National Institute for Health and Care Excellence


Appendix C: stakeholder consultation comments table

Consultation dates: 10 to 24 July 2017

<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Overall response</th>
<th>Comments</th>
<th>NICE response</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Infection Association</td>
<td>Yes</td>
<td>No comments</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
<tr>
<td>The Pernicious Anaemia Society</td>
<td>No</td>
<td>CFS/ME is often diagnosed when there is no other explanation for a patient's continual tiredness. It needs to be thoroughly examined and guidelines issued</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
</tbody>
</table>
VIRAS Stakeholder Comment on:
The NICE Guideline CG53

Abbreviations
CBT ................cognitive behaviour therapy
CFQ ...............Chalder fatigue questionnaire (or scale)
CFS ................chronic fatigue syndrome
GET ................graded exercise therapy
M.E. ...............myalgic encephalomyelitis
NICE ...............National Institute of Clinical and Care Excellence
PF .................Short-form 36 physical function subscale
QMUL ............Queen Mary University London
RA ................rheumatoid arthritis
SMC ...............standardised specialist medical care (PACE Trial Control Group)

The NICE Guideline CG53 states
"6.3.1.1…"
"CBT is an evidence-based therapy for CFS/ME. It is a collaborative approach that aims to reduce the levels of symptoms, disability and distress associated with CFS/ME. CBT or psychological approaches to CFS/ME do not imply that symptoms are psychological, 'made up' or in the patient's head. CBT is used as part of the overall management for many conditions, including cardiac rehabilitation, diabetes and chronic pain."

"6.3.1.2 Graded exercise therapy (GET)"
"GET is an evidence-based professionally mediated approach to CFS/ME involving appropriate physical assessment, mutually negotiated and meaningful goal-setting and education. An achievable baseline of physical activity is agreed, followed by individually tailored and planned increases in the duration of exercise[...], with the objective of improving symptoms and functioning."

These statements contain inaccurate information that is likely to mislead doctors and patients. The PACE Trial (White et al. 2011) produced substantial evidence about the use of CBT and GET as therapies for CFS. The PACE Trial data (2016) shows unequivocally that these treatments provide no objective benefit to patients with M.E. or CFS. The data in Table 1 shows that the treatment effects with CBT and GET, are by convention and usage small to negligible and they do not reach clinical significance (Jacobson, Follette & Revenstorf. 1984).

Table 1

| Treatment effect sizes for CBT and GET with 3 outcome measures |

Thank you for your response.
Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
In the PACE Trial, the difference between CBT or GET compared to the SMC control group with the Chalder Fatigue Questionnaire (CFQ) is insignificant at a mere 3 points, as shown in Table 2. The minimum detectable change of the CFQ is ~9 points and ‘normal’ fatigue is 12 points or less (see appendix 1).

Table 2

<table>
<thead>
<tr>
<th>Trial arm</th>
<th>Effect measure</th>
<th>Chalder Fatigue Questionnaire</th>
<th>SF-36 Physical Function subscale</th>
<th>6 Minute Walk Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBT</td>
<td>Cohen’s d</td>
<td>-0.486</td>
<td>0.302</td>
<td>0.053</td>
</tr>
<tr>
<td>GET</td>
<td>Cohen’s d</td>
<td>-0.334</td>
<td>0.269</td>
<td>0.294</td>
</tr>
<tr>
<td>GET</td>
<td>Correlation r</td>
<td>-0.165</td>
<td>0.133</td>
<td>0.145</td>
</tr>
</tbody>
</table>

The difference between CBT or GET compared to the control group with the SF-36 Physical Function subscale (PF) is negligible as shown in Table 3. The minimum detectable change for this measure is ~25 points, the general population mean for those not reporting long-standing illness is 92.5 and for those with long-standing illness it is 78.3. (see appendix 2).

Table 3

<table>
<thead>
<tr>
<th>Trial arm</th>
<th>Effect measure</th>
<th>SF-36 Physical Function subscale</th>
<th>6 Minute Walk Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBT</td>
<td>Cohen’s d</td>
<td>-0.236</td>
<td>0.149</td>
</tr>
<tr>
<td>GET</td>
<td>Correlation r</td>
<td>-0.165</td>
<td>0.133</td>
</tr>
</tbody>
</table>
The PACE Trial data shows that the appearance of a treatment effect was created by a minority of only around 10% of participants. If CBT or GET were authentically able to “reduce the levels of symptoms, disability and distress associated with CFS/ME”, then significant benefits should have been reported by the majority. The minority effect is evidently the result of poor participant selection, placebo, deference, coercion and other participation phenomena.

Furthermore, participants that provided subjective ratings indicating that they had improved on one measure, frequently had results in other measures which contradicted their claims to have improved. This was particularly evident with results from the only objective measure published, the Six Minute Walk Test, which frequently contradicted any reasonably good subjective ratings given for the Primary Outcome Measures. At outcome, the mean walk distance of >90% participants in all groups did not match the walking ability of an average, healthy person in their seventies. Only two participants reached the Casanova et al (2011) average for 40-49 year olds and one of those was in the control group.

Furthermore, 50% of participants in the control group improved five times more than 50% of either the CBT or GET groups with the CFQ and ten times more for the SF36 physical function measure. This difference was more than three times larger than the supposed overall ‘treatment effect’ of CBT and GET.

Therefore it is false and misleading to claim that “CBT is an evidence-based therapy for CFS/ME”, and imply that this therapy can, “reduce the levels of symptoms, disability and distress associated with CFS/ME”. The PACE Trial data shows unequivocally that CBT does not reduce the levels of patient’s symptoms or disability.

It is false and misleading to claim that, “GET is an evidence-based professionally mediated approach to CFS/ME”, thereby implying that this therapy can treat or benefit patients with CFS. The PACE Trial data shows unequivocally that GET made no difference to participant’s symptoms or disability compared to normal medical care. Most significantly, one year of exercise therapy only produced a sub-clinical advantage in walking ability and left >90% of GET participants unable to match the walking ability of an average healthy person in their seventies.

REFERENCES


Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53


APPENDIX 1

Hoffman et al evaluated fatigue in 196 myasthenia gravis patients with the CFQ and reported a mean rating of 15.6(6.2). The PACE Trial Protocol states that a Bimodal CFQ score of 3 or less, is a “threshold having been previously shown to indicate normal fatigue”. This converts to a median of ~12 in Likert scoring (0 to 33). Pouchot et al (2008) state that the CFQ has a “minimal clinically important difference” (MCID) of 9.9 in rheumatoid arthritis. Goligher et al (2008) found that the MCID with the CFQ was 7.0 (95% CI) in patients with systemic lupus erythematosus. Pettersson et al (2015) estimated the MCID with the CFQ was 9.42 (95% CI) in patients with systemic lupus erythematosus. Van Kessel et al was a clinical trial of CBT (n=35) and Relaxation Therapy (RT. n=37) for Multiple Sclerosis patients. 72 matched healthy controls had a mean CFQ score of 12.5 (5.24).

References


APPENDIX 2
Ruta et al, carried out a test-retest reliability study of the SF36 in 233 British rheumatoid arthritis (RA) patients, representing 4 classes of RA with an average age of 56 and mean SF36 physical function score of 31. Ruta et al (1998) found that the "Size of individual SF-36 score difference with 95% confidence" is 23.8. Steffen and Seney (2008) studied 36 parkinsonism patients whose mean physical function score was 57 (SD.23) and determined that the minimal detectable change with 95% confidence was 28. Stulemeijer et al (2004) found that their adolescent control participants on the ‘waiting list’ for CBT, had 10 points improvement with the SF-36 physical function subscale at five months, which is 2 points higher than White et al's (2011) claim for a “clinically useful difference” rating. Population norms are 92.5 for no long-standing illness and 78.3 for those reporting long-standing illness (Jenkinson et al. 1993).

References


Thank you for your response.
Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic
Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

<table>
<thead>
<tr>
<th>Royal Liverpool University Hospital, CFS/ME services</th>
<th>Yes</th>
<th>No new evidence base</th>
</tr>
</thead>
<tbody>
<tr>
<td>I believe that there should urgently be additional information added to section 1.2.2 on the assessment of people with CFS/ME and to the NICE pathway.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Thank you for your response.
Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

<table>
<thead>
<tr>
<th>PoTS UK</th>
<th>No</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>If there is a definite plan to update the guideline within the next year (not clear from proposal) then the decision may be acceptable.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Thank you for your response.
Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

<table>
<thead>
<tr>
<th>Royal College of Paediatrics</th>
<th>Yes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>If there is a definite plan to update the guideline within the next year (not clear from proposal) then the decision may be acceptable.</td>
<td></td>
<td></td>
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</table>

Thank you for your response.
Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Studies, reviews and surveys published since 2007 have reported that CBT and GET have only mild to moderate benefits in people with ME/CFS (e.g. Malouff JM et al. Clin Psychol Rev 2008;28:736–45; ME Association 2015; ME/CFS Illness Management Survey Results; Wearden et al. BMJ 2010;340:c1777; White et al. Lancet 2011;377:823–36).

Furthermore, there is growing evidence that GET is associated with a significant worsening of symptoms in a large number of people (e.g. Kindlon T. Bull IACFS ME 2011;19:59–111; ME Association 2015; ME/CFS Illness Management Survey Results).

In summary, the main treatment recommendations of the 2007 NICE guideline are either ineffective for the great majority of people with ME/CFS (in the case of CBT), or may be causing actual harm (in the case of GET).
<table>
<thead>
<tr>
<th>North London ME Network</th>
<th>No</th>
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</thead>
<tbody>
<tr>
<td><strong>The guideline badly needs updating. It is not acceptable to our members that the main treatments offered to people with ME/CFS on the NHS are graded exercise and CBT.</strong></td>
<td></td>
</tr>
<tr>
<td>The North London ME Network was founded in 1992 and represents and assists patients with this condition in north London. The feedback we have received from our members is that graded exercise (GET) either results in no improvement in the condition or it makes people worse, on occasion very substantially worse. A few members have found CBT helpful, but some found it ineffective or harmful.</td>
<td></td>
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<tr>
<td>One of our members went through a graded exercise programme combined with CBT which led to a major and permanent deterioration in her condition, to the extent that afterwards she could no longer walk at all and years later is still housebound. It is shocking that treatments which have the capacity to harm patients so significantly are still being recommended for people with ME/CFS.</td>
<td></td>
</tr>
<tr>
<td>The sickest member in our organisation died at age 48 from complications of ME, having spent years in a nursing home unable to sit up, speak, digest solid food or have normal bowel movements. He had, before he deteriorated too much, been hospitalised twice and each time came out of hospital sicker than he went in because the staff simply did not understand his condition or listen to his needs. He was put through an inpatient graded exercise programme which contributed to his further decline.</td>
<td></td>
</tr>
<tr>
<td>ME/CFS is a condition into which far too little physiological research has been carried out in the UK. But research does increasingly suggest that the ME/CFS label covers a number of subgroups, and it has been shown that these can be identified by differing gene expression profiles. It is clear to us from the experience of our members that if exercise programmes are to be continued for patients with ME/CFS there must first be research examining which subgroups, if any, may benefit from graded exercise/CBT programmes and which may be harmed. Whether the individuals who can benefit from GET are a specific subtype of ME or whether they are simply further along the road to recovery already needs to be established before any more patients are put through such programmes with the inevitable outcome that some will deteriorate as a result.</td>
<td></td>
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</table>

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
We are aware that some people with ME/CFS do benefit to some extent from carefully structured exercise programmes. We would draw NICE’s attention to the US researcher and ME specialist Dr Nancy Klimas, renowned for her work in this field, who uses a very specific and individually tailored exercise/activity programme with her patients. The programme is administered only after the patient has been through thorough physiological testing and is only carried out by a specially trained physiotherapist. In-depth physiological testing is never or very rarely offered to patients with ME/CFS in this country and we feel that this is a major mistake. We would recommend the NHS investigates the Klimas programme and considers it for use in the UK.

We would also point out that in the absence of any effective help from the NHS some of our members have tried a number of complementary therapies. One member reported that she would be unable to get out of bed without Co-enzyme Q10 and magnesium supplementation, which is part of a programme recommended by the British ME specialist, Dr Sarah Myhill. Others have been helped by herbal medicine, acupuncture and the Perrin osteopathic treatment for ME.

But unfortunately it seems that none of these therapies can be prescribed by the NHS, so many of our members cannot afford approaches which could ameliorate their symptoms and improve their functioning. Instead all they are offered – if they are offered anything at all - is an approach which makes a significant minority worse – sometimes permanently - and leads to no ongoing improvement for the majority. This is a totally unacceptable situation with an illness which places such a burden on this country, both in terms of patient suffering and cost to the state due so many being unable to work for long periods.

Finally, we note that the US CDC has dropped GET and CBT from its list of recommended treatments for ME/CFS. We very much hope NICE recommends the NHS follows suit.

### Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

<table>
<thead>
<tr>
<th>Association of British Neurologists</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurologists in the UK are not usually involved with the diagnosis and management of CFS/ME but we do see many patients with this condition when it overlaps with other neurological presentations. The Association of British Neurologists also takes an interest in the disorder as one that is common, disabling and distressing and involves abnormal nervous system functioning.</td>
<td></td>
</tr>
<tr>
<td>It will be important at some stage to update the guideline to take into account data from several large trials including the PACE trial and the GETSET trial. These tend to strengthen the view expressed in the original guideline that Graded Exercise therapy and Cognitive Behavioural Therapy are moderately effective, and do help some people with CFS, including some that make a recovery.</td>
<td></td>
</tr>
<tr>
<td>In addition there are several papers which show that outcomes in routine clinical practice are similar to those seen in trials. The latter study shows that the outcomes are better in the Netherland than the UK. A very recent evaluation of specialist services across the UK was conducted, for example, of 440 patients at 1 year again showing that outcomes are similar to those seen in trials.</td>
<td></td>
</tr>
</tbody>
</table>

Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
<table>
<thead>
<tr>
<th>FORWARD-ME</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Appendix C</strong>: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53</td>
<td>10 of 209</td>
</tr>
</tbody>
</table>

Such studies also reinforce the idea that recovery does occur in some patients even though in others it remains a chronic condition.


We respect the authority of NICE to evaluate current evidence on its own terms, and we respect the authority that underlies its conclusion that recent research offers no substantial challenge to the current guideline. We suggest, however, that NICE exceeds its authority in assuming that patients, physicians and mental health practitioners need only be informed of its own evaluation of research. For this reason we request revisions of the current guideline so that it presents a truthful, neutral picture of debate among respected authorities about the nature and optimal management of CFS/ME.

Our request is based on two central ethical considerations. (1) We submit the current guideline fails to respect “patient choice”, and “the right of individuals to make informed choices about healthcare (NICE – Social Value Judgments 2.1)

No information is more important to any patient who pursues medical care for symptoms than the fact that their condition is understood by some respected health authorities to require biological testing, treatment and physician support. For this reason (barring unusual cases of therapeutic privilege) there is no situation in which this information is not of material importance to a patient with CFS/ME. Similarly, while we respect NICE’s interpretation of recent research on CBT and graded exercise therapy (GET), no reasonable person would imagine that a patient gives informed consent to these interventions without knowledge that some respected health authorities conclude (a) that there is “insufficient evidence to determine the effectiveness of CBT on the outcome of global improvement” (AHRQ, 2016 Addendum) and (b) that GET involves “potential harms” (HHS Chronic Fatigue Syndrome Advisory Committee 2015).

Thank you for your response.
Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
(2) We point out the “legislation on human rights, discrimination and equality requires that patients are not denied access, or have different or restricted access, to NHS care because of their disability …or other status” (NICE – Social Value Judgments 6.0). Failure to inform physicians and mental health practitioners of the US conclusion that CFS/ME is a biological medical condition that requires biological care obstructs patients’ access to biological care. This obstruction singles out CFS/ME patients as somehow uniquely undeserving of access when facing a demonstrable possibility of need.

<table>
<thead>
<tr>
<th>Patient and Client Council</th>
<th>No</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Patients and service users are seriously concerned about existing guidelines. Please refer to our published Position Paper which outlines this: <a href="http://www.patientclientcouncil.hscni.net/uploads/research/ME-CFS_Position_Statement.pdf">http://www.patientclientcouncil.hscni.net/uploads/research/ME-CFS_Position_Statement.pdf</a></td>
</tr>
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Thank you for your response.

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<table>
<thead>
<tr>
<th>Inclusion London</th>
<th>No</th>
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<tbody>
<tr>
<td></td>
<td>Inclusion London believes that NICE guidelines should updated following a full independent review of the current data as recommended by Dr Charles Bernard Shepherd,</td>
</tr>
<tr>
<td></td>
<td>Dr Shepherd says in his paper: ‘….However, patient evidence has repeatedly found that cognitive behaviour therapy is ineffective and graded exercise therapy can make the condition worse. The PACE trial methodology has been heavily criticised by clinicians, academics and patients. A re-analysis of the data has cast serious doubts on the recovery rates being claimed. The trust of patients has been lost. The medical profession must start listening to people with myalgic encephalomyelitis/chronic fatigue syndrome if trust is going to be restored.’</td>
</tr>
<tr>
<td></td>
<td>Please see his paper at: <a href="http://journals.sagepub.com/doi/pdf/10.1177/1359105317703786">http://journals.sagepub.com/doi/pdf/10.1177/1359105317703786</a></td>
</tr>
<tr>
<td></td>
<td>We believe the review should also include data from ‘experts by experience’ i.e. those with chronic fatigue syndrome and M.E. such as the survey conducted by Action for M.E. mentioned below.</td>
</tr>
<tr>
<td></td>
<td>Inclusion London has been contacted by people with M.E. raising concerns that NICE does not intend to update the guidance. We believe that NICE should be listening to ‘experts by experience’</td>
</tr>
<tr>
<td></td>
<td>People with M.E. feel so strongly that the NICE guidance needs reviewing that a petition has been started: <a href="https://www.change.org/p/petition-the-nice-guideline-for-cfs-me-is-unfit-for-purpose-and-">https://www.change.org/p/petition-the-nice-guideline-for-cfs-me-is-unfit-for-purpose-and-</a></td>
</tr>
</tbody>
</table>

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
At the time of writing the petition had nearly 14,000 supporters.

