • Autoimmune diseases such as rheumatoid arthritis, lupus • Cardiac disease	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude and identify other diagnoses. The committee have now included examples of investigations that might be carried out when ME/CFS is suspected. The discussion section of Evidence review D- Diagnosis includes a list of differential diagnosis and conditions that commonly occur

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				• Endocrine disorders such as diabetes, Addison's disease, thyroid disease, menopause • Infectious diseases such as tuberculosis, HIV/AIDS, chronic hepatitis, Lyme disease • Intestinal diseases such as Coeliac or Crohn's disease • Malignancies • Mitochondrial Diseases • Neurological disorders such as multiple sclerosis, Parkinson's disease, myasthenia gravis • Primary psychiatric disorders and substance abuse (but not clinical depression (but not clinical depression as this can co-exist) • Significant pulmonary disease • Primary sleep disorders such as sleep apnoea • Functional Neurological Disorder Possible co-existing conditions: allergies, fibromyalgia, irritable bowel syndrome, multiple chemical sensitivities, hypermobility, Ehlers Danlos Syndrome.	in people with ME/CFS. These include many of the examples you list.
Welsh Association of ME & CFS Support (WAMES)	Guideline	011	7	1.4.2 Remove: specialist team Replace with: ME/CFS service, consultant or GP with special interest. We do not believe a specialist team is the only possible or likely way that services will be delivered in Wales.	Thank you for your comment. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I- Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres

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					A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.
Welsh Association of ME & CFS Support (WAMES)	Guideline	011	11	Remove: specialist team Replace with: paediatric ME/CFS service or paediatrician We do not believe a specialist team is the only possible or likely way that services will be delivered in Wales in the future.	Thank you for your comment. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I- Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.
Welsh Association of ME & CFS Support (WAMES)	Guideline	011	13	*1.5 Assessment and care planning by a specialist ME/CFS team* We welcome the recommendation that there should be specialists or professionals trained to offer support to people with ME/CFS. We do not believe a 'specialist team' is the only possible or likely way that services will be delivered in Wales. Assessment and care could equally be carried out by a group of professionals in local ME/CFS services based in primary care. We therefore recommend changing the heading to say 'ME/CFS service' or even 'ME/CFS professionals'.	Thank you for your comment. Based on the evidence (Evidence reviews A.B,C,D and I) and the committee's experience referral to ME/CFS specialist care was recommended for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. ME/CFS specialist teams where seen as the most appropriate place for people with ME/CFS to access support with GPs providing ongoing support and review. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I- Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people

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					with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams
Welsh Association of ME & CFS Support (WAMES)	Guideline	011	17	We welcome the highlighting of the importance to take a full history, but are surprised that this is not done by the GP before diagnosis, as this could affect the diagnosis. Perhaps this should talk about expanding the GP's history to avoid putting the person with ME/CFS through the same process twice. Is it the intention that this history be done a medical professional?	Thank you for your comment. After considering the stakeholder comments the committee agree to revise this recommendation to, 'carry out and record a holistic assessment to confirm a diagnosis and inform the care and support plan.'. This makes it clearer that the assessment is also the basis for the care and support plan. This is assessment is more detailed than the one carried before referral (see Evidence review I for further information on assessment in ME/CFS specialist teams).
Welsh Association of ME & CFS Support (WAMES)	Guideline	012	3	More detail is needed about the method of assessing physical function. Health professionals need to be reminded that physical assessments that involve raising the heart rate. If assessed by questionnaire, then guidance needs to be given on which are sensitive enough for use with people with ME/CFS	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	013	12-13	We welcome the recommendation of home visits for the severe and very severe ME/CFS patients but are concerned that many moderately affected people will find a long visit to a clinic causes PESE.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult. In the Access to care section of the guideline home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.

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Welsh Association of ME & CFS Support (WAMES)	Guideline	013	5	Add: 'knowledge' before 'skills and abilities'. If newly diagnosed, a person's knowledge base about the illness could be minimal and limit their ability to make these choices.	Thank you for comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.). In line with this the bullet points have been deleted as this is reflected in the aims of a care and support plan. The personalised care and support plan is based on the person's needs and includes the areas listed. The plan is developed in collaboration with the person with ME/CFS and explores their aims *and the management of their health and well-being within the context of their whole life and family situation. It should be proportionate, flexible and coordinated and adaptable to a person's health condition, situation and care and support needs.*
Welsh Association of ME & CFS Support (WAMES)	Guideline	013	14	*1.11.27 Refer to the following for advice on treating pain:* A warning should be added here not to refer to the recent NICE guidance on chronic pain as GPs have been using it to deny people with ME/CFS pain medications.	Thank you for your comment. The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that when managing any co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account.

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Welsh Association of ME & CFS Support (WAMES)	Guideline	014	19-21	Add: often, but doesn't always, involve periods of remission… This highlights that some people remain ill for years without any let up.	Thank you for your comment. After considering the range of stakeholder comments on this bullet point it has been edited to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS.
Welsh Association of ME & CFS Support (WAMES)	Guideline	014	30-31	Add after 'self managed': but not cured…	Thank you for your comment. After considering the range of stakeholder comments the first recommendation in the section on managing ME/CFS has been edited to,' Be aware that ME/CFS symptoms can be managed but there is no currently no treatment or cure (non-pharmacological or pharmacological) for ME/CFS.' The following section on energy management also includes that energy management is not curative. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. This point is made later and then reinforced in the management section of the guideline and for this reason your suggestion has not been added to the recommendation.
Welsh Association of ME & CFS Support (WAMES)	Guideline	015	3	Add after 'than in adults': but do not give false hope	Thank you for your comment. This committee agreed that this point does not add any further clarity to the recommendation and has not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	015	10	Add after 'help the person': achieve the best quality of life possible	Thank you for your comment. This committee agreed that this point does not add any further clarity to the recommendation and has not been added.

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Welsh Association of ME & CFS Support (WAMES)	Guideline	015	24	Care needs to be taken to ensure that the document linked to makes it clear when there are different laws, guidance outside England.	Thank you for your comment. All NICE guidelines and quality standards apply to Wales and are subject to Welsh legislation. See https://gov.wales/national-institute-health-and-care-excellence-nice-guidelines for Guidance for health boards, trusts and other stakeholders on how to follow NICE guidelines.
Welsh Association of ME & CFS Support (WAMES)	Guideline	016	6-8	*"Safeguarding assessments in people with confirmed or suspected ME/CFS should be carried out or overseen by health and social care professionals who have training and experience in ME/CFS"* Concern has been expressed by patients and carers about the level of competence of those professionals carrying out safeguarding assessments. Too many families have suffered for years at the hands of misguided professionals so we wish to see the addition of the words 'up-to-date' before 'training and experience in ME/CFS'. Misguided views of ME/CFS will linger for some years and hopefully new insights will be revealed regularly by research, so an up-dated training every year or 2 would protect families affected by ME from avoidable distress. It is also unclear who should carry out a safeguarding assessment if there are no ME/CFS specialists or doctors with a special interest in the country where the patient resides, as is the case in Wales.	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. 'up-to-date' does not add any further clarity to the recommendation and for this reason your suggestion has not been added. The committee agree there is inequity in access to ME/CFS services and throughout the guideline have made recommendations to improve access to care where services do not exist.
Welsh Association of ME & CFS Support (WAMES)	Guideline	016	12-13	The legislation relevant to mental health includes the Mental Health (Wales) Measure 2010 https://www.legislation.gov.uk/mwa/2010/7/contents	Thank you for your comment and information. We note that all NICE guidelines and quality standards apply to Wales and are subject to Welsh legislation. See https://gov.wales/national-institute-health-and-care-excellence-nice-guidelines for Guidance for health boards, trusts and other stakeholders on how to follow NICE guidelines.

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Welsh Association of ME & CFS Support (WAMES)	Guideline	016	6	Replace: Safeguarding assessments in.. With: If safeguarding assessments are needed in… The current wording could be interpreted by professionals with a psychological view of ME/CFS to mean that safeguarding assessments should always be considered, so clarification is needed.	Thank you for your comment. After considering the stakeholder comments this section has been reordered and the now second recommendation has been edited to,' *If* a person with confirmed or suspected ME/CFS needs to be assessed'.
Welsh Association of ME & CFS Support (WAMES)	Guideline	017	21-22	1.8 Access to care – add bullet point 1.8.1 Service providers should ensure people with ME/CFS can access health and social care services by: • Offering support to employ and manage care workers Support needs to be given to help people with ME/CFS adequately undertake the employment and management of their own care workers, either as live-in carers or as care workers employed under the Direct Payments system, as the patient may not be cognitively strong enough to deal with all the intricacies of employing one's own staff. This support needs to be ongoing for the whole period of time that this additional support from paid staff needs to go on for.	Thank you for your comment. The employment of care workers is not in the remit of NICE and your suggestion has not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	017	20	1.8 Access to care We welcome the listing of some reasonable adjustments which could make it possible for many people with ME/CFS to access health and social care services. On the few occasions that patients have been provided with them in Wales they have made a significant difference to the families' ability to cope with distressing situations. Adjustments were easier to obtain across health, social care and education when an advocate with a knowledge of the person with ME's situation has sufficient authority to influence on their behalf. e.g. a named contact or lead health professional. Ideally this person should be an expert on ME/CFS but as this is not possible in Wales a consultant or	Thank you for your comment and information.