Action for M.E. surveyed 2000 people with M.E (i.e. experts by experience). The survey results showed that nearly half of those that had tried GET or GAT made them a bit or much worse, see more details below:

Of those that had tried GET (23%):

- 35% said they found it helpful or very helpful, 18% said it resulted in no change, and 47% said it made them a bit or much worse.

Of those that had tried GAT (15%)

- 48% said they found it helpful or very helpful, 19% said it resulted in no change, and 34% said it made them a bit or much worse.


There are many papers by academics questioning the legitimacy of the PACE trial:

For instance:

- **PACE-GATE: An alternative view on a study with a poor trial protocol** (Bart Stouten)
  http://journals.sagepub.com/doi/pdf/10.1177/1359105317703787

- **PACE investigators’ response is misleading regarding patient survey results** (Karen D Kirke).
  http://journals.sagepub.com/doi/pdf/10.1177/1359105317703787

- https://www.researchgate.net/publication/309351210_Studies_on_Cognitive_Behavioral_Therapy_and_Graded_Exercise_Therapy_for_MECFS_are_misleading

The conclusions in the paper, ’Can patients with chronic fatigue syndrome really recover after graded exercise or cognitive behavioural therapy? A critical commentary and preliminary re-analysis of the PACE trial’ (2016) were,

‘The claim that patients can recover as a result of CBT and GET is not justified by the data, and is highly misleading to clinicians and patients considering these treatments’.

Authors Carolyn Wilshire, Tom Kindlon, Alem Matthees and Simon McGrath. The paper is available at: http://www.tandfonline.com/doi/full/10.1080/21641846.2017.1259724

Concerns have been raised that Graded Activity Therapies (GAT) and Graded Exercise Therapies (GET) do more harm than good, see the following papers by Tom Kindlon:
### Mast Cell Action

**No**

I believe that there should be additional information added to section 1.2.2 on the assessment of people with CFS/ME and to the NICE pathway.

**Royal College of Psychiatrists**

**Yes**

We support the view that the guideline on chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) should not be updated. The surveillance was brought forward to 2017 following a challenge based on potentially important new evidence. Evidence from a total of 155 reports was assessed by the surveillance team and topic experts. We found that the reporting of how the assessments were undertaken was rigorous and transparent; for example the controversy over

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<table>
<thead>
<tr>
<th>The ME Association</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>The ME Association is shocked and surprised to learn that the expert group appointed by NICE to review all new relevant research evidence on clinical assessment, diagnosis and management of ME/CFS has concluded that there is no need to review or update the 2007 NICE guideline (CG 53) on ME/CFS.</strong></td>
<td></td>
</tr>
<tr>
<td>The MEA consistently takes the position that key parts of the 2007 NICE guideline on ME/CFS are unfit for purpose. In particular, recommendations relating to the use of cognitive behavior therapy (CBT) and graded exercise therapy (GET) for everyone with mild or moderate ME/CFS are inappropriate and need to be revised.</td>
<td></td>
</tr>
<tr>
<td>We believe this is also the position taken by the vast majority of people with ME/CFS. We therefore published an online petition supporting our position and are carrying out an MEA website survey that gives people an opportunity to support the NICE guideline on ME/CFS if they wish to do so.</td>
<td></td>
</tr>
<tr>
<td>The MEA petition, calling for a review of the guideline, opened on Monday 10th July. This has attracted over 14,000 signatures in less than two weeks. The petition can be viewed here: <a href="https://www.change.org/p/petition-the-nice-guideline-for-cfs-me-is-unfit-for-purpose-and-needs-a-complete-revision?recruiter=744708136&amp;utm_source=share_petition&amp;utm_medium=copylink&amp;utm_campaign=share_petition">https://www.change.org/p/petition-the-nice-guideline-for-cfs-me-is-unfit-for-purpose-and-needs-a-complete-revision?recruiter=744708136&amp;utm_source=share_petition&amp;utm_medium=copylink&amp;utm_campaign=share_petition</a></td>
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<tr>
<td>The wording and current results from the MEA website survey, which opened on Tuesday 11th July, are as follows:</td>
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**Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53**

| **PACE data was discussed and the PACE data was set aside when considering other evidence from RCTs and systematic reviews. The results of these other studies remained in-line with NICE guidelines on GET and CBT.** |
| **Graded Exercise Therapy (GET) is shown to reduce post-exertion fatigue more than control treatments (White et al 2011), and Graded Exercise Self-help (GES) is also shown to be a safe treatment that may reduce fatigue (Clark et al 2017).** |
| Several recent papers show that outcomes in routine clinical practice are comparable to those seen in trials (Stahl et al 2013; Worm-Smeitink et al 2016). The latter study shows that the outcomes are better in the Netherlands than the UK (Worm-Smeitink et al 2016). An evaluation of specialist services country wide following current NICE guidelines on assessment and treatment was conducted (Collin & Crawley 2017), showing significant benefit for around a third of patients a year after treatment. |
| On these grounds we can see no rationale for updating the current NICE guideline on chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy). |

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Thank you for your response. Note that, in line with the **guidelines manual**, Committee members and topic experts for the published guideline are surveyed for their opinions on the relevance of the published guideline, recent developments in the topic area and their knowledge of any new important evidence since publication of the guideline. This intelligence is considered alongside the new evidence identified through the surveillance review. However, the decision to update or not update a guideline remains with NICE’s Guidance Executive. This is the case for all surveillance review topics. |

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
Do you think the NICE guideline for CFS/ME is working for you?

- Yes - I think it is (0%, 2 Votes)
- Yes - but it could be better (1%, 3 Votes)
- No - I think it needs a minor review (1%, 7 Votes)
- **No - I think it needs a major review (95%, 565 Votes)**
- I am not sure (1%, 4 Votes)
- What's the NICE guideline? (3%, 16 Votes)

Total Voters: **597** (at 4pm on Friday 20 July)

MEA website link: [www.meassociation.org.uk](http://www.meassociation.org.uk)

The principle reason we believe the NICE guideline must be reviewed is because it is no longer ethical to produce a ‘one size fits all’ guideline to the management of ME/CFS. The current guideline basically consists of recommending CBT and/or GET for everyone with mild or moderate ME/CFS. However, it fails to acknowledge differing views on both the value and potential harm that can occur when these two treatments are used as primary interventions for the majority of people with ME/CFS.

We also have a number of other reasons, especially in relation to assessment and management of people with severe ME/CFS. These are set out in our response to question 2.

Ethically speaking, we believe the only way forward is for NICE to revise the 2007 guideline on ME/CFS to ensure that:

(a) physicians and patients are fully informed about the reality of the international debate on the acceptability, effectiveness and safety of CBT and GET

(b) people with ME/CFS are provided with information and guidance on approaches to management that they consistently report as being helpful and

(c) there is meaningful information and guidance on the assessment and management of people with severe ME/CFS.

The current UK guidance from NICE on the management of ME/CFS is 'stuck in the past', is unethical, and is not acceptable to the patient community.

If this unethical position continues following the stakeholder consultation process, The MEA will be left with no option but to continue to campaign for the NICE guideline to be reviewed.

<table>
<thead>
<tr>
<th>Action for M.E.</th>
<th>No</th>
<th>Action for M.E. strongly disagrees with the proposal not to update the guideline for the following reasons:</th>
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<tbody>
<tr>
<td>Thank you for your response.</td>
<td></td>
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Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53
1. There is not, at the present time, a conclusive evidence base for treatments for CFS/M.E., including those recommended in the guideline, such as CBT and/or GET.

2. The current evidence base has led major international health agencies, including the Centers for Disease Control and Prevention in the US, to alter their guidance regarding CBT and GET.

3. NICE has an ethical obligation to present a full, accurate and balanced picture of current international clinical practice when it comes to managing and treating CFS/M.E. The existing guideline does not do this.

We provide further details on each of these points below.

1. There is not, at the present time, a conclusive evidence base for treatments for CFS/M.E., including those recommended in the guideline, such as CBT and/or GET.

The guideline must reflect that there is a mixed evidence base for its treatment recommendations of CBT and GET.

The research published since the last review of this guideline has provided a range of different findings. Whilst there have been some which may support the recommendations in CG53, others challenge those recommendations. There is no consensus.

The current guideline states that “Cognitive behavioural therapy (CBT) and/or graded exercise therapy (GET) should be offered to people with mild or moderate CFS/M.E. and provided to those who choose these approaches, because currently these are the interventions for which there is the clearest research evidence of benefit” [NICE 2007, CFS/ME: Diagnosis and management]. The guideline does not offer further information on the quality, quantity and validity of this research evidence.

As outlined in the NICE proposal, the data from the PACE trial is currently part of an ongoing debate over the quality of the trial. The meta-analysis Cochrane review on GET [Larun et al 2017, Exercise therapy for chronic fatigue syndrome] concludes that there is a significant effect on fatigue and physical functioning only when the PACE data is included. The review also recognises the “considerable heterogeneity” in results across all trials, and recommends further research to explore this.

Other reviews have concluded that exercise for patients with CFS/M.E. can be harmful [Twisk 2017, Dangerous exercise. The detrimental effects of exertion and orthostatic stress in Myalgic Encephalomyelitis and chronic fatigue syndrome, Physical Medicine and Rehabilitation Research Vol 2(1)], indicating that risks of potential harm should be considered when determining appropriate treatment for patients with CFS/M.E. The heterogenous results outlined in the Cochrane review (2017) also indicate that sub-groups of patients are either not benefitting from, or are reacting adversely to, GET.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
The Cochrane review on CBT [Price et al 2008, *Cognitive behaviour therapy for chronic fatigue syndrome in adults*] does not include data from PACE, and states that the evidence base is "limited to a small group of studies", and that there is "a lack of evidence on the comparative effectiveness of CBT alone or in combination with other treatments."

The NICE proposal states that the 'direction of effect' is consistent across the evidence base, showing improvement for some patients following CBT or GET intervention. The proposal further states that, should the PACE data be downgraded or set aside in a new review, other evidence from RCTs and systematic reviews shows benefits from CBT and GET.

The guideline's core recommendation on treatment, that CBT and/or GET should be offered to people with mild or moderate CFS/M.E. does not acknowledge that the results for these treatments are disputed. The guideline ought to reflect that there is a mixed evidence base for these treatments. They can help some patients, but the results demonstrating this are heterogeneous and not significant, except when a trial which is currently subject to scientific scrutiny as to the validity of its results is included.

2. The current evidence base has led major international health agencies, including the Centers for Disease Control and Prevention in the US, to alter their guidance regarding CBT and GET.

Major international health agencies in the US have altered their guidance, demonstrating the lack of consensus resulting from the evidence base, which has led to varying policy and practice in the management and treatment of CFS/M.E.

We comment above on the mixed evidence base for efficacy of CBT and GET and our concern that the NICE proposal to maintain CG53 without updating means excluding up-to-date information about the current body of research regarding best clinical practice for patients with CFS/M.E. The mixed (and developing) evidence base is fostering ongoing debate in the academic and clinical community over what forms of intervention ought to be recommended for patients and treatment guidance is changing as a result in other parts of the world.

US health agencies, such as the Centers for Disease Control and Prevention, have changed their guidance on the condition to remove references to CBT and GET [Centers for Disease Control and Prevention, *Myalgic Encephalomyelitis/Chronic Fatigue Syndrome*, https://www.cdc.gov/me-cfs/index.html accessed 21 July 2017] and the New York State Health Commissioner recently informed clinicians that CBT/GET were recommended “in the past” [https://drive.google.com/file/d/0B37JHmPXER6JZkZRd0hIalA2bUE/view accessed 21 July 2017]. These changes in policy and practice signal a divergence in what conclusions can be drawn from the evidence base with regard to treatment and management approaches.

The changing stance of US medical agencies has occurred since the 2015 Institute of Medicine report, *Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: redefining an illness* [Institute of Medicine 2015, *Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an*...
### Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

“illness, National Academies Press]. This report proposed tighter diagnostic criteria, and concluded that “it is clear from the evidence compiled by the committee that M.E./CFS is a serious, chronic, complex, multisystem disease that frequently and dramatically limits the activities of affected patients.” These conclusions have resulted in US practice moving away from the behavioural treatments that were advocated previously.

It is not a question of one agency being right, and another being wrong. The reality is that it would be unethical to maintain a NICE guideline that fails to inform patients of the range of views on biological care and management strategies for CFS/M.E.

The current CG53 was issued in 2007 when there was a greater consensus around recommended interventions. The context is now much changed, and continuing to recommend CBT and/or GET without mentioning that there is not a clinical consensus around their efficacy is to provide incomplete guidance to clinicians and misrepresent current international practice to patients.

3. NICE has an ethical obligation to present a full, accurate and balanced picture of current international clinical practice when it comes to managing and treating CFS/M.E. The existing guideline does not do this.

Not acknowledging the inconclusive and disputed evidence of the effectiveness of CBT and GET has serious implications for patients accessing medical care and for clinicians obtaining informed consent.

Medical ethics place a duty on health organisations to ensure that patients can access healthcare, even in cases where there is diagnostic uncertainty. Care cannot be withheld due to uncertainty over what form of care would be most appropriate and effective for the patient. Additionally, patients have a right to autonomy, exercised through informed consent to a particular health intervention.

These ethical principles are endorsed in NHS England’s Core Principles. [NHS Core Principles, http://www.nhs.uk/NHSEngland/thenhs/about/Pages/nhscoreprinciples.aspx, accessed 21 July 2017] Principle 1 states that “the [NHS] is designed to diagnose, treat and improve both physical and mental health. It has a duty to each and every individual that it serves and must respect their human rights.” Principle 4 states that “patients… will be involved in and consulted on all decisions about their care and treatment.” This right to consultation is further enshrined in NHS policy on Shared decision making. [NHS, Shared Decision Making, https://www.england.nhs.uk/ourwork/pe/sdm/, accessed 21 July 2017]

In Appendix A of the NICE proposal, under Shared decision-making 1.1.1.1 it is stated, that in order to ensure shared decision-making, the healthcare professional should “provide information about the range of interventions and management strategies as detailed in this guideline.” If there is additional information that is not detailed in the guideline, then professionals could be in the situation of acting in accordance with the guideline but not complying with NHS England’s Core Principles.
In accordance with the NICE guideline as it stands, a clinician would recommend CBT and/or GET as the best-evidenced interventions and the patient may agree to take part in these interventions. In such a situation, the patient is not being told all the relevant information that would impact on their decision when consenting to these treatments. The patient is not aware that:

- a meta-analysis of the overall body of evidence produces significant results in favour of GET only when the data from a disputed trial is included; the PACE trial is sufficiently disputed that the NICE proposal accounts for the possibility of these results being downgraded or set aside
- the overall body of evidence in favour of CBT, in its most up-to-date Cochrane review, is not significant
- medical agencies internationally have considered this evidence base and produced conflicting guidance.

This information is sufficiently significant that it can be reasonably concluded that the patient is not able to give informed consent in making this decision. It also contravenes the NICE consensus statement on shared decision making [NICE, Shared Decision Making Collaborative: A consensus statement, https://www.nice.org.uk/Media/Default/About/what-we-do/SDM-consensus-statement.pdf accessed 21 July 2017] which states patients should be able to have “informed preferences”, based on the “options, outcomes and uncertainties” of care or treatment options.

Furthermore, when the patient is not informed of alternative care interventions, their access to these interventions is effectively withheld.

In giving an unconditional recommendation of CBT and/or GET, the guideline precludes the provision of other healthcare approaches, such as biological care in the form of pharmacological treatments for individual symptoms or other techniques for managing symptoms. Given the international difference over recommended approaches, patients have a right to access these alternatives as a means to improving their condition. Inasmuch as the guideline does not acknowledge these alternatives, a patient is prevented from accessing this potentially beneficial healthcare. In this way, the current NICE guideline could prevent patients from improving their health.

In recommending CBT and GET as interventions, and not providing more information on alternatives, the guideline is also missing an opportunity to embed a personalised medicine approach in the treatment of CFS/M.E. As stated above, it is unethical to withhold access to treatments that may improve the health of patients. Suggesting a range of treatments, and acknowledging that their efficacy varies in different patient groups, increases the likelihood of a patient accessing a course of treatment that will be effective for them. In continuing to recommend CBT and/or GET for patients in a ‘one size fits all’ approach, the current guideline limits the likely effectiveness of treatment for patients, as only the sub-group which responds positively to these treatments will see their health improve.

In Wales, the NHS is adopting principles of prudent healthcare to ensure greater value from healthcare systems for patients. An underlying principle is that "any service or individual providing a
service should achieve health and wellbeing with the public, patients and professionals as equal partners through coproduction.” [Welsh Government, Prudent healthcare, http://gov.wales/topics/health/hhswnes/prudent-healthcare/?lang=en accessed 21 July 2017] It is difficult to see how this can be achieved if the NICE guideline does not provide either clinicians or patients with the current international understanding to underpin decision-making.