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				paediatrician with the necessary authority and respect can make things happen within his/her own team and has the ability to liaise effectively with specialist colleagues. GPs can find it harder to do this. There have been many occasions however when adjustments have been refused because the diagnosis was not accepted or there was a lack of understanding of the severity of the illness and possibility of harm. This has led to an increase in symptoms, relapse, sense of being ignored, depression and even suicide.	
Welsh Association of ME & CFS Support (WAMES)	Guideline	018	19-24	Add: Failure to provide access to health or social care can lead to complications, relapse, increased weakness and even death. Refusal recently by a hospital in Wales to accept the severity of a severely ill patient's condition and make adjustments to enable her to enter hospital for investigations, meant she died at home much earlier than she should have and in unnecessary discomfort and distress.	Thank you for your comment and information.
Welsh Association of ME & CFS Support (WAMES)	Guideline	018	3-5	Add: Provide support to locate patient ambulance transport if necessary.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	018	24	Add: and financial support.	Thank you for your comment These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	019	9-29	We welcome the inclusion of this consideration of the difficulties people with ME/CFS experience in a hospital setting. We recommend an additional bullet point: Consider whether a hospice or palliative care setting might be more appropriate.	Thank you for your comment. This recommendation considers how the hospital environment could be adapted and not where people should be admitted for this reason your suggestion has not been added.

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Welsh Association of ME & CFS Support (WAMES)	Guideline	019	21-29	*keep stimuli to a minimum, for example by:* We recommend an additional point: Keep tests and investigations to a minimum	Thank you for your comment These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	021	11-12	1.9.2 *Offer to liaise on the person's behalf (with their informed consent) with 12 employers, education providers and support services* We welcome the acknowledgement that employers, education providers and support services will need information to effectively understand the limitations ME/CFS places on people and enable them to provide support. Clarification is needed on who, within the health service, could liaise.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS and not who should be delivering all the aspects of care (Evidence review I _Multidisciplinary care (Benefits and Harms section). The multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse.
Welsh Association of ME & CFS Support (WAMES)	Guideline	021	14	*adjustments needed* The difficulty many people with ME/CFS have experienced in accessing adjustments, some of which are not often required for people with other disabilities and limitations, would suggest that it is important to give examples. Add: including home schooling, working from home, flexible or reduced hours, providing transport, designated parking space, a quieter work area with lower light settings, speech to text software, text to speech software, audiobooks, ergonomic assessment, or a place to rest when needed.	Thank you for your comment. Further information in types of adaptions and adjustments are included further in this section and in the committee discussion in evidence review A and the points your raise are highlighted there. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable

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					and for this reason your suggestion has not been added to the recommendation.
Welsh Association of ME & CFS Support (WAMES)	Guideline	021	15	As the recommendations in NICE guidelines are provided for Wales, as well as England, we believe it would be appropriate to list the appropriate legislation instead of saying 'or *equivalent statutory guidance*' https://dera.ioe.ac.uk/562/7/100603medguideanceen_Redacted.pdf	Thank you for your comment. We note that all NICE guidelines and quality standards apply to Wales and are subject to Welsh legislation. As such equivalent statutory guidance includes Welsh legislation. For this reason your suggestion has not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	022	6-7	*'Give parents and carers information about education, health and care plans and how to request one from their local authority.'* For this guidance to be helpful to people in Wales, and not misleading, the equivalent guidance in Welsh education should be referenced. The Welsh Government has not adopted the Education, Health and Care Plans mentioned here. In Wales pupils or students with ME/CFS would be considered to have 'Additional Learning Needs' and schools and colleges would be required, in law, to develop an appropriate person centred 'Individual Development Plan' with multi-agency input. (Additional Learning Needs and Education Tribunal (Wales) Act 2018)	Thank you for your comment. All NICE guidelines and quality standards apply to Wales and are subject to Welsh legislation. See https://gov.wales/national-institute-health-and-care-excellence-nice-guidelines for Guidance for health boards, trusts and other stakeholders on how to follow NICE guidelines.
Welsh Association of ME & CFS Support (WAMES)	Guideline	022	14	The guideline recommends that the specialist team consists of health and social care professionals with expertise in a range of areas. We recommend that a list of potential specialities also be included as this will make it more apparent what is needed when commissioning discussions take place. Patients should have early access to a Doctor(s) and Occupational Therapist. Early Occupational Therapy assessment and support is essential, within a month of diagnosis, and a patient might also need:	Thank you for your comment and information. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (see Evidence review I _Multidisciplinary care).

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				• district or community nurse input to enable procedures to be carried out at home, • social care • physiotherapy • dietetic support • psychological support • speech therapy There is no clear recommendation of whether a specialist team should be located in tertiary or primary care, although there is acknowledgement that care might be 'managed in primary care and 'supported by advice and direct clinical consultation from a specialist team'.(1.10.2 line 5-6) In Wales, a country with many rural communities, the *Primary Care Model* aims to develop 'seamless care and support at or close to home' bringing in a wider range of professionals to develop services within localities or 'clusters'. https://gov.wales/primary-health-care-html This model is more beneficial to people with ME as it reduces harmful & expensive travel for patients, makes home visits for the severely affected easier, taps into an existing practice of ongoing care. All of the above services should be available in the community within easy reach and at home, if necessary. Centralising services and running 'take it or leave it/ all in one' courses in a major centre could lead to many people with ME/CFS being overlooked and unable to access help. The guideline should clarify that basing specialist teams in either primary care or tertiary care could be considered as possible models. Leaving it vague makes it harder for stakeholders to engage with commissioners. Team leadership	The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *Service design* This guideline focused on clinical recommendations and the committee did not comment on the design and delivery of services, including who leads services as this is determined locally. A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes local and regional teams. *Access to services* The committee agree there is inequity in access to ME/CFS services and throughout the guideline have made recommendations to improve access to care however it was not within the committee's remit to make specific recommendations on service design and delivery. *Implementation* There are areas that may need support and investment, such as access to specialist teams, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. *Audit*

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				There is no guidance given on who should lead the specialist team. Psychologists currently lead the CFS and fatigue services in Wales, which has been one of the disincentives to people with ME to access the services. While clinical psychologists have a role to play in supporting people with ME/CFS to cope with their illness, it is not appropriate that they should bear the responsibility for overseeing the care of a 'complex, chronic medical condition affecting multiple body systems'**.** We believe the team should be led by a specialist consultant**,** GP 'with special interest' or 'paediatrician with special interest'. In Wales few doctors currently have an interest in, or accept responsibility for, diagnosing and caring for pwme, but neurologists, a rheumatologist and an endocrinologist have all had some input into the care of pwme in Wales at some point, and immunologists elsewhere in the UK. We believe a medical professional with a strong interest in the condition is more important than the speciality itself. WAMES endorses the 2014 Welsh Government Task & Finish Group Report recommendation that: 'There is scope for some flexibility in deciding which speciality (or specialities) should take the lead, but the home should not be located in mental health services." http://wames.org.uk/cms-english/wp-content/uploads/2014/10/me_cfs-task-and-finish-group-report-and-recommendations-aug-2014.pdf We would like the guideline to specify that mental health, psychiatrists and psychologists should not lead an ME/CFS team.	The committee agree that audit is an important part of measuring performance in services but this guideline focused on clinical recommendations, the development of audit systems was not included as an area in the scope and the committee are unable to make recommendations in this area. Your comments will also be considered by NICE where relevant support activity is being planned.

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				Combination services Another disincentive for people with ME/CFS to attend a specialist service is when 'fatigue' services attempt to cater for both 'CFS' and Fibromyalgia / pain patients. Research into exercise intolerance makes it clear that different approaches are needed towards activity and pain management for pain patients and ME/CFS patients, and we believe that while it might be appropriate to combine some services for ME/CFS with other medical conditions, it is not appropriate for ME/CFS services to be located in a pain clinic, and it is important to clarify this in the guideline. Implementation The implementation of specialist teams in Wales would be extremely challenging and expensive to set up. Two Health Boards have previously discussed setting up services, but they were unable to advertise them to patients, due to lack of trained staff and funding. Work was undertaken in one Health Board to look for suitable existing services which could accommodate pwme, but time, money and effort would be needed to increase capacity and persuade staff that ME/CFS was a serious enough condition to warrant their attention. Existing neurological clinics across Wales could offer an appropriate community rehab service to people with ME/CFS (based on maximising function within a patient's existing limitations) but they do not all have long term funding or capacity to cater adequately for existing neurological patients without adding a significant number of ME/CFS patients to their waiting lists. Add: The performance of local ME/CFS services should be regularly audited.	

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Welsh Association of ME & CFS Support (WAMES)	Guideline	023	7-10	*Give people with ME/CFS (and their family members and carers, as appropriate) a named contact* We welcome the recommendation that people with ME/CFS be given a named contact to coordinate their management plan, but foresee large implementation challenges. This is not common practice within NHS Wales and could be difficult logistically and have significant cost implications, even if the concept were acceptable to medical practices and health boards.	Thank you for your comment. The committee have modified the recommendation so that the named contact could be in primary care or in the ME/CFS specialist team. This should make it easier to implement. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as improved access to services, to implement some recommendations in the guideline. guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned.
Welsh Association of ME & CFS Support (WAMES)	Guideline	023	12-15	1.10.4 *Provide parents and carers of children and young people with ME/CFS 13 with details of a named professional in the specialist team who they can contact with any concerns about their child's health, education or social life.* We welcome the recommendation for parents and carers to be given a named contact to contact with concerns about their child's health, education or social life, but as a specialist team is not a realistic possibility in many locations, advice should be provided by a Physician, Paediatrician or GP with specialist knowledge and experience or a local ME/CFS service.	Thank you for your comment. Throughout the guideline there is reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support plan and supervision for the management of some symptoms. A description of ME/CFS team has been added to the terms used in the guideline and this includes local and regional teams.
Welsh Association of ME & CFS Support (WAMES)	Guideline	023	5-6	*Care for people whose ME/CFS is managed in primary care should be supported by advice and direct clinical consultation from a specialist team.* As a specialist team is not a realistic possibility in many locations change the wording:	Thank you for your comment. The committee agree there is inequity in access to ME/CFS services and throughout the guideline have made recommendations to improve access to care including