The guideline states that CBT and GET are currently “the interventions for which there is the clearest research evidence of benefit.” This is largely down to a lack of research on alternative approaches. For example, many patients with CFS/M.E. report that pacing is helpful in managing their condition. Action for M.E.’s 2014 patient survey found that 85% found pacing helpful, 12% found it made no change and 4% said their condition got worse (cf. 54%, 34%, and 12% for CBT and 48%, 19%, and 24% for GET respectively) [Action for M.E. 2014, M.E.: Time to deliver, https://www.actionforme.org.uk/uploads/pdfs/me-time-to-deliver-survey-report.pdf], CG53 acknowledges this patient opinion, but states that healthcare professionals should advise patients that “there is insufficient research evidence on the benefits or harm of pacing.” The guideline ought to identify alternatives to CBT/GET as an area for further research in order to ensure that there is a well-rounded evidence base. This is particularly the case given the disputed nature of evidence on CBT and GET, and that US medical agencies have recommended management approaches such as pacing based on patient experience.

The strength of patient feeling regarding CG53 is demonstrated through a petition [http://bit.ly/2zbXlmM, accessed 21 July 2017] which has gained more than 14,000 signatures as of 21 July 2017 and calls for a full review of the guideline. The experiences of people with CFS/M.E., both in the UK and internationally, support that CBT and/or GET treatments do not constitute an appropriate universal approach to effectively managing the condition and indicate the need to consider a wider range of biological treatments and other management approaches that, altogether, will offer the best efficacy in improving the health of patients.

Reissuing the 2007 guidance makes it difficult for patients and clinicians to be aware of the current international context in managing M.E and make informed decisions about patient care. There is an obligation to inform patients there is not unanimity in the medical field regarding treatment and management approaches. Informed consent is not in place if healthcare professionals and patients are not comprehensively aware of the current medical position, and patients are being denied access to biological medical care or other management approaches if they are not being made aware of other options which could be potentially beneficial to their health.

British Association for CFS/ME

We thank you for the opportunity to comment and for the rigorous and comprehensive ten-year surveillance report. We appreciate that NICE wishes to wait on the possibility of a further Cochrane review on CBT, incorporating the PACE trial, and other evidence, before considering whether to review the guidance. However, we would urge NICE to commit now to a comprehensive review and updating

Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic
of guidance CG53, for the reasons detailed below. Our comments are restricted to adult patients. Given the time constraints, we have listed key references only.

1. The surveillance review describes a substantial amount of research published in the past 10 years, and further key research has been published since the end of that review (Jan 2017). As practitioners working with patients affected by this serious and debilitating condition(s), the past decade of research has developed our understanding of the disorder and its management. Thus, we must disagree with NICE when you assert that all of this research is either wholly consistent with or not deemed to impact recommendations developed in 2007. We are concerned that this sends an erroneous message to patients, healthcare practitioners, researchers, commissioners, and others such as benefit assessors.

2. Members of BACME are doctors, psychologists, therapists, nurses, and others who are dedicated to supporting patients with CFS/ME, so we are deeply concerned by continuing controversies, misperceptions, and other issues that surround these disorders. It is significantly difficult for patients, and practitioners, dealing with illness that is not well defined nor well understood, and that has no specific treatment available aimed at bio-pathological processes. We believe that NICE is best placed to attempt to clarify what can be agreed on and what remains uncertain. We believe that avoidance of the issues pertaining to diagnostic criteria and potential aetiologies does not best serve the patients and their health professionals. We are not expecting NICE to fully resolve such issues, but we feel it vital to acknowledge their existence, and to do so within the guidance document that most people read. It is not sufficient that these discussions are embedded in large technical review documents.

For example, we would favour including something akin to the following information:

Various diagnostic criteria exist for post-viral fatigue syndrome (PVFS), CFS, ME and other syndromes. Each set of criteria defines different populations though they overlap. We do not know whether these represent different disease entities, a disease spectrum, or similar final common pathway(s) of disease and this awaits further advances in aetiological understanding. It is likely that some people diagnosed with CFS/ME have alternate primary diagnoses (one example, as supported by published and unpublished evidence is that joint hypermobility syndrome (Hypermobile Ehlers-Danlos Syndrome) is substantially prevalent in CFS/ME populations (Nijs et al. J Manipulative Physiol 2006; 29: 32-39 and paediatric studies). NICE criteria 2007 were developed from evidence, and aim to provide practical criteria that are useful for healthcare provision. It is vital that such criteria are neither too inclusive nor too restrictive. Research requires more specific criteria and we favour analyses in intervention trials that explore more than one definition.

Further work on diagnostic criteria or adoption of new criteria such as SEID (systemic exertion intolerance disorder) is likely to cause more confusion and uncertainty. Instead, we await potential biomarkers to guide disease definitions. However, we recognise that PVFS, ME, and Fatigue, Not otherwise specified, are distinguished differently in the ICD-10 and this may have impacts. Research has variously indicated CNS and autonomic abnormalities, chronic immune activation, and psychosocial factors, such as traumatic life events, which may be involved

fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
in pathogenesis, though this seems likely to vary between patients. We therefore advocate moving away from an organic versus functional dichotomy and instead describing the likelihood of neuropsychoimmunological interactions. Recent additional analysis from the PACE trial has identified 5 potential subgroups (Williams et al. Psychol Med 2017; 47; 1454-65). Together with clinical experience, we can recognise several archetypal phenotypes – PVFS, ‘pure’ CFS with good efficacy (both likely to involve less impairment and better prognosis); CFS/ME with comorbid mood disorders (more likely history of childhood trauma); a group with multiple comorbidities which fits criteria for ME symptoms (and is likely to have most severe impairments and poorer prognosis); plus a mixed group. We note the description of an avoidant-inactive group but note the possibility that underdiagnosed or not yet described pathologies, such as joint hypermobility syndrome, and disorders of muscle and energy metabolism might indeed cause certain activities to be harmful. We also acknowledge that a purely physical understanding of any disease is restrictive, that this may hamper GP diagnosis, and recovery, so we favour a biopsychosocial model, which is consistent with interventions offered as rehabilitation rather than treatment.

3. We would urge NICE to consider providing summary detail to support certain recommendations. We note the first recommendation (1.1.1.1) that healthcare professionals provide information on CFS/ME and interventions. Yet, this information is not specified fully, can be complex and subject to interpretation, and research, and our experience suggests that many GPs feel ill-equipped in this respect. For example, we would like to see a more extensive description of intervention effects. Population studied, nature of interventions, effect size, number needed to treat, serious adverse events, etc. are important measures that would be given in other NICE guidance and reviews. Debate over the PACE trial in particular has highlighted the complexity of defining outcomes, especially with variable diagnostic criteria used in trials. As practitioners, we need to be able to communicate what a particular research outcome might mean in terms of clinical impact for the patient. Given also the significantly variable natural history of CFS/ME, we support a more general outcomes approach, including evidence from PROMs, and that utilised by Collin and Crawley (BMC Health Serv Res 2017; 17:488), which questioned patients in 11 specialist centres as to whether they were ‘very much or much better’, ‘a little better’, ‘no change’ ‘a little worse’, ‘worse or very much worse’. We would favour intervention trial data presented in this stratified way so that patients and practitioners can understand the proportions likely to benefit or worsen. This would also allow meaningful comparisons between trials.

4. Current estimates suggest that around 8000 patients are seen in specialist services, so the majority of patients seen by health services are under GP care. Specialist service provision is unequal depending on geographical area and severity of disability. Evidence shows that many GPs have uncertainty over making a diagnosis (Chew-Graham C et al. BMC Family Practice 2010; 11:16;) which we find unsurprising given the complexities involved, whereas a major part of specialist medical care involves making a diagnosis or diagnoses (Broughton J et al. BMC Family Practice 2017; 17: 384). We also note recent evidence that patients diagnosed with CFS/ME have been seen with increased frequency for some years prior to diagnosis. (Collin et al. BMC Family Practice 2017; 18: 60). This is critical evidence
of an increased burden on primary care, which increases further immediately following diagnosis. We suggest that earlier suspicion of CFS/ME is needed, and NICE may wish to consider recommendations regarding tools for information provision and training for GPs (Bayliss K et al. BMC Family Practice 2016; 17:66). We note that GPs feel they can play a particularly important role in excluding other conditions. (Bayliss K et al. BMC Family Practice 2014; 15: 44). We suggest that NICE reviews section 1.3.1.1 as GPs may or may not be able to make an early diagnosis, depending on circumstances, resources, and skills. Moreover, we believe that referral to specialist care should not simply be guided by severity, but should also consider length of illness, diagnostic uncertainty, and comorbidities. It needs to be recognised that no interventions are recommended at present, for severely affected patients and those who do not recover. Long-term support services may not be commissioned for this group in primary or specialist care.

5. The section on specialist CFS/ME care needs some revision. Although BACME members are often involved in delivering CBT and GET, we believe the guidance and recommendations are too simplistic and do invite controversy. We would prefer a more open and detailed approach to describing intervention effects (as described above and found in various NICE documents on different conditions and interventions). We would urge that the guidance also includes the following points:

The rationale behind CBT and GET, and their delivery by clinicians with specialist training. Common misperceptions are that these are prescribed primarily to treat psychological issues or inactivity/avoidance of exercise. Instead, the goals are variable, but may be considered rehabilitative, depending on the patient’s clinical situation and social context. Goals may include assisting a person to maximise their efficacy, functioning, well-being, acceptance, and social inclusion.

The NICE guidance is relied upon for commissioning services. Thus we suggest that different evidence-based ways of delivering CBT/GET need to be detailed in the guidance (eg, groups, online) to guide commissioning. We are also concerned about the commissioning of CBT and GET as ‘pure’ services, not within a package of care or in accordance with the general principles of the guidelines (eg, adapted to patient circumstances and preferences). This may be due to the lack of detail regarding the evidence base in the guidance as many trials studied these interventions within specialist services and/or broader care packages.

It needs to be acknowledged that the impact of CBT and GET is variable in different patients, and we are concerned that noting the overall superiority of an intervention in a trial or systematic review does not provide comprehensive information for patients, practitioners advising those patients in primary care, and therapists delivering care. The PACE trial follow-up (Sharpe et al. Lancet Psychiatry 2015; 2: 1067-74) is difficult to interpret given that many but not all patients received further intervention. However, this may lend credence to the idea that a flexible and variable approach to what interventions are delivered and when, in specialist care, is likely to be of some help in a substantial proportion of patients.

Research and experience suggests that the proportion who will have some improvement is around two-thirds. This is in agreement with Collin and Crawley’s recent data, and previous findings, which we would paraphrase as roughly a third of patients will get better or very
much better, a third of patients experience some improvement, and a third, no change or worsening. In addition we consider that around 1-2 out of ten patients may recover, while the same proportion may get worse or much worse.

Outcomes in various therapeutic trials overall appear somewhat better than those from historical natural history studies. We understand the issues involved in such comparisons, but there is a need to acknowledge that outcomes remain far from desirable in all patients. We would appreciate greater understanding that it is common in research trials to study well-defined and specific interventions, but that clinical practice can utilise a more flexible and adaptive approach that is best suited to an individual patient and therapist.

The benefits of such an approach have been studied by Vos-Vromans et al in the FatiGo trial, which compared CBT with a multidisciplinary rehabilitation approach, which included elements of CBT but also mindfulness, body awareness therapy, pacing, and gradual activity increase, all delivered in a rehabilitative context. MRT was found superior to CBT alone in clinically meaningful ways (Vos-Vromans D et al. J Intern Med 2016; 279: 268-82). The experience of many BACME members supports the use of ‘third wave’ therapies, such as mindfulness, mindfulness-based stress reduction (MBSR), acceptance and commitment therapy (ACT) and compassion-based strategies, as part of a package that includes CBT/GET, adaptive activity planning, and other skills development.

6. Pharmacologic management. We question the particular highlighting of amitriptyline (1.6.3.2) and note the following references.


We also feel that rintatolimod (Mitchell WM. Expert Rev Clin Pharmacol 2017; 9: 755-70), rituximab (Fluge et al. PLoSOne 2015; 10: e0129898), and anakinra trials (Roerink et al. Ann Intern Med 2017; 166: 577-64) are worthy of mention, even though they are respectively, not licensed in the UK/EU for CFS/ME, lack sufficient evidence base at present, or have been proven ineffective.

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
- 29% of respondents stated that CBT improved/was helpful.
- 53% reported no change in their symptoms.
- While 18% reported a worsening of their symptoms after CBT therapy.

The Kirklees and Calderdale ME group have asked Healthwatch Kirklees to find out why there is a huge discrepancy between the results of large-scale patient surveys and the claims made for the effectiveness for CBT as promoted by the authors of the 2011 PACE trial. The use of CBT as a treatment for any/CFS patients could be seen by people who have ME as inappropriate and based upon scientifically flawed beliefs about the illness. Most patients who we spoke to who have undergone CBT treatment are told that the NHS uses a biopsychosocial model for the illness. Patients are expected to answer endless questions about their low mood or anxiety during therapy. As a matter of routine GP's prescribe anti-depressants for ME patients telling them this will improve their mood and consequently their illness will improve. Healthwatch Kirklees could not find any evidence that long-term treatment of ME/CFS patients with antidepressants will bring any improvement in their illness. Kirklees and Calderdale Independent ME Support Group calls upon NICE to withdraw CBT from its guidelines as a recommended treatment for ME/CFS.

**GET**

In our 2015 survey we addressed this issue of GET treatment as to whether it made people's illness more or less manageable.

- 6% of respondents reported that GET made their illness more manageable.
- 6% said it neither improved their symptoms nor made them worse.
- 40% of respondents said that GET made their illness less manageable.

This picture is supported by numerous large-scale patient surveys conducted by the two biggest ME medical charities in this country: the ME Association and Action For ME. Between 2001 and 2015 these two charities carried out five large scale patient surveys. (An analysis of these surveys is provided by Karen De Kirke in the Journal of Health Psychology, 1 May 2017.)

It is worth pointing out, that the Centres for Disease Control and Prevention, in the United States has updated its website information for ME/CFS and has removed previously recommended treatments such as CBT and GET.

**Diagnostics**

The current NICE guidelines state that a diagnosis for ME should be made after other possible diagnoses have been excluded and the symptoms of persisted for four months in an adult. In 2015 the Department of human health and five other federal agencies, the United States asked the Institute of Medicine (IOM) to develop evidence-based criteria for the diagnosis of ME/CFS. In its report, the IOM stated that: "Regarding the duration of the illness, the proposed criteria require six months to make a diagnosis. In light of evidence that most other causes of similar fatigue do not last beyond six months." Under the current NICE guidelines, there is a danger that people are being diagnosed with ME/CFS who do not have the illness. Feedback from Kirklees and Calderdale
| The 25% ME Group | No | We are strongly of the view that what is required, as of now, is for CG53 to be withdrawn. We say this in view of aspects of the content and the way that certain recommendations are being interpreted and applied in clinical practice; this continues to have significant adverse consequences for M.E. patients. We will substantiate this perspective in our further comments. Question: When reviewing a guideline / considering whether there is need for review, under what circumstances is it considered appropriate to take cognisance of the impact on patients of application of a guideline’s recommendations in clinical practice since publication? |

Independent Support Group would like to call upon NICE to adopt the IOM evidence-based criteria that requires a period of six months to make a diagnosis.

The majority of the group Healthwatch spoke to regarding the current NICE guidelines for making a diagnosis of ME/CFS, felt that the guidelines are too broad and fail to take into account the advances in scientific understanding of the illness. The Kirklees and Calderdale Independent ME Group would urge NICE to adopt the IOM evidence-based criteria for making a diagnosis of ME/CFS. It should be pointed out that the Centres for Disease Control and Prevention in the United States have now adopted the IOM criteria.

Please find these below:

"Diagnosis requires patient have the following three symptoms:
1. A substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social or personal activities, that persists for more than six months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong,) is not the result of ongoing excessive exertion, and is not substantially alleviated by rest, and
2. Post exertion malaise*
3. Unrefreshing sleep*

At least one of the two following manifestations is also required:
1. Cognitive impairment*
2. Orthostatic intolerance*

"Frequency and severity of symptoms should be assessed. The diagnosis of ME/CFS should be questioned if patients do not have the symptoms at least half of the time with moderate, substantial or severe intensity."

Thank you for your response. Regarding your specific questions:
Q When reviewing a guideline / considering whether there is need for review, under what circumstances is it considered appropriate to take cognisance of the impact on patients of application of a guideline’s recommendations in clinical practice since publication? The impact on patients of guideline recommendations is always an appropriate consideration in surveillance review decisions. Any relevant information NICE is made aware of in this area, whether from evidence searches,
We note that the present consideration of whether or not to review is solely predicated on an appraisal of subsequent research publications. While a thorough and balanced appraisal of subsequent publications is of course right and proper, it is insufficient in this case. This guideline was contentious from the start, with the National Institute giving short shrift to many reasoned concerns raised in the course of guideline development (https://www.nice.org.uk/guidance/cg53/history).

Many such concerns remain pertinent to this day.

Question: When reviewing a guideline / considering whether there is need for review, under what circumstances is it considered appropriate to thoroughly review the existing guideline (in addition to looking at any new information that may suggest an update)?

We are further concerned at the change in 2014 to presenting a skeleton guidence on-line, whereby the Institute has seen fit to strip away the substance, leaving only the recommendations: some being bland ‘no brainers’ which tell the health professional nothing of substance, while others require heavy caveats (discussed below).

Curiously, the core guideline is now referred to as ‘evidence’ and is simply described as ‘containing details of the methods and evidence used to develop the guideline’. We doubt if any health professionals ever look at it.

The above is of concern in relation to coverage on the patient group we represent, severely affected M.E. patients. We will come back to this point in responding to Q 07. (Since there is evidence that people can and do become severely affected through mismanagement, we are commenting on all aspects of CG53.)

[P2] Regarding the proposal to liaise with Cochrane about the possibility of updating Cochrane review on CBT to include data from the PACE Trial, the following are necessary pre-conditions if people with M.E. are to have full confidence in the reported findings of such a review:

(i) Regarding the PACE trial, consideration must include the recently divulged anonymised individual patient data.

(ii) Editorial responsibility must be vested in a group other than the ‘common mental disorders’ group, M.E being neither particularly common, nor a mental disorder.

[P3] Regarding the conclusion that “until and unless further research suggests otherwise, the NICE diagnostic criteria for CFS/ME remain valid” - may we enquire: What research, if any, underlies these diagnostic criteria?

As far as we are aware:

No empirical basis has been detailed for these criteria. Unlike, say the diagnostic protocol set out in the ‘Canadian Criteria’ which explicitly stipulates such credentials [Carruthers, B. et al.: 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.]

The description set out in CG53 has have never been subject to research or feedback from healthcare professionals or patients themselves, will be considered. The evidence considered by the present surveillance review included feedback from a patient representative and patient survey data. Additionally any information received during the consultation related to impact on patients also informed the final review decision. This will be passed onto developers for consideration during the update of the guideline.

Q When reviewing a guideline / considering whether there is need for review, under what circumstances is it considered appropriate to thoroughly review the existing guideline (in addition to looking at any new information that may suggest an update)?

The purpose of a surveillance review is to examine whether current recommendations remain relevant and appropriate. This is based on a combination of looking at the existing recommendations alongside new evidence and information that may indicate an impact on the guideline. The surveillance review can comment on the need for existing recommendations to be amended or deleted as well as the need to add new recommendations.

Q What research, if any, underlies these [i.e. NICE’s] diagnostic criteria?

The evidence considered when formulating the recommendations for diagnosis can be found in the full version of the guideline.

Q Does NICE consider it appropriate, in principle, to provide doctors and other healthcare professionals with information about any potential risks of the management strategies recommended in CG53?

As you note, NICE CG53 recommendation 1.1.1.1 states ‘Shared decision-making between the person with CFS/ME and healthcare professionals should take place during diagnosis and all phases of care. The healthcare professional should: […] Provide information about the range of interventions and management strategies as detailed in this guideline (such as the benefits, risks and likely side effects).’ Ensuring that healthcare
We note with concern that the description of the recent (2017) Cochrane review on Exercise fails
to place the reported findings in context, in two important respects:
(i) the review is described as incorporating data on the PACE trial, while failing to mention that this
review was carried out before the individual participant data was released. It is a matter of record that
a recently published reanalysis according to the original trial protocol showed even more mediocre
result than the now infamous paper published in the Lancet in March 2011.
(ii) the consultation document fails to cite the authors’ conclusion in full - in addition to the sentence
cited, the authors note:

- that there are a range of outcomes regarding which nothing can be said (crucially for
  patients, these include pain and quality of life)
- that “Reported results were obtained from patients who were able to participate (not from
  those too disabled to attend clinics); these results were inconclusive as to type of exercise
  therapy and showed heterogeneity.”

This failure to place the updated review in an appropriate context is notable, and in our view
symptomatic of a wider failure in the consultation document to seriously grapple with the import of
any information - new or old - that would temper the recommendations of CG53 towards something
more in line with patient experience.

We respectfully request that these caveats are introduced to staff in the NHS as a matter of
urgency, and that they impact on a genuine review of CG53 without delay.

Further to the above, please take cognisance of this publication, which concerns both Cochrane
& PACE:

Controversy over exercise therapy for chronic fatigue syndrome: key lessons for clinicians
and academics  Alex J. Mitchell; B J Psych Advances (2017), vol. 23, 145–148

This states:

“… Larun et al. [i.e. Cochrane] predominantly relied on statistical means and standard deviations for
each symptom measure outcome. (These statistics were not revised after primary data were finally
released.) It should be noted that these symptom measures are probably the least meaningful type
of statistical data. They demonstrate differences between groups, but not how many individuals
improved or even the percentage of improvement. …

Independent re-analysis examined data for recovery at the end of the [PACE] trial and findings were
also disappointing (Matthees 2016).

The recovery rates using a priori thresholds were as follows: 3.1% for specialist medical care alone,
6.8% for CBT, 4.4% for GET and 1.9% for adaptive pacing therapy, with no significant differences
between groups.

The PACE authors themselves maintained that CBT and GET were associated with significantly
increased recovery rates of 22% at 52-week follow up, compared with only 8% for adaptive pacing
therapy and 7% for specialist medical care alone (White 2013).
Both reports were different from the editorial claims that appeared in the BMJ at the time of initial publication of the PACE study, which suggested that 28–30% of patients recover using CBT and GET (Knoop 2011). Long-term follow-up at 2.5 years found that any differences apparent between treatment arms at 52 weeks were lost as adaptive pacing and specialist medical care caught up with CBT and GET (Sharpe 2015).

Regarding the Cochrane review of CBT, the consultation document likewise simply quotes a single sentence, out of context. In this case, the first sentence from the abstract’s conclusions, cited below:

“CBT is effective in reducing the symptoms of fatigue at post-treatment compared with usual care, and may be more effective in reducing fatigue symptoms compared with other psychological therapies. The evidence base at follow-up is limited to a small group of studies with inconsistent findings. There is a lack of evidence on the comparative effectiveness of CBT alone or in combination with other treatments …”

In addition, the detail of the conclusions are tentative and heavily caveated:

**Main Results:** “….Findings at follow-up were heterogeneous and inconsistent.”

**Plain Language Summary:** “However at follow-up, the results were inconsistent and the studies did not fit well together, making it difficult to draw any conclusions.”

**Author’s Conclusions - implications for practice:**

“The benefits of CBT in sustaining clinical response and reduction of fatigue symptoms at short and medium term follow-up are inconclusive. The benefits of CBT in improving physical functioning and reducing depression, anxiety and psychological distress at post treatment and at follow-up are also uncertain.

…. findings are based on a small body of evidence in which other therapies were designed as attention placebo controls, which limits confidence in the findings obtained. The body of evidence for CBT compared with relaxation or support and education at short and medium term follow-up is very small, heterogeneous and inconclusive.

…. Currently there is a lack of available evidence on the effectiveness of CBT as a stand-alone intervention or in combination with other interventions compared with usual care or other types of treatment (including immunological therapies, pharmacological therapies, exercise, complementary/alternative therapies and nutritional supplements) for CFS.”

**We respectfully request that these caveats are introduced to staff in the NHS as a matter of urgency, and that they impact on a genuine review of CG53 without delay.**

Regarding the relevance or otherwise of PACE to people with M.E., please note the stated perspective of the PACE trial authors:

*The PACE trial paper refers to chronic fatigue syndrome (CFS) which is operationally defined; it does not purport to be studying CFS/ME but CFS defined simply as a principal complaint of fatigue that is disabling, having lasted six months, with no alternative medical explanation (Oxford criteria).*

PD White, KA Goldsmith, AL Johnson, R Walwyn, HL Baber, T Chalder, M Sharpe, on behalf of all the co-authors, writing to Richard Horton, editor, the Lancet.
Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

And, in the paper as published in The Lancet:
“The PACE findings can be generalised to patients who also meet alternative diagnostic criteria for chronic fatigue syndrome and myalgic encephalomyelitis but only if fatigue is their main symptom.”

Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. PD White et al., The Lancet, Volume 377, Issue 9768, 5-11 March 2011, Pages 823-836

We respectfully request that this information is provided to staff in the NHS as a matter of urgency, and impacts on a review of CG53 without delay.

Q 01 & Q 02 Support & Information needs
Regarding Information Needs, current recommendations are that healthcare professionals should provide accurate information, and in a variety of formats, if appropriate. This could be said of the NHS response to any condition and it scarcely requires a guideline development process to establish this. Without an indication of what specific information is accurate, nor how health professionals might become aware of this accurate information, this recommendation is vacuous.
Please consider and clarify. In doing so, please take due cognisance of the following comment.

Regarding ‘Shared decision-making’ [Ps 6-8], and the reference to the recommendation for provision of information regarding risks in respect of the range of interventions and management strategies as detailed in this guideline. [rcd. 1.1.1.1], together with the consideration of a 2015 court judgment on this subject:

It is remarkable that the Consultation Document concludes that this has no implications for CG53, citing the present recommendations regarding informing about risk [inc. 1.6.2.2] This completely side steps the issue of whether or not and in which way / to what extent the interventions recommended in CG53 hold potential for risk, and whether or not CG53 has an obligation to appraise health professionals on this subject.

Question: does NIHCE consider it appropriate, in principle, to provide doctors and other healthcare professionals with information about any potential risks of the management strategies recommended in CG53?

The principle ‘First, do no harm’ is flouted in CG53
As well as continuing patient reports of sustained deterioration on following guidance given by health practitioners in good faith on the basis of this Guidance, there is a body of research revealing that patients have specific physiological characteristics which constitute grounds to conclude that they can and will deteriorate on exercise.

We are aware that deterioration in an M.E. patient can and does occur following activity that does not come close to exercise, but nonetheless would be encompassed by the National Institute’s definition of ‘exercise’, as set out in CG53: “Any form of physical activity that uses the major muscle groups of the body. Activities of daily living (for example, brushing hair or getting dressed), sitting up in bed and walking about are all exercise in the context of this guideline.”
We note that the glossary is contained in the full guideline which is not available to practitioners in the latest [2014] iteration; in our view this circumstance has significant consequences in terms of steering health professionals away from ability to adequately assess risk.

Regarding risk, awareness of risk, and reasons for risk - an illustration, from a patient who has experienced many relapses, despite having improved sufficiently to work for some time now:

"I was unlucky in that there was no real diagnostic test at that time to prove it was actually an organic illness. Nowadays, the clubs would take a blood sample, measure your T-cells, and you would rest until your blood cells were at such a level that it would be safe for you to go back to training. Those days we didn’t have that level of science, so I was out doing laps of the track when I should have been resting.

I still read some medical advice to ME people to do exercise, and certainly from my point of view that is the worst possible thing that anyone could tell me to do.”


It is telling when a patient has more insight into the appropriate management of the illness than the National Institute for Health & Care Excellence.

We note that CG53 presently states: “Little or no evidence was found for the effectiveness of sleep management, rest, relaxation or pacing for people with CFS/ME.” and presents no reason to hold that ‘rest’ may be vital.

The section on ‘Provision of Care’ supplies a range of bland recommendations - with no indication of considerations that are relevant in achieving them in this context.

The surveillance review has done nothing to establish to what extent practitioners are in a position to provide accurate information, to what extent patients consider that they are offered what CG53 states should be offered, what an ‘individualised management plan’ might look like in practice, nor how effective these are, where they exist.

Please be aware that at least some of the medical education on this subject is abysmal, as revealed by responses to an FOI to Scottish medical schools which showed that, where taught at all, ‘CFS’ is taught as a somatoform disorder. The indications are that - through no fault of their own - graduate doctors are variously unaware or downright misinformed about this illness; this makes provision of adequate and accurate information post graduation vital in order to ensure safe and effective patient care.

Q 03 What are the existing case definitions for CFS/ME in adults and children? What evidence exists to substantiate or validate these case definitions?

We note that much of the Consultation Document’s content at Q 04 concerns case definition i.e. Q 03. Regarding coverage presented at Q 03, we note the ‘Topic Expert Feedback’: “Topic experts referred to a list of research findings and papers worldwide and categorisation of biological abnormalities and dysfunctions and infections found in ME”.

May we please have something about the considered implications of this material?
Q 04 Are there any substantiated or validated evaluations to support the diagnosis of CFS/ME in adults and children?

The heading ‘Topic Expert Feedback’ at Q 04 reveals some peculiar thinking, past and present, concerning diagnostic criteria (Q 03).

PAST: “In the scoping meeting prior to developing NICE guideline CG53, there was a discussion on this with near unanimous consensus from stakeholders supporting broadly defined diagnostic criteria. This was to allow the inclusion of the vast majority of people with CFS/ME, which more narrowly defined criteria would exclude.”

Taking this argument to its logical conclusion, diagnostic criteria could reasonably encompass the whole population - this being a sure and certain way to ensure that ‘people with CFS/ME’ will be included.

In establishing clinical criteria in respect of any disorder, the objective should be both a suitable degree of specificity and sensitivity - in other words, delineating a patient group and only the patient group.

“A corollary of this was that it allowed the inclusion of the majority of trials, which have typically used broad diagnostic criteria.”

This is portrayed as a positive feature of the trials. Yet it is illogical to apply the findings of trials using one set of clinical criteria to a patient group delineated by another set of criteria. It may also be highly risky to the patients concerned.

PRESENT: “The expert was unaware of concerns about inclusion criteria of trials in CFS/ME, ..”

It is questionable to look only at clinical picture in defining a disorder and then adopt the findings of research based on patients with a different clinical picture. We note that None of the research studies use ‘NICE’ criteria.

The positions taken are that ‘CFS/ME’ is diagnosed clinically, any testing being done for exclusionary purposes only and the approach to patients is dictated by the reported findings of controlled trials.

**It is therefore appropriate - indeed essential - that these two groups are the same i.e. the clinical criteria used to recruit to trials must be identical to the clinical criteria for identifying the patients to whom the results are applied.**

We respectfully submit that flouting this principle holes CG52 below the waterline.

This section reflects no awareness of current diagnostic practice. There is a massive problem, in terms of:

- people with M.E. being treated as though suffering from chronic fatigue for non-medical reasons (somatoform disorder)
- people with other disorders being given a ‘CFS’ misdiagnosis

**Three contributions at the 2010 Invest in M.E. conference collectively illustrated the importance of appropriate diagnostic protocols and the adverse consequences of failure to achieve this.**
1. Presentation by Prof Brigitte Huber concerning a research study that had had to be halted when it became clear that it wouldn’t be possible to recruit enough participants to give the findings sufficient ‘power’. Asked to account for this, presenters observed “there aren’t any doctors out there diagnosing” and “you have to be able to diagnose properly”.

2. Presentation by Prof Leonard Jason, illustrating that the lack of a specific, sensitive, and clearly agreed diagnostic protocol implies that research findings that purport to be about this patient group may not in fact be so.

Prof Jason noted that a case definition must be reasonably sensitive - i.e. it must effectively ‘capture’ the vast majority of the patient population who have the disorder in question and specific – i.e. it must not include a substantial proportion of patients who don’t have the disorder at all. Specificity is particularly important when looking into a relatively low incidence disorder such as M.E., since a small margin of error on specificity can lead to research subjects with the disorder concerned being swamped by inclusion of even a small proportion of the population of patients with a much more widespread condition.

3. That the consequence of these difficulties was the advocacy of inappropriate interventions was clear from the observations of Dr Paul Cheney, who had made a study of the cellular energy defects in cardiac function. He reported: “we see cardiac diastolic dysfunction in almost every case” and that “there are patients whose diastolic dysfunction is so low/poor that they would fit well into a cardiac ward awaiting transplant”. He was later asked to respond to a question from the floor: “In view of the widespread diastolic dysfunction what are the implications of using graded exercise as a therapeutic intervention?” Dr Cheney provided a carefully considered response, including that advice that patients should “move within the limits of your illness”. On graded exercise, however, he was unequivocal: “The whole idea that you can take a disease like this and exercise your way to health is foolishness. It is insane.” This view was based on his research findings on appropriately diagnosed patients, with 100% exhibiting diastolic dysfunction on head up tilt table test.


The ‘Oxford’ criteria are mentioned here in the section on diagnosis, despite being clearly pitched as research criteria:

Q 04 concerns whether or not patients can be identified based on some form of diagnostic testing. The Impact statement makes this assessment of emerging biomedical evidence:
“There was also evidence on metabolites, microRNA and cytokines to diagnose CFS/ME, and that the temporal lobe might be implicated in CFS/ME pathophysiology. However, this evidence was reported by single studies and further research to confirm results is needed.”

This may be a perfectly valid statement in terms of implications for diagnostic in the present climate. However patients are done a dis-service by failure to consider the knock on implications of such
emerging findings for patterns of care. They cannot both be suffering from an illness that has no medical basis - or, none that cannot be attributed to the secondary effects of inactivity, as the research studies underpinning CG53’s management recommendations assert - and also be carrying these abnormalities. Both professionals and patients will be helped by high profile sharing of these emerging findings.: even if they presently have no implications for diagnostic practice, they can and do have implications for how patients are perceived and managed.

Q 05 Does the evidence show that any particular intervention or combination of interventions is effective in treatment, management or rehabilitation of adults and children with a diagnosis of CFS/ME?

Under the heading ‘Specialist CFS/ME care / Cognitive behavioural therapy, graded exercise therapy and activity management programmes’ we note that CG53’s core recommendations are described separately as ‘CBT’ and ‘GET’. However in terms of what the patient is asked to do, these are much the same i.e. increasing activity. We will therefore consider these together.

CBT a generic concept - as the term ‘drug’ is generic. Its substance depends on the cognitions identified as irrational and/or dissonant and the behaviour deemed maladaptive. Professionals therefore need to be made aware of what form it should take.

In terms of the research studies underpinning CG53, exercise is a behaviour deemed appropriate to overcome the impact of aberrant illness beliefs concerning the detrimental impact of activity on physical function and wellbeing. CBT studies differ from the exercise studies in that patients are provided an ‘explanation’ of why they are being asked to do this.

A reading of the relevant research papers reveals the title chosen does not always reflect the content precisely in this regard. A study may be described as ‘exercise therapy’ in the title, but pertain to exercise in combination with a cognitive change component. When reviewing studies for NIHCE, any such studies have been categorised according to the title, and not the substance of the study. This clearly may have implications for data analysis, and the existing comparison of ‘exercise’ and ‘CBT’ studies.