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				advice should be provided by a Physician, Paediatrician or GP with specialist knowledge and experience or a local ME/CFS service.	reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support plan and supervision for the management of some symptoms. A description of ME/CFS specialist team has been added to the terms used in the guideline and this includes local and regional teams. *Service design* This guideline focused on clinical recommendations and the committee did not comment on the design and delivery of services as this is determined locally.
Welsh Association of ME & CFS Support (WAMES)	Guideline	024	23	After 'when symptoms are improved' Add: 'and have been stable for some time'	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to,' uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse).
Welsh Association of ME & CFS Support (WAMES)	Guideline	027	19	Add: Advise and/or provide aids to prevent future problems, such as a Tilt-in-space chair, a profiling bed, personalised wheelchair, commode, over-toilet seats, walk-in shower with seat, walking sticks at the correct height etc.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added
Welsh Association of ME & CFS Support (WAMES)	Guideline	027	19	Add an additional final bullet point: Advise and/or provide information and aids to correct problems arising from enforced immobility once function begins to improve such as wedged shoes to aid walking.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added
Welsh Association of ME & CFS	Guideline	029	11	Insert third bullet point: incorporating extra periods of rest and sleep as needed	Thank you for your comment. The following section on symptom management includes sleep and rest. The committee noted that there was a lack of evidence identified for rest and sleep strategies and the committee were

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Support (WAMES)					unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice. This applies here and advice on rest and sleep should be part of the personalised collaborative physical activity or exercise programme.
Welsh Association of ME & CFS Support (WAMES)	Guideline	029	19	Add a bullet point (or link to an entry in the list of terminology) on the nature of rest - lying down with eyes shut, meditation, or sleeping – not watching TV. People generally have a very flexible' view of what constitutes rest!	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual.
Welsh Association of ME & CFS Support (WAMES)	Guideline	030	3-12	As research has highlighted that OI is fairly common in ME/CFS and specialists are few, we recommend adding more information about the condition and how it impacts other symptoms in ME/CFS e.g.: Symptoms include dizziness, fatigue, brain fog, palpitations, pallor, nausea and fainting. In severe cases, symptoms can be triggered just by sitting up. Orthostatic stress can trigger Post Exertional Symptom Exacerbation (PESE) in people with ME/CFS. The most common forms of OI are Postural Orthostatic Tachycardia Syndrome (POTS), Neurally Mediated Hypotension (NMH), and orthostatic hypotension (OH). These syndromes are not mutually exclusive. Patients with ME/CFS can also have orthostatic intolerance with significant reduction in cerebral blood flow without any associated changes in blood pressure or heart rate.	Thank you for your comment and information. In the suspecting ME/CFS section of the guideline orthostatic intolerance is identified as one of the symptoms that are commonly associated with ME/CFS. The committee made a consensus recommendation to raise awareness about this. The committee did not make any recommendations on the management of orthostatic intolerance noting that although this can be straightforward it this can involve advice on diet, carrying out daily activities and activity support and should be tailored to the person taking into account their other ME/CFS symptoms. The committee noted medicines usually prescribed for OI can worsen other symptoms in people with ME/CFS and should only be prescribed or overseen by a clinician with expertise in orthostatic intolerance. (see evidence review G).

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				ME/CFS patients are often unable to tolerate a full tilt table test, which can trigger a relapse in their illness. Instead, diagnosis may be made using the NASA 10 Minute Lean Test. 1. There is a need for links to where can doctors find basic management & prescribing advice 2. There is a need for links to online training courses for health professionals	
Welsh Association of ME & CFS Support (WAMES)	Guideline	030	2	Add last bullet point: It may be necessary not to complete an activity if the length or impact of the activity has been underestimated. Resting could fend off a flare or relapse and enable a return to the activity sooner.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Welsh Association of ME & CFS Support (WAMES)	Guideline	030	2	Insert additional point **after 1.11.23** Sleep: • In the early stages of the illness, hypersomnia is common. It is important that people with ME/CFS listen to their bodies and sleep as much as they need to. This gives the best chance of recovery and functional improvement in the long term. • Hypersomnia can also happen during flares and relapses. As always, patients should listen to their bodies in order to get out of the flares or relapses. • Standard "sleep hygiene" practices may not always be appropriate in ME/CFS, such as strictly limiting daytime sleep.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.