The study design identified for identifying evidence relevant to responding to this question is confined to randomised or controlled clinical trials

We are aware that the ‘National Institute for Health and Care Excellence’ work to a strict protocol in developing guidelines, a core plank being adoption of the reported findings of controlled trials. In common with ‘NIHCE’ Clinical Guidelines in general, the management and treatment guidance in CG53 rests on - and only on - on the reported findings of such trials. Only randomised and/or controlled trials were included in presenting evidence to the Guideline Development Group. The trials on increasing activity were then plucked from among the rest simply on the basis that there were more of them. In other words - solely on the basis the overall number of trials reporting positive outcomes. Against this background, we have a number of significant concerns.
For analysis of randomised trails results to be robust, it is essential that certain conditions are fulfilled:

(i) the intervention and control groups must be, in aggregate, comparable in all respects and distinguished only by the fact that one group undergoes the intervention and the other does not; in the case of random allocation of participants to intervention and comparison groups, sufficient numbers must be involved in the trials to produce a controlled; large numbers are required in order to achieve this.

(ii) trial participants must all suffering from the same disorder, this being the disorder that the clinical guideline in development is concerned with.

In our view, the body of research studies that fed into CG53 management recommendations fails on both counts:

(i) the trails, even in aggregate, involve relatively small numbers; the RCT method of assessing evidence on the relative merits of interventions was never intended to permit firm conclusions based on such small numbers

(ii) there is no reason to believe that trial participants were all suffering from the same disorder, and indeed there are a strong grounds on which to form the opposite view. (Relatively, the failure of a clinical guideline for use in the UK NHS to recognise that ‘PVFS, ME, and The Chronic Fatigue Syndrome’ are quite separate to the behavioural disorder ‘fatigue syndrome’ is remarkable.1

We therefore submit that the evidence base on which CG53 management recommendations are based is insufficiently robust to permit firm conclusions.

Random allocation of participants to intervention and comparison groups is deemed the optimum method of control when recruiting to trials, but actually of value on in so far as it succeeds in achieving matched intervention and comparison groups.

Question: which of the randomised trials considered in CG53 and in this review were successful in achieving matched intervention and control groups?

Regarding the possible impact of reanalysis of PACE data on recommendations for exercise and CBT, the consultation document rests the case for no need to review, no matter what emerges from this exercise, on the existence of prior evidence that points in the same direction as the present official interpretation of PACE.

This clearly puts the spotlight on this other evidence. It is far from thoroughly robust.

For example, the change of outcome criteria for PACE following failure of FINE has a precedent in earlier research, where the criteria used to judge outcomes were changed at the later stage of assessment. The former criteria, if used, would have showed no benefit to intervention group over comparison (control) group. The trial in question was influential because it followed up participants over a longer period than any of the other CBT trials (five years):

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1 This despite repeated WHO confirmation of the distinction, and confirmation from government that the WHO’s classification is accepted - most recently in House of Lords short debate 4th July 2017 [Parliamentary Under-Secretary of State, Department of Health, Lord O’Shaughnessy].

This publication looked at various outcomes six months after completion of a course of CBT (or relaxation, in the case of the comparison group). The presentation of findings hinges on whether or not patients “achieved good outcomes”, with criteria for improvement related to a specific outcome measure - the degree of improvement shown on the physical functioning scale of the Medical Outcomes Study Short-Form General Health Survey.

A further publication looked at outcomes at five year follow up stage:


No significant difference was observed between CBT and relaxation groups on the original outcome measure. No mention is made of the prior use of this measure as the key determinant of “good outcomes”. The assessment takes a different approach to reporting findings, with prominence accorded self rating of improvement. (Even so, the positive findings applied to just 17 patients who had had CBT, and 10 who had had relaxation therapy, and the difference between the two groups only just met the threshold of statistical significance.)

Also, in summarising results, the authors refer to significantly more of the ‘CBT’ patients meeting ‘criteria for complete recovery’. While noting that levels of physical functioning, fatigue, general health, and symptoms were no better in this group than among controls. On scrutiny of the data, it emerges that none of the various components specified as being required for a participant to be considered to be ‘completely recovered’ showed a significant difference between the CBT and control groups at the five year follow up stage (though the situation is not directly comparable in respect of one of these measures, concerning employment).²

A further example - this trial was influential because it had recruited more participants than other CBT trials.

² Aggregate figures for numbers in full or part time work are given. However, the ‘complete recovery’ component measure specifically required full time employment. These figures aren’t given. When assessed for outcome those in the CBT group who were working worked significantly more hours per week than their working counterparts in the comparison group, so it would seem likely that relatively more of them were in full time employment. However, that more of the CBT group than the control group were in employment before the trial began. In all other respects, though, the components of the measure of ‘complete recovery’ correspond exactly to outcomes which are reported as not significant. All in all it is hard to see how the employment measure alone could justify the assessment of greater likelihood of ‘complete recovery’ among the CBT group.
trials for CFS:

and because a cost effectiveness analysis was subsequently carried out:

CG53 quotes a sample size of over 270 in respect of this study, making it the largest of the behavioural trials. However, this tends to give a misleading picture of the numbers involved due to the high drop out rate and the three group structure of the trial (‘CBT’ and two comparison groups). The number of participants who received CBT and in respect of whom complete data regarding outcomes was available was 59. Even fewer supplied complete information on service resource use, so that when the cost effectiveness analysis was subsequently carried out data for just 37 CBT patients was available.

Yet it is on the basis of this analysis that the National Institute for Health and Clinical Excellence rest their conclusion that ‘CBT’ is cost effective.

In so far as the intervention of increasing activity may be helpful to some patients currently subsumed under a broad brush ‘chronic fatigue (syndrome)’ label, as applied in the UK during the decade since CG53 published, it is not helpful to all.

CG53 recommends increased activity - with or without a cognitive ‘explanation’ to patients - as the interventions with the best evidence; however this is solely predicated on the number of trials reporting benefit of the interventions.

There is no attempt to distinguish patients who may benefit, from others for whom these interventions would be a waste of time and money, and - crucially, from others still for whom exercise - or CBT exhorting to exercise - is harmful.

Some 25% ME Group members were not severely affected by M.E. until undertaking exercise.

This core point must be recognised if harm is to be avoided.

In this connection it is instructive to compare CG53 and the present consultation document with the deliberations of the Chief Medical Officer’s Working Group report (2002), which advises that:

- Lack of evidence of effectiveness may not always indicate that a therapy has no benefit, because insufficient research may have been undertaken to quantify the effect.
Moreover, data from surveys of patients and clinical experience suggests that, even when good-quality evidence is available, findings of those studies may not be generalisable beyond the groups of patients included in the research.

However, good clinical practice methods and clinical experience predict that a blanket application of therapeutic approaches shown to be effective in trials does not necessarily benefit all patients.

Annex 5: Evidence

and, having weighed up the significance of survey findings indicating a high incidence of adverse responses to ‘CBT’ and ‘GET’, considers that:

- The data clearly indicate that the York review results do not reflect the full spectrum of patients’ experience.

Annex 3: Patient Evidence

We are confident that removal of data from ‘Oxford’ criteria studies alters conclusions. Please note:

Chronic fatigue syndrome prevalence is grossly overestimated using Oxford criteria compared to Centers for Disease Control (Fukuda) criteria in a U.S. population study James N. Baraniuk - Department of Medicine, Georgetown University, Washington, DC 20007; Fatigue: Biomedicine, Health & Behavior; Preprint Date: July 21, 2017

URL: http://www.tandfonline.com/doi/full/10.1080/21641846.2017.1353578

“Results: The Oxford criteria designated CFS in 25.5% of 2004 males and 19.9% of 1954 females. Based on quadrant analysis, 85% of Oxford-defined cases were inappropriately classified as CFS. Fukuda criteria identified CFS in 2.3% of males and 1.8% of females.”

The import of this for patient care must be grasped.

Further problem with ‘Oxford’ criteria is that they are never, to our knowledge, applied as intended. Sharpe MC et al. A report - Chronic Fatigue Syndrome: Guidelines for Research Journal of the Royal Society of Medicine, 1991, 84, pp118-121 makes it clear that, while the criteria will encompass a range of patients, subgrouping is intended in analysing and presenting results - for example, it should be noted, in reporting data, which patients had a viral onset.

We note that Sir Michael Rawlins, then chair of the National Institute for Clinical Excellence, delivered a powerful speech critiquing sole reliance on controlled trials:

“The evidence discussed in Sir Michael’s Oration has only one purpose. It is the basis for informing decisions about the appropriate use of therapeutic interventions in routine medical practice. Such decisions have to be made at various levels but with critical consequences for patients, their families and society. They include the decisions that physicians make for individual patients as well..."
as assessing whether interventions are safe, effective and cost effective for healthcare systems as a whole. Mistakes can have repercussions at all levels. Randomised controlled trials (RCTs), long regarded at the 'gold standard' of evidence, have been put on an undeserved pedestal. Their appearance at the top of "hierarchies" of evidence is inappropriate; and hierarchies, themselves, are illusory tools for assessing evidence. They should be replaced by a diversity of approaches that involve analysing the totality of the evidence-base.

There is a presumption that, in general, the benefits shown in an RCT can be extrapolated to a wide population; but there is abundant evidence to show that the harmfulness of an intervention is often missed in RCTs.

Sir Michael argues that observational studies are also useful and, with care in the interpretation of the results, can provide an important source of evidence about both the benefits and harms of therapeutic interventions.”

[Harvean Oration to Royal College of Physicians, 2008]

Pharmacological interventions: we note that “No topic expert feedback was relevant to this evidence”. May we ask why the Institute failed to enlist the services of a topic expert who was in a position to say something about the evidence on pharmacological interventions?

May we suggest that this situation is rectified?

We direct attention to prior failure to adequately discuss the findings of controlled trials of immunological therapy, and anti-viral therapy, in CG53 and in the present consultation document.

Q 06 Review and ongoing management

Just one page long and having identified no evidence on the subject, this section is nonetheless one of the strongest in CG53 in our view. A degree of progress could be made were these recommendations to be implemented in practice.

The surveillance review is confined to a brief and completely inconclusive discussion of defining recovery, hinging on a systematic review paper from 2014 providing quality of life research. There is nothing concerning review and ongoing management in the NHS, as such.

There is a desperate need to start listening to patients on this subject, and for health professionals to respond appropriately to patients rather than holding to a preconceived opinion of what should happen and blaming the patient when it does not.

Q 07 Key principles of care for people with severe CFS/ME

We suggest modification of the existing severely affected section & a higher profile. The 25% ME Group would be willing to contribute to this.
As presented in CG53, full version, this section lies on pages 303-313 of a 317 page document. In over six years of working with severely affected sufferers throughout the UK, I have yet to come across an instance where a health professional appeared to be aware of this information. Unfortunately this section contains the advice that similar principles i.e. increasing activity - can be applied to the management of severe M.E. as other forms. This is based on very scant published evidence, and runs directly counter to patient experience.

That said, there is some valuable information here, notably on home care. This information is now even harder to find, as the institute has seen fit to sideline the main guideline document as ‘evidence’ and strip away the substance of the guideline in what appears to health professionals on-line, leaving only the recommendations.

There is an urgent need for suitable information to be readily available to health professionals on the clinical presentation and management of severe M.E.

For example, professionals may be unaware that people with severe M.E. may become unable to swallow, and that the root of the problem is unlikely (at best) to be identified on routine Speech and Language Therapist (SALT) investigation. One of our members almost starved to death in an NHS hospital as a direct result. Others have suffered less dramatic but nonetheless troubling experiences stemming from NHS lack of awareness.

Health professionals also need to be aware that there is no robust research evidence for increasing activity in this patient group, and a great deal of evidence that a person with severe M.E. will require to be protected from sensory stimuli (light, sound, smell, for example) as well as activity.

We note with concern that there is no reference to the findings of the ‘FINE’ trial in this section, this trial having been pitched at severely affected patients. It failed to the supposition that similar principles of management apply. [This trial is reference 110 in the consultation paper]

**NB: there is no such thing as a ‘mild’ case of M.E.** This is one of the most disabling disorders there is. Reviewing multiple studies, a 2003 paper concluded: “The quality of life of ME/CFS patients shows marked diminution that is more severe than in many other chronic illnesses.” Indeed a US practitioner, presenting at a medical conference, has had to redesign the morbidity graph for the slide presentation, since no other category of patients had ever scored so low on the rating scale.

| Blue Ribbon for the Awareness of Myalgic | No | We most strongly do not agree with the decision not to update the guidelines, as we do not believe, in their current state, that they are fit for purpose, and that they perpetuate erroneous views of ME | Thank you for your response. |
Encephalomyelitis (BRAME) and CFS. NICE are ethically obligated to reflect the truth and the reality in a neutral way. As these guidelines stand, they are unethical, and obstruct patients receiving correct medical care.

We have been calling for the rewriting of the guidelines since they were published. I was a member of the guideline development group and could not sign up to the finished guideline, as I knew, despite how hard I fought in the meetings, and presenting evidence, to highlight the reality and impact of these complex and debilitating conditions, that the final document was not representative of ME or CFS, (apart from the patient statements) and had the potential to cause great harm by advocating ‘treatments’ that multiple research papers, and patient surveys, have shown to be unhelpful/harmful.

As there has been so much controversy about ME and CFS the WHO ICD10 G93.3 classification should be included in the guideline, to clearly inform health professionals that ME and CFS have been classified by WHO as neurological conditions since 1969. The NICE guideline has again failed patients by not acknowledging this, and the tone, language, and recommendations within the guideline including CBT and GET as ‘treatments’ have helped to perpetuate and reinforce the myth, that some have created, that (erroneously) ME and CFS are psychosomatic disorders. NICE is supposed, by its own ethics, to improve the healthcare of patients, not create potential harm, as it has with this guideline.

Patients have a right to medical care if they are ill, or if there is a significant possibility they are ill. The guidelines at the minute perpetuate a one-sided view of the condition, in our (and many others) opinion an erroneous view of the condition, particularly given the multitude of research papers showing ME and CFS are biomedical conditions, making it difficult for patients to receive biomedical tests, care and management – only being offered biopsychosocial approaches. This is not only unhelpful/harmful for ME and CFS patients giving poor outcomes, but in this time of austerity it is not cost effective, and is also preventing people with other conditions, who would truly benefit from CBT or Exercise therapy from receiving the management/treatment they need.

The guidelines need to clearly state that there is no cure for ME or CFS, not “there is no pharmacological cure”; which gives the false impression that there is a cure, it just is not pharmacological. It is well recognised that there is currently no cure, nor is there a management/treatment which is suitable for all – this very clearly needs to be placed in the guideline, as to infer anything else provides false hope, and can lead to patients not being able to provide an informed consent.

On the NICE website they state that

“NICE’s role is to improve outcomes for people using the NHS and other public health and social care services. We do this by:

- Producing evidence-based guidance and advice for health, public health and social care practitioners.
- Developing quality standards and performance metrics for those providing and commissioning health, public health and social care services.”
• Providing a range of information services for commissioners, practitioners and managers across the spectrum of health and social care.
• Evidence-based guidance and advice

Since 1999, we have provided the NHS, and those who rely on it for their care, with an increasing range of advice on effective, good value healthcare, and have gained a reputation for rigour, independence and objectivity. In April 2013 we gained new responsibilities for providing guidance for those working in social care.

NICE has failed completely for patients with ME or CFS, and the health professionals who are trying to care for them, on each of the above key points. The reputation for rigour, independence and objectivity, seems sadly lacking with these guidelines.

There are two central ethical considerations for an urgent review of the guideline:
1 – the current guideline fails to respect “patient choice”, and the “right of individuals to make informed choices about healthcare” (NICE Social Value Judgements 2.1)
2 – “legislation on human rights, discrimination and equality requires that patients are not denied access, or have different or restricted access, to NHS care because of their … disability … or other status” (NICE Social Value Judgements 6.0)

Given NICE’s own statement on their role and reputation above, how can NICE say that there is no need to update the guidelines when over the past year key points acknowledged by NICE themselves were:

1. Sympathising with the position we were in with the Guideline
2. Acknowledging that the guideline “did not meet our (patients’) needs and it did not meet theirs (NICE’s) either”
3. The Guideline failed to address the real issues in ME/CFS
4. It does not promote innovation
5. It had a disappointing impact on specialist care and commissioning issues.
6. NICE Guidelines are not mandatory - a guideline is basically a tool to help professionals and patients – a decision-making aid - not done anything wrong in not following the NICE Guideline if it addressed a local need.
7. In NICE it was evidence that drove guidance.
8. Difficult where an absence of any new evidence of effective interventions
If it is evidence that drives guidance with NICE, then NICE has been presented with a wealth of biomedical research evidence, patients survey and personal evidence, over the past 10+ years. This is not helped by NICE’s continuance to accept, in order to support its’ lack of need to update the guidelines, the results of the very controversial, and much challenged PACE trials.

There is much evidence showing that it was right to challenge the PACE trials. Not only were the results, when independently analysed, extremely unsuccessful, but the criteria used for entry into the programme was basically anyone with a fatigue condition – they were not studying true ME or CFS, with their multitude of symptoms. Even the team behind the PACE trials, in a letter to the editor of the Lancet, in response to criticism, states:

"In their letter, Peter White et al state: “The PACE trial paper refers to chronic fatigue syndrome (CFS) which is operationally defined; it does not purport to be studying CFS/ME”. The sentence continues by stating that the PACE Trial studied: “CFS defined simply as a principal complaint of fatigue that is disabling, having lasted six months, with no alternative medical explanation (Oxford criteria)”.”