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				- Where it is necessary to adjust a patient's sleep pattern to fit around work hours, education etc. melatonin or other sedatives can be tried. Changes should be made gradually in small increments. - Insomnia is a common problem. Melatonin, low dose amitriptyline or other sedatives can be tried. Start low and go slow – ME/CFS patients are very sensitive to medication and prone to side effects. On waking, patients often experience a period of profound weakness or paralysis, subjectively experienced as "heaviness" or "dead weight", in which they are unable to move. Advise patients to allow time for this to 'wear off' or reduce in severity when planning activities.	
Welsh Association of ME & CFS Support (WAMES)	Guideline	031	1-4	Change to: Managing abdominal pain and nausea 1.11.28 Encourage people with ME/CFS who have abdominal pain or nausea to keep up adequate fluid intake and advise them to try to eat regularly, taking small amounts often.	Thank you for your comment. This recommendation has been moved to the dietary management section. This section includes more advice on how to minimise complications caused by gastrointestinal symptoms. For this reason your suggestion has not been added.
Welsh Association of ME & CFS Support (WAMES)	Guideline	031	13-14	We welcome the advice to 'start low, go slow' when prescribing medication but are disappointed that there is no guidance for drugs that might be more or less helpful for people with ME. GPs always request practical advice like this.	Thank you for your comment. The evidence for any pharmacological interventions for ME/CFS was inconclusive with limited evidence for any one medicine and this was supported by the committee's clinical experience and consensus view. As a result the committee could not confidently recommend any medicines.
Welsh Association of ME & CFS Support (WAMES)	Guideline	032	8-10	We doubt that there is such a thing as a 'dietician who specialises in ME/CFS' in Wales! A major change in attitude would be needed to develop such skills and experts would need to be brought in from outside the country. The cost of pan-Wales training courses and consultations with a significant number of people with ME/CFS could be expensive so we see many challenges in implementing this. There is a need for training materials.	Thank you for your comment. The committee agree there is a lack of dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS.

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					The recommendation has been reworded to describe dietician as a 'dietician who has a special interest in ME/CFS', the committee recognised that currently dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas.
Welsh Association of ME & CFS Support (WAMES)	Guideline	032	21-23	*1.11.38 Refer children and young people with ME/CFS who are losing weight or have faltering growth or dietary restrictions to a paediatric dietitian who specialises in ME/CFS.* There is unlikely to be a paediatric dietician specialising in ME/CFS in Wales for some time, if ever, so we would like a warning to be added to this point. Weight gain and weight loss are a consequence of ME/CFS symptoms and are not necessarily the result of an eating disorder.	Thank you for your comment. The committee agree there is a lack of paediatric dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The recommendation has been reworded to describe paediatric dietician as a 'paediatric dietician who has a special interest in ME/CFS', the committee recognised that currently paediatric dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are paediatric dieticians that provide

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					expertise to ME/CFS services, special interest describes this group of professionals better. The committee discussion section of Evidence review G- non pharmacological management includes the rationale for ensuring children and young people are referred to a paediatric dietitian who understands the impact of ME/CFS on weight.
Welsh Association of ME & CFS Support (WAMES)	Guideline	033	2	Insert additional point after line 2: Consider Mast Cell Activation Syndrome and Coeliac Disease in patients with multiple food intolerances.	Thank you for your comment. Throughout the guideline the committee have recommended the importance of being aware of differential diagnoses and coexisting conditions, a coeliac screen is included in the list of investigations that might be considered in section 1.2. The committee hope that the recommendation to refer people with ME/CFS with a restrictive diet for a dietetic assessment will improve the identification and management of complications that people with ME/CFS can experience and they decided not to refer to any one particular condition**.**
Welsh Association of ME & CFS Support (WAMES)	Guideline	033	11	Add: abdominal pain	Thank you for your comment. This list includes examples of risk of malnutrition and unintentional weight loss identified by the committee and is not intended to be an exhaustive list.
Welsh Association of ME & CFS Support (WAMES)	Guideline	034	2-5	We query whether CBT helps people to manage ME/CFS symptoms, though it can help people come to terms with the shock of developing an illness and the distress of having to live with it long term. This sounds like a hangover from the view that changing illness beliefs can cure ME/CFS symptoms.	Thank you for your comments. **The committee specifically rejected the assumption that people with ME/CFS have 'abnormal' illness beliefs and behaviours as an underlying cause of their ME/CFS.** Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT **as described in the guideline** could be offered where this

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					is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Welsh Association of ME & CFS Support (WAMES)	Guideline	034	1	Change title to: Psychological support CBT is not the only form of psychological support that could be helpful to people with ME/CFS in learning to live with a chronic illness. It is also not the only form of psychological support offered to ill people in the NHS, though it may be the most expensive. There is a shortage of CBT practitioners in the NHS and therefore CBT is not a viable option for many people with ME/CFS. The waiting list could be long and patients might wish to try cheaper, more accessible therapies or one that suits their needs better, instead of CBT or while waiting for a CBT course to become available. We recommend emphasising that people with ME/CFS should be able to choose from a range of psychological and emotional support, as different approaches will suit different people. The options could include: supportive counselling; mindfulness; ACT (Acceptance and Commitment Therapy).	Thank you for your comment After considering the range stakeholder comments about the title not being representative of this section the committee edited the title of this section to remove psychological support recognising this only referred to CBT. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as training costs or access to services, to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed.

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Welsh Association of ME & CFS Support (WAMES)	Guideline	035	5-13	As this section is about psychological support we do not understand why a psychological therapy that aims to confront distressing emotions and anxieties should aim to tackle practical areas that are ideally the remit of an OT and/or nurse i.e.: *working together to adapt and refine self-management strategies to improve the person's functioning and quality of life, for example their sleep, activity and rest; developing a self-management plan; reviewing their plan regularly to see if their self-management strategies need to be adapted, for example if their symptoms or functioning change; developing a therapy blueprint collaboratively with their therapist at the end of therapy*. Developing a management strategy for dealing with overwhelming and unhelpful thoughts and emotions might involve behavioural changes, but is not the same as developing a strategy for managing energy, pain or other symptoms.	Thank you for your comment. After considering the range of stakeholder comments the first recommendation in this section has been edited to remove the word treatment. The committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The recommendation is clear that CBT is not curative. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness and if chosen by the person with ME/CFS delivered as part of the care and support plan and energy management plan. The CBT therapist would work with the other healthcare professionals that specialise in ME/CFS.
Welsh Association of ME & CFS Support (WAMES)	Guideline	037	1	We welcome the highlighting of the need to manage flares and relapses. Many people with ME/CFS in Wales are unfamiliar with the term flare and would talk about a mini-relapse or 'noticing danger signals', so this could be new terminology for some.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
Welsh Association of ME & CFS Support (WAMES)	Guideline	037	9	Add after 'temporarily reducing activity levels': and increasing periods of rest or sleep'	Thank you for your comment. The recommendation includes general strategies for people with ME/CFS, specific strategies would be individual to the person with ME/CFS and discussed as part of their care and support plan. The risk of including examples in a recommendation is that

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					they cannot be exhaustive and there is the risk these are taken as the only options available.
Welsh Association of ME & CFS Support (WAMES)	Guideline	038	8-9	Replace 'specialist team' With: ME/CFS service	Thank you for your comment. This has been edited throughout the guideline to ME/CFS specialist team.
Welsh Association of ME & CFS Support (WAMES)	Guideline	039	2-7	We welcome the recommendation that people with ME/CFS be offered a review at least once a year and more frequently "depending on the severity and complexity of their symptoms, and the effectiveness of any symptom management". Some carers of people with severe ME/CFS believe this will need to be much more frequent than once a year. As the condition changes over time, there may be periods of relatively better health and then relapses, which can last months, and it can be difficult to explain what has caused them. The condition can be very isolating and frightening for the person with ME/CFS and their carers, so having regular contact with the relevant health professionals is very important. However, some moderately and severely affected people with ME/CFS believe that annual reviews could be detrimental, especially if they require travel and visits to overwhelming locations like clinics. It could take many months for some people to recover from such a trip. The potential for short home visits or phone or video chats is essential to minimise harm. It would be helpful to add a section or comment here to highlight the implications for the severely affected. Because there is a danger that without review, other conditions (like Crohns, cancer etc.) or explanations for symptoms may be overlooked once the person has an ME/CFS diagnosis, we recommend that a short questionnaire be drawn up to be carried out at home before a review, to help identify which areas of	Thank you for your comment. The committee agree that some people with ME/CFS may require more regular reviews and the recommendation reflects this recommending people should be offered a review at least once a year. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The committee note that the review here is based in primary care and this would reduce the need for travelling to specialist centres. The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a change in symptoms are investigated. This should ensure that