Dr Mark Vink, in the Journal of Neurology and Neurobiology (10 January 2017) published his analysis of the PACE data and found that “If the effect of Specialist Medical Care had been removed from the analysis, then 0% and 1.3% of patients improved objectively with CBT and GET, respectively” and that “The objective individual participant data shows that in up to 82.2% and 79.8% of ME patients their health might have been negatively affected by CBT and GET, respectively..........These data confirm the conclusions of a number of studies that patient health was negatively affected by CBT and GET”

In Wilshire et al’s analysis of the data printed in the Journal of Fatigue: Biomedicine, Health and Behaviour (Vol 5, 2017, Issue 1). There results found “None of the changes made to PACE recovery criteria were adequately justified. Further, the final definition was so lax that on some criteria, it was possible to score below the level required for trial entry, yet still be counted as ‘recovered’. When recovery was defined according to the original protocol, recovery rates in the GET and CBT groups were low and not significantly higher than in the control group (4%, 7% and 3%, respectively).”


NICE cannot support a section of the guideline, and say it does not need to be updated, based on evidence which is highly controversial, and was not even studying people with the condition – where is NICE’s rigour, independence and objectivity?

In the USA, health authorities consider ME/CFS to be a biological condition, and that CBT and GET are not recommended for use in these patients, in particular due to the adverse effect of exercise.

In this time of austerity in the NHS, and the need to save funds, why does NICE continue to promote management/treatment that is unhelpful/harmful to patients, which can cause a deterioration in a patient’s condition, leading to a poorer outcome and more costs for the NHS. As well as patients
taking up valuable resources and spaces for CBT and Exercise Therapy from those who truly would benefit from it and need it. As with other chronic LTC, CBT could be used, when appropriate, as a supportive tool, to help patients come to terms with their condition, and find a positive way forward with living with the condition – it is not used as a ‘treatment’ or to change the belief that a person is ill when they have a biomedical condition. Likewise, as with other LTC, promotion is for a healthy and a balanced lifestyle, including activity, within their abilities, and coping mechanisms, not the type of CBT and GET that is given to people with ME or CFS.

It is time for NICE to say we will provide the best practice, even if that means admitting that we (NICE) got it wrong – real strength comes from acknowledging where mistakes have been made and rectifying them – that is where NICE will garner real respect. Professor Mark Baker NICE himself admitted the guidelines were not fit for purpose, so please let us all work together to create a balanced document that truly reflects the reality of living and managing these most complex and debilitating neurological illnesses ME and CFS, and provides advice that will truly help, not hinder, and have an adverse effect on the patient population.

The globally acclaimed and accepted ME International Consensus Criteria should most definitely be included within the guideline, whether there is a full revision of the guideline or not, as this allows accurate criteria for diagnosis of ME, and information about the condition to aid management of ME. http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2796.2011.02428.x/pdf along with the guide for medical practitioners found at http://sacfs.asn.au/download/me_international_consensus_primer_for_medical_practitioners.pdf

Following its publication in 2007, NICE also let us down by refusing to refute the existence of the NICE criteria. When I raised this concern, at the time it was being written, that the section on diagnosis could be misread by healthcare professionals, I was repeatedly assured that it is not a diagnostic criteria, merely a set of symptoms to prompt hcp to consider the diagnosis of ME, and that if it did start being misread in this matter that NICE would put out a statement clarifying this, and stating that it is not a diagnostic criteria – when my fears came to fruition on its publication, and I contacted NICE to send out the promised statement, nothing happened – you have an opportunity by updating these guidelines and sending out a statement to rectify this matter. When Professor Mark Baker was asked about this list of symptoms being erroneously used as the ‘NICE criteria’, he confirmed that ‘there is no such thing as a NICE criteria for ME/CFS’ (Forward ME meeting 22 June 2016). PLEASE clarify that this is the case, very clearly, in the much needed revision of the guideline

There is no place for the Oxford criteria within this guideline, and should be removed, as should research based on this. This has been discredited and the 2015 report from the US National Institutes of Health recommended that the single symptom approach to diagnosing patient should be abandoned. They concluded by saying that use of a broad case definition ie Oxford generated heterogeneous samples of people with a variety of fatiguing illnesses and that using it to study ME/CFS could “impair progress and cause harm”.

This guideline is not fit for purpose for the patient population, or the supposed values of NICE to promote quality healthcare – which is currently not the case for people with ME and CFS.
Please make it clear in the guideline that NICE Guidelines are not mandatory - a guideline is basically a tool to help professionals and patients – a decision-making aid - not done anything wrong in not following the NICE Guideline if it addressed a local need. This is something that has been confirmed by Professor Mark Baker and by the Supreme Court decision in the case of Montgomery v Lanarkshire Health Board (2015).

Please remember, that this guideline impacts on every area of patient’s and carer’s lives, as it is also used as a key document by other organisations eg Department of Work and Pensions, and so impacts on benefits, social care etc.

Hope 4 ME & Fibro Northern Ireland have been campaigning for some time to have graded exercise therapy (GET) and cognitive behavioural therapy (CBT) removed from the NICE guideline CG53 for “CFS/ME”. These therapies, when applied to patients with myalgic encephalomyelitis (ME), are widely reported to cause harm3,4,5. Many of our members have reported being harmed by medical pressure to exercise. E.g. One young man was put on an exercise bike by a neurologist, and the exertion caused him to collapse, vomiting, on the floor. The NICE guideline CG53 was used as justification for this patient’s treatment. This situation cannot be allowed to continue – it is time the CG53 guideline was reviewed and the recommendation for GET removed.

2. Patients worldwide support the removal of CBT and GET from the NICE guideline CG53. At the time of writing the ME Association petition, calling for a review CG53, has collected over 15000 signatures6 in the few days allocated for the consultation period. This substantial plea should not be ignored by those in control of NICE. CG53 is not working for patients. The guideline should therefore be reviewed immediately.

3. We regard patients who meet either the Canadian Consensus Criteria (CCC7) or the International Consensus Criteria (ICC8) to have the disease called ME. The Oxford criteria, have been shown to over diagnose9 patients with “CFS” (Note: In the USA ME, is often referred

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Please note that the aim of surveillance is to check that published guidelines are current and decide whether updates are needed. To do this, all surveillance reviews rely on assessing 2 elements that influence the decision to update a published guideline as outlined in the guidelines manual:

5 StopGET stories of harm from GET: http://www.stopget.org/sign-now/about-us/
6 ME Association Petition https://www.change.org/p/petition-the-nice-guideline-for-cfs-me-is-unfit-for-purpose-and-needs-a-complete-revision
This over diagnosis means that many trial subjects, selected via Oxford criteria, do not have the disease ME, yet the outcomes of these trials are still used to inform ME care decisions. The removal of all Oxford based studies from the list of studies informing the knowledge base for ME/CFS has been recommended by the Institute of Medicine (IOM) report “Beyond Chronic Fatigue Syndrome/Myalgic Encephalomyelitis: Redefining an Illness”\(^{10}\), and we agree with this stance. The USA Agency for Healthcare and Research Quality (AHRQ) has further issued an Addendum\(^{11}\) to its 2014 ME/CFS evidence review. This Addendum downgrades the conclusions on the effectiveness of cognitive behavioural therapy (CBT) and graded exercise therapy (GET). There can be no doubt that the CG53 guideline needs to be reviewed in light of this new understanding.

4. We regard the name “chronic fatigue syndrome/myalgic encephalomyelitis” (CFS/ME) to be misleading. Putting the words “chronic fatigue” at the front of the disease name gives a misleading impression to medical professionals. Indeed, the “fatigue” premise behind the name “chronic fatigue syndrome” ensures that many patients without the defining feature of post exertional symptom exacerbation\(^{12}\) will also receive a “CFS/ME” diagnosis. This dilutes the perceived severity of the disease ME, and is consequently detrimental to all those with ME, and particularly the most severely affected. Misdiagnosis (perhaps because of the inclusion of the word “fatigue” in the name) is an ongoing problem\(^{13}\). The CG53 guideline does not help this. The guideline needs to be reviewed, and we suggest the prefix “chronic fatigue syndrome” is removed.

5. The recommendations for CBT and GET have now been deleted from the clinical guidance recommendations in:
   a) The USA Center for Disease Control guidelines\(^{14}\)
   b) The Health Service Executive in Ireland guidelines\(^{15}\)

By doing this, these two countries have acknowledged the inappropriateness of using psychosocial therapies as a primary treatment for a physiological disease such as ME. The premise behind CBT and GET is summarised in the 2011 PACE Trial\(^{16}\). Here is what the PACE Trial has to say about these therapies:

**CBT:** “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

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12 CCC, ICC and IOM – as ref 5, 6 & 8 above.
14 USA Center for Disease Control guidelines now don’t include GET & CBT - [https://www.cdc.gov/me-cfs/index.html](https://www.cdc.gov/me-cfs/index.html)
15 Health Service Executive (Ireland) website have removed ref to NICE guidelines [http://www.hse.ie/eng/](http://www.hse.ie/eng/)
16 PACE trial [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3065633/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3065633/)
(fear of engaging in activity) and behavioural responses (avoidance of activity) are linked and interact with physiological processes to perpetuate fatigue. The aim of treatment was to change the behavioural and cognitive factors assumed to be responsible for perpetuation of the participant’s symptoms and disability.”

GET: “GET was done on the basis of deconditioning and exercise intolerance theories of chronic fatigue syndrome. These theories assume that the syndrome 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.”

(Note the PACE trial refers here to “CFS’, but the premise of these therapies is also applied to “CFS/ME’). This makes it clear that CBT and GET are based on psycho-social assumptions about the nature of ME. Now that the IOM report considers ME as systemic exertion intolerance disease (SEID) these therapies should be regarded as obsolete. It is time the UK followed the lead of the above enlightened countries and ceased to recommend either CBT or GET in the CG53 guideline.

6. Much of the research supporting CBT and GET (for the treatment of ME or CFS/ME) suffers from scientific flaws. These flaws can include: the premise on which the research is based; the selection of subjects, the methods used; and the interpretations of the study outcomes. The PACE Trial and subsequent publications have been widely criticised for a plethora of errors and these errors have not been adequately addressed by the PACE authors in their responses. Scientific review of other studies supporting the use of CBT and GET, is likely to throw up similar problems. Following scientific scrutiny of these studies, the basis for the inclusion of CBT and GET as treatment recommendations are unsupported by science. The removal of CBT and GET from CG53 is essential to preserve the scientific integrity of all NICE recommendations.

7. We were disappointed when reviewing the evidence for this surveillance document, to find that the review panel only assessed the abstracts of the publications they considered, rather than the full documents. The quote below demonstrates that the team were not even prepared to look beyond the abstract when they had a question in mind about one of the studies. Quote

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17 IOM report – as ref 8 above
18 PACE trial – as ref 14 above
21 Keith Geraghty http://journals.sagepub.com/doi/10.1177/1359105317714486
from page 12 of the document:\textsuperscript{23} “However, it was not clear from an assessment of the abstract if diagnostic validity and reliability were tested.” This lack of curiosity would not be acceptable in a student essay, so why it is acceptable here is unclear. This suggests that the decision not to review CG53 is based only on a shallow review of the evidence, and that little effort has gone into the appropriate investigation of the situation surrounding ME. Therefore, a more thorough and meaningful review is required.

8. We are concerned that the review panel have preferentially considered only one type of evidence. It is well known that there are currently two schools of thought regarding ME. The PACE Trial\textsuperscript{24} authors favour the psycho-social premise and therefore their CBT and GET treatments are designed assuming that no physiological disease lingers after the initial illness-triggering incident. This contrasts strongly with scientists who are studying the measurable physiological abnormalities in ME\textsuperscript{25} as part of an ongoing disease process. The two situations are as different from each other as the idea of a “Flat Earth” is from the recognition of the Earth as a spherical planet. Reading this review document, we are concerned that whilst the CG53 review panel mention the various physiological studies, they simply ignore them when considering whether to review the guideline. This level of bias is a major concern to patients everywhere. If there are indeed patients who suffer from a psycho-social fatigue (and who would therefore benefit from CBT and GET) then it is important to separate out these “chronically fatigued” patients from genuine ME patients, who have ongoing physiological problems with exercise, and for whom GET and PACE-style CBT are contra-indicated\textsuperscript{26}. Again, we call for an in-depth and appropriately informed review of CG53. We also call for an independent investigation into the membership of the review panel and the topic expert team, to ascertain why such an inherent psycho-social bias dominates.

9. We are concerned that throughout CG53, there is a recommendation for the “education” of medical professionals. However, this apparently laudable suggestion is somewhat moot without describing the nature of the education to be provided. Should this “education” promote the view that patients can heal themselves through their own efforts in completing GET and CBT then that “education” will, in our view, be worthless. Medical professionals need to recognise the physiological limitations imposed upon ME patients by the disease. Health care

\textsuperscript{23} Surveillance proposal consultation document July 2017 – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

\textsuperscript{24} PACE trial – as ref 14 above

\textsuperscript{25} Examples of studies showing physiological abnormalities can be found in the references section of this blog from the USA National Institute of Health here: https://directorsblog.nih.gov/2017/03/21/moving-toward-answers-in-mecfs/

\textsuperscript{26} Chronic fatigue syndrome: assessment of increased oxidative stress and altered muscle excitability in response to incremental exercise https://www.ncbi.nlm.nih.gov/pubmed/15715687
professionals should not be encouraged by inappropriate NICE recommendations to push patients to exercise more. Patients have clearly articulated the harms\textsuperscript{27} they have experienced from GET and CBT. The IOM panel\textsuperscript{28} reviewed thousands of documents to conclude that “exertion of any sort (physical, cognitive, or emotional)—can adversely affect patients in multiple organ systems”, yet the NICE surveillance review has discounted the validity of these reports, whilst still accepting as valid, psycho-social studies based largely on subjective patient outcomes. If the “education” of medical professionals is to be based on this psycho-social approach to ME, then it is likely that patients will continue to report problems with the treatments they receive. CG53 is obviously not fit for purpose while these harms continue to occur.

10. Graded exercise therapy as a name, implies that conventional “exercise”, should be followed by the patient. The guideline then suggests that this exercise should be progressed up to 50-70\% of maximum heart-rate, once the patient has been successful with low key exercise of up to 30 minutes. However, many ME patients find even the most basic non-exercise tasks place their heart-rates well above the 50-70\% range\textsuperscript{29}. It seems that the guideline was written assuming that patients would not try to reach the 50-70\% range themselves, when in fact the reverse is the case, and heart rate monitors are instead needed to prevent patients exceeding this heart-rate range on trivial activities. The CG53 guideline does not caution medical professionals about this issue, nor are the use of heart-rate monitors regularly suggested to patients. Members of our charity have found heart-rate monitoring to be helpful\textsuperscript{30}, and whilst no useful treatment is yet available, we believe that heart rate monitoring could help mild and moderate patients to safely manage their activities, thereby reducing the likelihood of further decline. To make better use of heart-rate recommendations, the CG53 guideline needs to be carefully re-drafted, taking into consideration both patient experience, and studies from clinicians with knowledge of the physical limitations of ME and of exercise physiology\textsuperscript{31}. This would require that CG53 is reviewed.

11. Considering the two schools of thought for ME (see point 8 above), it would seem to us that there are likely to be two cohorts of patients currently being subsumed under the umbrella term “CFS/ME”. Patients with an ongoing physiological disease process, who are unable to exert themselves without significant exacerbation of all their symptoms, are likely to have ME as defined by the CCC or ICC. Whilst ill, these ME patients will never benefit from GET or CBT (note: CBT is often applied to ME patients to persuade them to increase their activities in a

\textsuperscript{27} ME Association Survey - as ref 1 above
\textsuperscript{28} IOM report - as ref 8 above
\textsuperscript{29} Workwell presentations on heart rates http://www.workwellfoundation.org/research-and-latest-news/
\textsuperscript{30} Slide share on HR monitoring by Sally Burch: https://www.slideshare.net/SallyBurch/heart-rate-monitoring-and-nice-guideline-for-me
\textsuperscript{31} Workwell studies – as ref 27 above
manner similar to GET). However, patients who are more generally chronically fatigued (e.g. suffering from lifestyle burnout, fatigue resulting from depression, or perhaps a slow recovery after a fully resolved illness) might benefit from GET and CBT programmes as they restore a better lifestyle balance. We suggest that the review of CG53 considers how the guideline addresses this dichotomy. Perhaps it is time to consider that the same treatments are not applicable to both cohorts of patients? This would obviously require a complete review of CG53 with perhaps the creation of a brand-new guideline for ME. This way ME could be clearly separated from the more generalised chronic fatigue.

Severe ME is not appropriately covered in the current version of CG53, and the profound sensitivities of these patients are very poorly recognised by frontline medical professionals. Anecdotally we have heard of patient symptoms being discounted once the patient reveals that they have ME. We have also heard how patients within a hospital setting have been denied wheelchairs or appropriate assistance on the basis of ME not being a serious condition. As one carer told us, “The prejudice we have experienced from neurologists, doctors and consultants, has been devastating.”

Patients with severe ME are very susceptible to the extra exertion required for medical appointments, and the concentration required to respond to questions can be sufficient to cause a significant later exacerbation of all their symptoms. The system makes little provision for quiet and darkened resting spaces, and appropriate home visits are difficult to access. The CG53 guideline does not go far enough in describing the types of accommodations that might help the severely affected to access care.

Many severely affected patients report to us that visiting their doctor worsens their condition to the point that they wish they had not attended, and consequently these patients become almost invisible to the system, because their fragile state prevents them from accessing appropriate care. Patients tell us that they are afraid of their inactivity being interpreted as a form of malingering, and further that they fear a psycho-social interpretation being applied to their condition.

The parents of children with severe ME sometimes find that false allegations of child abuse are made against them. This can be due to a failure of the authorities to comprehend the nature of severe ME, as a highly disabling and intractable disease.

It seems the CG53 guideline does not sufficiently protect severe ME adults and children from such poor and inequitable treatment, nor from the assumption by some medical practitioners that their disability is a choice, or a mental health issue.

Finally, there is no acknowledgement of the very severe ME state where immobility, tube-feeding,

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32 Tymes Trust: [http://www.tymestrust.org/pdfs/falseallegations.pdf](http://www.tymestrust.org/pdfs/falseallegations.pdf)
paralysis, muscle spasms, severe cognitive dysfunction, and profound intractable pain may regularly affect the sufferer, such that they are too unwell to even tolerate the presence of family members in the room. That this very severe state may persist for years on end is not well recognised. These patients and their carers are left feeling abandoned by the health care system. CG53 therefore needs to be urgently reviewed.

### 1. Background:

In order to comment on the recommendation by NICE not to update the NICE guideline on Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) it is not sufficient merely to look for new evidence which has come about in recent years - one necessarily needs to look back on the original guidelines to understand what a failing they were and what they missed.

To comment on why a review of the guidelines is required it is necessary to repeat that the original guidelines were at fault and that they were rejected almost unanimously by the patient community. We use some of the comments from our original submission and from our later review in 2013 in the following points –

- The original NICE guideline put forward a psychosocial model for ME and promoted CBT and GET as the options for management. The biological model with evidence of inflammatory, immune, oxidative and nitro oxidative pathways as key areas was ignored. This was heavily criticised.

- The AGREE Instrument (Appraisal of Guidelines Research and Evaluation Instrument) with which NICE is obliged to comply in the formulation of all its Guidelines is specific: "The health benefits, side effects and risks should be considered when formulating the recommendations".

- NICE failed to conform to the AGREE Instrument which requires that NICE is obliged to give equal weight to three main sources of data: "evidence-based" medicine, usually deemed to be random controlled trials (RCTs); the opinion and experience of physicians with expertise in the area, and the opinion and experience of the patient group for whom the Guideline is intended.

- NICE did not abide by the European AGREE standards which govern guideline development.

- Invest in ME rejected the original NICE guidelines as unfit and has recommended them to be updated/rewritten.

- Invest in ME concluded that the basis of the NICE Guidelines was in viewing as broad a section of fatigue states as possible, where high quality biomedical research into ME was

Thank you for your response.

Please note that the aim of surveillance is to check that published guidelines are current and decide whether updates are needed. To do this, all surveillance reviews rely on assessing 2 elements that influence the decision to update a published guideline as outlined in the guidelines manual:

- Intelligence gathering on the perceived relevance of the guideline, which may include responses to questionnaires or external enquiries about the guideline recommendations

- Abstracts of primary or secondary evidence that has been published since the end of the search period for the guideline

It is the role of the developers to consider the full text studies when they are conducting full systematic reviews for the guideline update.

We note your concerns about the FITNET-NHS trial. However, this was just an example of ongoing research identified through the surveillance review and not the only ongoing evidence we are aware of on this topic.

Q: Were there any patients, carers, service users and the public involved in the current surveillance team? The surveillance review considered the views of a patient representative. Additionally the public consultation has been responded to by a broad range of stakeholders representing the groups you identify.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have
ignored. Essential research showing the multi-system nature of ME was not considered or discussed.

- NICE exhibited a bias toward promoting a predetermined one-size fits all approach to ME by continually highlighting CBT and GET therapies despite widespread derision from ME patients.

- The original NICE guidelines left both healthcare professionals and patients in a state where they became, and have become, of little use to anybody – neither to patients nor to healthcare staff. Patients were dissatisfied with the guidelines. Doctors were afraid to venture outside of the NICE guidelines in case they were taken to the GMC by individuals and groups with vested interests in perpetuating the myths about ME being a behavioural disorder.

- There was almost universal condemnation of the guidelines by patients, patient support groups, most ME charities and even healthcare providers.

- Over twenty internationally renowned ME/CFS experts provided Statements in support of the Claimants’ case for the Judicial Review of the National Institute for Health and Clinical Excellence (NICE) Clinical Guideline on “CFS/ME” that was brought by ME/CFS sufferers [Statements of Concern about CBT/GET provided for the High Court Judicial Review of February 2009 http://www.investinme.org/Article-361%20Statements%20of%20Concern%20CBT-GET%20JR%20Feb09.shtml ]

We believe these comments are still valid today. No evidence has been produced to contradict these statements.

So, before even beginning to analyse the Surveillance proposal consultation document, one must state categorically that the NICE guidelines were already on very shaky ground and that cannot be ignored.

It was no small matter that the very population for whom the NICE guidelines were supposedly intending to benefit were, instead, forced to take NICE to a Judicial Review, such was the dissatisfaction with the guidelines and it was plain for all to see that patients were not listened to.

Recommendations not to update NICE guidelines must first reflect on whether the existing Guidelines are valid – and they for the most part are not.

It was Professor Mark Baker, director of NICE in 2014, who said in a Forward-ME meeting (http://www.forward-me.org.uk/25th%20June%202014.htm ) decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
"Turning to the ME/CFS Guideline specifically, the Professor said that it did not meet our needs and it did not meet theirs (NICE's) either."

Professor Baker had been in post for two years at that time

Regarding the Surveillance proposal consultation document –

2. **NICE** states that

   - The NICE Board sets our strategic priorities and policies, but the day to day decision-making is the responsibility of our Senior Management Team (SMT).

Therefore, it would be worthwhile to note from the outset that accountability must remain then with these staff and functions. Should any patient be affected deleteriously by the guidance in NICE then these people in NICE must be made accountable.

Going forward then any harm coming to patients by these guidelines and from any decision not to update them must be seen to be caused by the NICE Board and SMT and accountability must be taken by those members.

3. **NICE** states –

   "NICE is committed to involving patients, carers, service users and the public in the development of its guidance and other products. By involving the very people for whom the guidance will be relevant, we put the needs and preferences of patients, carers, service users and the public at the heart of our work."

   [https://www.nice.org.uk/media/default/About/NICE-Communities/Public-involvement/Public-involvement-programme/PPIP-leaflet-1.pdf](https://www.nice.org.uk/media/default/About/NICE-Communities/Public-involvement/Public-involvement-programme/PPIP-leaflet-1.pdf)

   Were there any patients, carers, service users and the public involved in the current surveillance team?

4. From reviewing the Surveillance proposal consultation document we believe NICE is already displaying its predisposing bias in favour of the Biopsychosocial (BPS) lobby and therapies – something which we believe undermines this whole Surveillance proposal consultation process and requires independent scrutiny.

As early as the first page NICE refer to a study of internet-based cognitive behavioural therapy in children and young adults. This study has already been heavily criticised by patients as flawed research.

A very strange choice of an example for ME guidelines – if one assumes that NICE is really being objective.
5. NICE states –
“Evidence consistent with, or not deemed to impact, current recommendations was found in the following areas: general principles of care; presentation; diagnosis; general management strategies after diagnosis; referral to specialist CFS/ME care; specialist CFS/ME care; review and ongoing management; and key principles of care for people with severe CFS/ME.”
We find this implausible.

The USA Institutes of Medicine (IOM) report, the NIH P2P report, the revelations regarding the flawed PACE trial - all have affected diagnosis, ongoing management, specialist care, referrals.

6. NICE states -
“Topic experts agreed with the conclusions of the surveillance team about the 3 US reports which were that no impact on the guideline was anticipated. They indicated that until and unless further research suggests otherwise, the NICE diagnostic criteria for CFS/ME remain valid.”

The current NICE guidelines require Post Exertional Malaise (PEM) as a core symptom which is correct.
But then they make “physical or mental exertion makes symptoms worse” as one of the optional symptoms. This does not make sense.

The IOM report called for the use of Oxford criteria to be dropped – which the PACE Trial and many other CBT and GET studies have used.

This therefore undermines completely the reasoning not to update the already flawed NICE guidelines and the dependency on PACE to prove anything.

NICE must take note of IOM, NIH, AHRQ and CDC decisions.
Not to do so would be negligent.

The NICE board is directly accountable for any decision not to remove CBT and GET from recommendations and this must be taken into account by any future damage caused by NICE recommendations.

7. NICE have not publicised who the “Topic Experts” used in the Surveillance proposal consultation process were.
This information must be publicised.

To do otherwise will reinforce the view that the Surveillance proposal consultation document has been solely influenced by the viewpoints from BPS supporters.
It is also not correct for NICE to decide itself who these Topic Experts are without the public being able to know and comment.

Under 1.5 Who is involved in this document it states -
"When developing guidelines, NICE involves people who might be affected by the guideline recommendations in a collaborative and transparent way."

Why has this not been performed for this review which is important for patients?
Why are patients or patient groups not involved?
We do not accept that NICE has been transparent.
This calls into question the validity of this document.

8. NICE need to downgrade CBT and GET just as USA has done.

The ‘definitive’ PACE trial long term outcome did not show any benefit and scientists from around the world have called for its retraction or re-evaluation.

The CDC has updated their website about ME/CFS to use the 2015 Institute of Medicine report and has removed Graded Exercise Therapy (GET) and Cognitive Behavioural Therapy (CBT) from its recommendations https://www.cdc.gov/me-cfs/about/index.html.

The USA Agency for Healthcare Research and Quality (AHRQ) also downgraded CBT and GET. The USA CDC is not recommending CBT/GET so UK guidelines are at odds with both NIH and CDC recommendations.


9. The CBT described by NICE for CBT is not the same supportive CBT as for other chronic illnesses.

CBT developed for CFS/ME is directive and based on the premise that CFS/ME is perpetuated by wrong illness beliefs and inactivity leading to deconditioning.

CBT for CFS/ME is aimed at "addressing any over-vigilance to symptoms.

This sort of CBT is not prescribed to other chronic illnesses and it should not be recommended for CFS/ME.

Cancer patients, for example, are told to monitor and report their symptoms, not ignore them.

As such, this is dangerous and NICE stating the opposite should mean that the NICE board and the NICE Senior Management Team must be answerable in court for any damage made to patients who carry out this advice.
NICE will be accountable if it ignores the advice to withdraw this unsound recommendation.
NICE would be negligent.
10. NICE states

"The experts also gave their thoughts on the current status of diagnostic criteria in NICE guideline CG53 and elsewhere, in light of these reports. Their comments included:

The HHS Chronic Fatigue Syndrome Advisory Committee state: ‘A priority should be placed on developing biomarkers and diagnostic tests... research has neglected many of the biological factors underlying ME/CFS’. Whereas in the UK there may be increasing acceptance of CFS/ME in the umbrella of functional neurological disorders.”

This comment above is far beyond NICE’s remit and takes it into dangerous and uncalled for areas which will be opposed by ME patients.

NICE states that the UK considers CFS/ME as a functional (i.e. nothing wrong pathophysiologically) neurological disorder whereas US considers it neurological.

NICE is part of the Department of Health (DoH) – a department that always confirms that ME is neurological.

How is it possible that NICE accept this statement for UK when numerous government health departments including Department of Health have constantly reassured that they consider ME as a neurological disorder, no mention of functional?

NICE cannot disregard the WHO and the UK government’s official position on ME being a neurological disease.

The WHO ICD-10 lists Postviral Fatigue Syndrome and ME in G93.3 (CFS indexed to it) and the current Beta ICD-11 draft also has Postviral fatigue syndrome, ME and CFS under “Other disorders of the nervous system”.

Functional Neurological Symptom Disorders have their own classification and there is no mention of PVFS, ME or CFS in that category.

UK* Functional neurological symptom disorder (FNSD) is a condition in which patients experience neurological symptoms such as weakness, movement disorders, sensory symptoms and blackouts. The brain of a patient with functional neurological symptom disorder is structurally normal, but functions incorrectly.”

So while the US priority is to find biomarkers and diagnostic tests the UK (with NICE) is trying to brush this off by placing CFS/ME under an umbrella of FND and treat it with CBT and GET as there is nothing wrong biologically, they say.
<table>
<thead>
<tr>
<th>This statement has to be withdrawn.</th>
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<tbody>
<tr>
<td>This seems, again, to have been heavily influenced by the BPS lobby – which makes us again wonder what the real agenda is of NICE and who were the NICE-selected Topic Experts.</td>
</tr>
<tr>
<td>It may be so that a FOI act will be required to reveal the identities of the Topic Experts, who chose them and what links they have to insurance companies and/or other organisations or individuals which have vested interests in perpetuating a view of ME being a behavioural disorder.</td>
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11. The dismissal by NICE of the AHRQ's finding of a lack of evidence once Oxford is excluded is negligent.

(Post-exertional Malaise being hallmark of CFS/ME yet research based on Oxford criteria that do not require PEM are being considered)

NICE guidelines state post-exertional malaise and/or fatigue is required but then it says "physical or mental exertion make symptoms worse" is optional.

PEM by CCC, ME-ICC, and IOM definitions includes symptom exacerbation following exertion.

So NICE either does not know what PEM is or else does not take it seriously either. This is negligence by NICE. NICE must be made accountable for any damages caused from this negligence.

12. NICE makes a point about shared decision making with regard to the guidelines - but this does not apply to patients with work-related insurance coverage as insurance companies demand patients go through CBT/GET regimes (and NICE recommends these) before getting their payments.

As patients do not get better undergoing these therapies there is often a long and distressing process to fight the injustice.

Again NICE must be accountable for damages, and costs, relating to the burden brought on to patients by this erroneous and negligent recommendation.

13. NICE should withdraw evidence of CBT/GET and not sit on the fence by saying that it does not do so "and none of the papers reporting on the PACE trial have been retracted".

There is no point in NICE stating that none of the papers have been retracted. This is an establishment attempt to stop real debate and is so disingenuous of NICE. That is passing on the responsibility and NICE reviewers should have enough scientific expertise to make the decision on the evidence base of CBT/GET themselves. |
QMUL spent £200k+ trying to stop PACE data being made available to the public. The Lancet has its own failings that it should be dealing with. We know that the editor of the Lancet is not responsible – refusing to engage and discuss despite multiple attempts to force retraction and failing to answer this charity’s letters [http://www.investinme.org/IIMER-Newslet-1511-01.shtml]. We make this point to enforce the view that NICE cannot base decisions on the flawed editorial policies of journals who have their own reasons for failing to listen to academic and patient opinion demanding the retraction of their papers.

14. As the NHS is in financial trouble then it would be far more beneficial for the patients and the NHS if honest and up-to-date information about the disease was given, help with information about education and work provided and monitoring of patients regularly to avoid missing other illnesses that may hide in this population.

Psychological supportive services should be provided only to those who really need them. It is a misuse of scarce funding to force CBT and GET – failed therapies which have no evidence base – on to patients who do not want them.

NICE is imprudent in wasting scarce financial resources.

This is a matter for the government to act upon.

15. NICE state that "Peer-reviewed study reports were assessed by abstract.”

For such an important document as this Surveillance proposal consultation it is not good enough to rely on reading abstracts only as they do not reveal methodological flaws and peer reviewing has been shown to be inadequate in the "gold standard" PACE trial for example.

This is a major failing that should invalidate the Surveillance proposal consultation document.

16. The NICE document states – regarding the PACE Trial –

"The authors have responded to these criticisms in an FAQ, and have re-analysed the main outcome measures according to the original protocol with similar results to those in the primary PACE results paper i.e. reduced fatigue and increased physical function. However, many commentators continue to dispute the PACE trial findings.”

This should be changed to “many informed and knowledgeable commentators.”.

Reanalysis by Matthees et al states -
“This re-analysis demonstrates that the previously reported recovery rates were inflated by an average of four-fold.”


This is significant enough to make it mandatory for NICE to remove all references to the PACE Trial for any judgement to be made.

NICE cannot use PACE for anything other than to reject its previous guidelines comments. Continuing to use PACE Trial references to justify the bias inherent in this document will make the Surveillance proposal consultation document invalid and a further review process will be required. It is negligent of NICE not to remove PACE Trial data for purposes of this Surveillance proposal consultation.

17. NICE seems to accept Cochrane reviews without question. Yet the Cochrane reviewers such as Dr Larun have conflicts of interest as they have co-authored with the investigators of the papers they are reviewing. 
https://jcoynester.wordpress.com/2016/03/20/why-the-cochrane-collaboration-needs-to-clean-up-conflicts-of-interest/

This is unacceptable. The Cochrane CFS/ME reviews are not considered to be unbiased. Cochrane is not a safe choice and is not independent. NICE must hand over the review to an independent body. We do not consider NICE to be independent. We do not consider Cochrane, as it has been seen so far with regard to ME, to be either independent or unbiased.

18. Under Summary of evidence from surveillance
In Q-01 and Q02 it states “Provide information on returning to work or education”
How is this possible? With its welfare reforms the current government has been determined to take this out of the doctor’s hands and give to corporate parasites who are made responsible for determining work and benefits yet have no knowledge of the condition.

The NICE guidelines have done nothing to help with this.

19. NICE states - “Healthcare professionals responsible for caring for people with CFS/ME should have appropriate skills and expertise in the condition.”
How is this possible? There is no specialism in CFS/ME thanks to NHS policies and this is a false view painted by NICE.
NICE has to take some responsibility for no expertise in CFS/ME being developed due to NICE’s faulty beliefs about this disease.