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				discussion a review should prioritise. It can be difficult for people with ME/CFS to think clearly enough in the middle of a consultation to remember all the key points, especially if also negotiating transport or technological difficulties. A recommendation for monitoring and reviews were included in the 2007 CFS/ME guideline and to our knowledge this was not implemented in Wales so we foresee implementation challenges going forward.	changing or new symptoms are not overlooked and appropriate investigations are done. This has been reinforced in the flare up and relapse section of the guideline. Implementation All NICE guidelines and quality standards apply to Wales and are subject to Welsh legislation. See https://gov.wales/national-institute-health-and-care-excellence-nice-guidelines for Guidance for health boards, trusts and other stakeholders on how to follow NICE guidelines.
Welsh Association of ME & CFS Support (WAMES)	Guideline	039	8-10	1.14.3 *When undertaking a review in primary care, ensure you have access to the person's management plan and (if relevant) discharge letter from the specialist ME/CF team.* Replace: *discharge letter from the specialist ME/CF team.* With: letters from the person's named coordinator and/or ME/CFS service. Ensure relevant decisions are placed in the patient's central record / management plan. If there is to be a named coordinator then that is the person that should be able to help the person with ME/CFS, carer and health and social care professionals to access any and all relevant information for any activity. The assumption here seems to be that the person doing the review is not a member of the 'team', but this might not be the case. The named contact for a person with ME/CFS is likely to be a member of this team term and will be needed for the term of the illness – in most cases lifelong. 'discharge letter' could give the impression that people often recover and no longer need a review. The wording needs to be rethought.	Thank you for your comment. After considering the stakeholder comments this recommendation has been edited to 'clinical communications from the ME/CFS specialist team, including (if relevant) discharge letter' to be broader. The review is done in primary care and while part of the multidisciplinary team not usually part of the ME/CFS specialist team, the named contact could be in primary care or part of the ME/CFS specialist team. The care that people have is tailored to their circumstances and so it is important that at the review all the necessary information is available. Discharge The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no

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					one single model of care. Some of the committee members described experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support.
Welsh Association of ME & CFS Support (WAMES)	Guideline	039	21-22	As there may not be a specialist team available, we suggest the wording is changed to refer the person with ME/CFS to their local ME/CFS service or specialist physician	Thank you for your comment. The ME/CFS specialist team and special interest in ME/CFS is defined in the terms used in the guideline and can include a local ME/CFS service or a specialist physician.
Welsh Association of ME & CFS Support (WAMES)	Guideline	040		We welcome the highlighting of the need for training for both health and social care professionals but we consider there to be major challenges to implementation. It has been our experience that most 'training' in NHS Wales has been carried out by professionals sharing their thoughts and experiences, without realising how much they do not know. There has been a reluctance to 'buy in' expertise, and when that has happened GPs have expressed the need for detailed practical guidance on diagnosis and pharmacological prescribing, which is not contained in this guideline. There needs to be guidance on the need to urgently include training for doctors and other health professionals in the undergraduate medical curriculum, postgraduate Physician, Paediatric and General Practice curriculums and all continuing education programmes. The widespread lack of knowledge and misunderstanding about ME/CFS amongst the medical profession means that there needs to be an urgent programme to redress this and raise the profile of ME/CFS. This cannot be optional or it will take too long to right the wrongs of the past 50 years. National NHS services should be required to appoint an ME/CFS lead in each health board and trust, with the responsibility of	Thank you for your comment. The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. Your comments will also be considered by NICE where relevant support activity is being planned.

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				educating and raising awareness. Such a recommendation was made by the Welsh Government in 2014 but health boards largely ignored it. What guidance can NICE give to make implementation likely? We welcome the recognition that training and awareness-raising needs to be extended to social services – many Local Authorities in Wales allocate a named senior officer to be a 'champion' for a particularly vulnerable group, e.g. a Champion for Autism. This person has a lead role in terms of advocating for this vulnerable group, awareness raising, training and liaising with service user / carer groups and statutory and third sector agencies, and implementing national strategies, etc. This is a practice that could be extended to ME/CFS	
Welsh Association of ME & CFS Support (WAMES)	Guideline	040	16-23	There are no specialist services with knowledgeable physicians in Wales who can produce or support training programmes. Services offering courses for people with ME have expertise in Bio Psycho Social (BPS) versions of CBT and GET for CFS or pain. They are not knowledgeable in ME/CFS. We therefore recommend that guideline specifies: • the evidence-based content of the programmes be developed by, and with the support of, doctors and paediatricians with significant experience of ME/CFS (not specialist services) and who take a biomedical approach to the condition. • Trainers should also have expertise in medical education. • The experiences of ME/CFS patient organisations, as well as individual patients should be utilised as an overview of ME/CFS experience can add to the varied experiences of individuals.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. This recommendation has been edited to,' ME/CFS' specialist services. This reflects the evidence in Evidence reviews A and B and the committee's experience that ME/CFS specialist services provide valuable training, information and support to non specialists and people with ME/CFS.

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Welsh Association of ME & CFS Support (WAMES)	Guideline	041	9-11	More descriptive examples of 'activity' should be included as this is a common term and people with no experience of ME/CFS will fail to understand that automatic movements and reactions in healthy people are 'activity' which can cause symptom deterioration in people with ME/CFS.	Thank you for your comment. The definition of activity includes physical activity, the committee decided not to include examples of any activity (physical, cognitive, emotional or social) as any list of examples cannot be exhaustive and there is the risk these are taken as the only options available.

**None of the stakeholders who comments on this clinical guideline have declared any links to the tobacco industry.*