20. NICE state that –

1.1.3.2 Every person diagnosed with CFS/ME should be offered: information about the illness (see section 1.1.2) acceptance and understanding assistance negotiating the healthcare, benefits and social care systems assistance with occupational activities including work and education if appropriate (see section 1.4.5).

1.1.3.3 An individualised management plan should be developed with the person with CFS/ME, and their carers if appropriate. The plan should be reviewed and changes documented at each contact. It should include:

- relevant symptoms and history
- plans for care and treatment, including managing setbacks/relapses
- information and support needs
- any education, training or employment support needs
- details of the healthcare professionals involved in care and their contact details.

and then states

**Surveillance decision**

This review question should not be updated.

Yet despite all these fine words none of this happens for a person with CFS/ME.

NICE guidelines are ineffectual

21. NICE states -

“. It was concluded that physicians could improve diagnosis and treatment of CFS/ME through insight from the experiences of people with CFS/ME.”

This shows the hypocrisy of NICE – or rather of those influences who control what NICE promote.

Before NICE has stated the rights of the patient.
Then NICE states that “GPs should explore the patient’s illness beliefs before referral”
Then NICE state that “physicians could improve diagnosis and treatment of CFS/ME through insight from the experiences of people with CFS/ME.”

Patients do not want CBT or GET – yet NICE is so compromised by the BPS influences that you make quite contradictory remarks.

NICE also state –

“The authors concluded that GPs should explore the patient’s illness beliefs before referral to maximise patient engagement in therapy.”
and
“During the 3-year surveillance review, a qualitative study concluded that GPs could elicit and
explore patients’ CFS/ME beliefs before referral to specialist care.”

This is totally bogus. Are there any other conditions where these sort of questions are asked before patients get a referral
to a specialist? Does this have to happen if it does not happen for MS, cancer, dementia, other
diseases?
We think not.

Does NICE not think that the patients should also ask the GP’s illness beliefs about ME?
Perhaps NICE can add that to their recommendations.

22. NICE state
“Some issues were raised around consent to treatment. NICE guideline CG53 includes the sections
‘Your responsibility’ and ‘Patient-centred care’ which explain in detail the considerations that
healthcare professionals should make when implementing the guideline, including fully involving
patients and carers in decision-making, providing appropriate information, and that the guideline is
not mandatory.”
One of the few points we agree with NICE.
We believe this statement should be at the start of the NICE guidelines (in its current form) –
marked clearly and boldly in a disclaimer box – for all to see before reading further -

The recommendations in this guideline are not mandatory.

23. It strikes us that throughout the document that the “topic Expert” ought to be the patient.
Did any patients take part in this review?

24. NICE states -
“An educational programme was developed whereby CFS/ME continuing education materials were
distributed to healthcare professionals at conferences.”

Does NICE evaluate the education being provided?
If not then why not?

Invest in ME Research has held 12 International Biomedical Research Conferences on ME and 7
International Biomedical Research Colloquiums but despite invitations each year none of the UK
health authorities have accepted an invitation to attend these.
However, the US NIH and CDC representatives have attended and found them useful.
25. NICE states - Post-exertional malaise (PEM) is a required symptom for NICE diagnosis but strangely "physical or mental exertion makes symptoms worse" is optional yet NICE accepts qualitative research papers for its review that do not require PEM, namely Oxford Criteria which have now been rejected by US health authorities.

NICE dismiss criticism of use of the Oxford criteria – obviously because in doing so it would invalidate the NICE pre-determined decision not to update the original guidelines.

All research references based on Oxford criteria need to be removed from the Surveillance proposal consultation document.

26. If NICE say CFS/ME (their term) is now considered FND then why are CFS patients still banned from donating blood even if they are recovered?

NICE cannot even define recovery in the context of CFS/ME it seems.

"CFS : Post Viral Fatigue Syndrome
I am sorry but unfortunately, we cannot accept a donation if you have this condition or if you have previously had the condition even if you are now recovered.”

https://my.blood.co.uk/knowledgebase/index/C

27. NICE are deliberately waiting for additional studies from known BPS protagonists and for the flawed PACE Trial to be incorporated into Cochrane so that they can then update the guideline based on these totally false and flawed views.

Yet NICE do not consider the current Phase III multi-centre placebo controlled rituximab trial almost finishing in Norway.

One would be cynical to believe that NICE were deliberately attempting to force through a BPS agenda for CFS/ME guidelines ahead of the possible good results coming from the Norwegian Phase III rituximab trial.

We are cynical.

We believe this is an establishment effort to falsify the view of CFS/ME and use bogus, chronologically dependent information to skew a decision on CFS/ME which will avoid taking into account the Norwegian trial results.

This should be publicised.

It makes the NICE Board and SMT to be acting in an immoral and corrupt way, if true, and is therefore negligent. If true, this will need further investigation and scrutiny by parliament.
28. Asking for removal of GET from the NICE guidelines is not enough. CBT needs to be removed for the reasons stated above.

29. NICE states -
“A qualitative study described the development of an epidemiological case definition to distinguish CFS/ME from other chronic fatiguing conditions. However, it was not clear from an assessment of the abstract if diagnostic validity and reliability were tested.”

Why did not the Topic Expert reviewers check the full paper?
Surely it is important for NICE to be more accurate. This is shoddy work from NICE and calls into question the competence of the Topic Experts that NICE themselves selected.

30. NICE states -
“The comments regarding the need for the Oxford criteria to be retired do not impact directly on the guideline because it recommends a different diagnostic approach than the Oxford criteria.”

The evidence for CBT and GET that NICE currently recommend rely on studies that used Oxford Criteria which are broader than the current NICE Criteria so the decent thing to do the same as the US AHQR and downgrade CBT and GET. Even the CDC website has removed CBT and GET from its pages.

31. NICE states –
“The experts also gave their thoughts on the current status of diagnostic criteria in NICE guideline CG53”
And
“there are no gold standards by which one set of criteria can be said to be better or worse than any other.”

Yet did not Professor Peter Littlejohns, NICE Clinical and Public Health Director, state the following after patients took NICE to a judicial review –
“The 2007 guideline was welcomed by patient groups as an important opportunity to change the previous situation for the better, helping ensure that everyone with CFS/ME has access to care appropriate for the individual. Today’s decision means that the NICE guideline is the gold standard for best practice in managing CFS/ME”. NICE contradicting itself again.
32. NICE states –
“The comments regarding the need for the Oxford criteria to be retired do not impact directly on the guideline because it recommends a different diagnostic approach than the Oxford criteria. In terms of NICE excluding studies using Oxford criteria from evidence reviews for the guideline, as one of the topic experts stated: broadly defined diagnostic criteria in the NICE guideline (which was supported by almost all stakeholders during scoping) allow the inclusion of the vast majority of people with CFS/ME, and a corollary of this was that it allowed the inclusion of the majority of trials, which have typically used broad diagnostic criteria. Further, topic experts had no concerns about the inclusion criteria of trials in CFS, and it was also noted by topic experts that there is no gold standard definition of chronic fatigue syndrome.”

This is madness.

All researchers are stating at our Colloquiums that Oxford criteria and the broad range of less stringent criteria inhibit research. We do not wish to have “...the inclusion of the majority of trials, which have typically used broad diagnostic criteria.” For guidelines for CFS/ME. It is completely negligent and pointless to do this.

33. Recently this from Professor James Baraniuk of Georgetown University Medical School, Washington, USA

"Results: The Oxford criteria designated CFS in 25.5% of 2004 males and 19.9% of 1954 females. Based on quadrant analysis, 85% of Oxford-defined cases were inappropriately classified as CFS. Fukuda criteria identified CFS in 2.3% of males and 1.8% of females." The Oxford criteria were untenable because they inappropriately selected healthy subjects with mild fatigue and CIF and mislabeled them as CFS."

This says it all.

CIF stands for Chronic Idiopathic Fatigue.

NICE may say this was not available to them. Well it is known to NICE now!

And this only strengthens the argument to remove all research based on Oxford criteria – a case which was already strong before the Surveillance proposal consultation but is now overwhelming. NICE must withdraw all research referencing or based on Oxford criteria. To do otherwise would be negligent.

34. NICE states -
“Topic expert feedback Topic experts highlighted evidence on maternal anxiety and depression associated with chronic disabling fatigue in adolescents 13 years old. This evidence has been summarised in the 10 year surveillance summary section.”

Why is this research being discussed by NICE topic experts as it not about CFS or ME but chronic fatigue which can be caused by almost anything?

It needs to be removed.

35. NICE states -
“People with CFS/ME have reported pacing to be helpful in self-managing CFS/ME. However, healthcare professionals should advise people with CFS/ME that, at present, there is insufficient research evidence on the benefits or harm of pacing.”

Was the PACE trial supposed to study pacing (Adaptive Pacing) as one of the arms? If NICE can state that CBT and GET are beneficial and without harm then surely the form of pacing that was studied in the “gold standard” PACE trial would show the same?

There is no evidence of benefits or harms of sleep hygiene for CFS/ME either but NICE gives advice on sleep!!

36. NICE states -
“The therapist should adhere closely to empirically grounded therapy protocols.”

Here again we need to point out that the often made remark that CBT is used in other chronic illnesses such as heart disease, diabetes, cancer etc. but these are supportive CBT therapies not the directive ones as in CFS/ME.

37. Page 26
“Undertake an activity analysis to ensure that the person with CFS/ME is not in a ‘boom and bust’ cycle before they increase the time spent in exercise.”

There is no evidence that CFS/ME patients are “in boom and bust” cycles.

38. Page 32
“Trials using Oxford criteria were eligible when developing NICE guideline CG53, and topic experts had no concerns about the inclusion criteria of trials in CFS. It was also noted by topic experts that there is no gold standard definition of chronic fatigue syndrome.”

NICE guidelines require Post-Exertional Malaise (PEM) as a key symptom in CFS/ME yet it accepts research using Oxford Criteria that do not require PEM as reliable evidence. How can this be scientific?
39. Pages 29 to 36 seem to accept evidence for CBT and GET uncritically. Instead of going through the flaws of these reviews we would like to refer to a submission sent to us by a supporter XXXXXXXX has emphasised that any implication that CBT or GET are actually treatments for CFS/ME causes real harm to a large number of patients, creating false expectations in members of the medical profession, government bodies, employers or insurance companies, badly affecting the way that they are treated.

Here are XXXXXXXX’s points which we would like to put forward -

- You were written to in 2012 to draw your attention to an analysis of the PACE trial on the use of Cognitive Behaviour Therapy etc. on CFS/ME. A small group of us with scientific backgrounds had major concerns about the methodology, analysis and conclusions of this trial, but you explained that your advice was based mainly upon peer-reviewed studies rather than individual comments.

- Due to the persistent difficulties in obtaining the data, it has taken a long time to be able to produce such an analysis, but there are now a number of peer-reviewed articles that clearly demonstrate the failure of CBT and GET to produce any measurable improvement in the functioning of patients with CFS/ME.

- ‘PACE-gate’: when clinical trial evidence meets open data access http://journals.sagepub.com/doi/full/10.1177/13591053166675213

- PACE trial claims of recovery are not justified by the data http://www.tandfonline.com/doi/pdf/10.1080/21641846.2017.1299358


- Do graded activity therapies cause harm in CFS http://journals.sagepub.com/doi/full/10.1177/1359105317697323

- CBT and objective assessments in CFS http://journals.sagepub.com/doi/abs/10.1177/1359105317707215

- The existing inclusion of CBT as a possible treatment for CFS/ME continues to cause great concern in the patient community due to the false expectations that this engenders, amongst the medical profession, insurance companies, government agencies and employers.
- The situation is utterly different from the way in which CBT is considered as possibly helping some patients to cope with conditions such as heart disease: the difference between being considered an effective treatment and being offered as support for a condition is of major importance in the real world.

- As for GET, it is clear that the risks of this approach causing harm is far too great. The evidence to suggest it is safe is far too weak, and the results from large-scale surveys of patients clearly indicate major concerns.

- As a mathematician who has studied both statistics and experimental psychology, I find it astounding that NICE continues to put forward CBT and GET as potential treatments for CFS/ME on the basis of studies which would be decried were they to support acupuncture or homeopathy:

- a reliance on subjective responses to unblinded treatment would never be tolerated in alternative medicine – how can they retain any respect here?

- You finally have some peer-reviewed evidence showing that these therapies are neither curative nor treatments for CFS/ME: is it not time that your advice reflected that position?

40. The CBT prescribed by NICE for CFS/ME is not the same supportive CBT as for other chronic illnesses. CBT developed for CFS/ME is based on the premise that CFS/ME is perpetuated by wrong illness beliefs inactivity and fear avoidance leading to deconditioning. CBT for CFS/ME encourages patients to ignore their symptoms and keep on going even if they have set backs. This sort of CBT is not prescribed for other chronic illnesses.

41. NICE states -
"Topic experts highlighted the qualitative study on the SMILE trial which reports on the experience of service users (patients and parents/carers) for children with CFS/ME."

This study has never been published so why does NICE even mention this?
Another flaw in the NICE Surveillance proposal consultation.

Lightning Process practitioners have been reported to the Advertising Standards Agency several times. An unregulated, unaccountable pyramid business has no place in treatment of people with ME.

It was unethical to expose children to this in a study in the first place.
Including this is a shameful act by NICE and their so-called “Topic Experts” – and brings yet again into doubt the make-up of these NICE selected persons who are controlling the future of people with ME in the UK.

42. Nice states
“It was considered appropriate to wait for more evidence before adding a definition of recovery to the guideline.”

We find this statement astonishing as the current NICE guideline states “Most people with CFS/ME will improve over time and some people will recover and be able to resume work and normal activities.”

More appalling statements by NICE.

43. NICE state –

In RR – 03 What is the prevalence and incidence of CFS/ME in different populations?
No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

The Deputy Chief Medical Officer of England admitted that the CMO does not know the prevalence of ME in UK and that no figures are kept. See http://www.investinme.org/IIME-Newsletter-1701-01.shtml
Therefore, this decision is incorrect as no prevalence and incidence figures exist.
It surely also show another failing in NICE as we are nowhere nearer to understanding the scale of the problem. The NICE guidelines have done nothing to help in this area.

44. There are serious implications for children implicit in the document.
It is interesting that NICE document in their surveillance-review-proposal a link to How effective is FITNET-NHS for children and young adults with CFS/ME?
NICE gives prominence to FITNET, an un-blinded trial that does not even require NICE criteria (post-exertional malaise optional unlike NICE), yet makes no mention of the Norwegian Phase III multicentre double blinded, placebo controlled rituximab trial that is going to be published in 2018.

The FITNET trial appears to be on chronic fatigue not ME (or CFS/ME).
FITNET is a study already ridiculed by patient groups. It indicates already to us that NICE exhibits bias toward a BPS approach to ME.

45. At a meeting organised by Invest in ME with Dr Martin McShane, Director of Domain Two, NHS Commissioning Board, was presented with evidence of families of ME patients being prosecuted due to their children having ME and the healthcare staff dealing with the cases not understanding the disease process sufficiently. This is far from uncommon.
Dr McShane stated that he understood the family’s anger and said he would feel exactly the same if he was in their situation. He expressed his apologies and acknowledged the need to balance the system to ensure that situations such as this would not occur and that a major task was to alleviate stress for patient and carer.

He said he heard what the parents were saying.

This means that the NICE guidelines have failed as the guidelines still allow this intolerable situation to occur. We need to address the major flaw in the NICE guidelines – namely its bias toward promoting a predetermined one-size fits all approach to ME by continually highlighting CBT and GET therapies despite widespread derision from ME patients.  

This was in March 2013 – many years after the NICE guidelines were created and with ample chance for the NICE guidelines to have “worked” if there was seen to be any use for them.

This clearly demonstrates that the NICE guidelines have failed as the guidelines still allow this intolerable situation to occur. We need to address the major flaw in the NICE guidelines – namely its bias toward promoting a predetermined one-size fits all approach to ME by continually highlighting CBT and GET therapies despite widespread derision from ME patients.

46. The PACE trial as well as any of the other CBT/GET trials for CFS/ME are unblinded with subjective outcomes making them worthless. NICE would not accept drugs on that kind of evidence.

47. We would like to use the following abstract from Emeritus Professor Jonathan Edwards of UCL to point out the inadequacies of the PACE Trial in this paper—

PACE team response shows a disregard for the principles of science
http://journals.sagepub.com/doi/full/10.1177/1359105317700886

“The PACE trial of cognitive behavioural therapy and graded exercise therapy for chronic fatigue syndrome/myalgic encephalomyelitis has raised serious questions about research methodology. An editorial article by Geraghty gives a fair account of the problems involved, if anything understating the case. The response by White et al. fails to address the key design flaw, of an unblinded study with subjective outcome measures, apparently demonstrating a lack of understanding of basic trial design requirements. The failure of the academic community to recognise the weakness of trials of this type suggests that a major overhaul of quality control is needed.”

The paper concludes –
“White et al. (PACE PI) conclude that they stand firmly by the findings of the PACE trial, presumably because of their inability to understand its basic flaws. As has been suggested by others, the flaws are so egregious that it would serve well in an undergraduate textbook as an object lesson in how not to design a trial. Its flaws may have only been widely appreciated recently simply because those involved in trial design in other disciplines were unaware of its existence. Now that they are aware, there appears to be near unanimity. The patients have been aware of the problems for several years, and all credit to them for their detailed analyses. In my experience, most of the people with a deep understanding of the scientific questions associated with CFS/ME are patients or carers. To suggest that when these people voice their opinions they are doing a disservice to their peers seems to me inexcusable.”

48. In 2013, at the 6th Invest in ME Research International ME Conference, Dr Clare Gerada (chair of Royal College of GPs) stated that GPs knew very little about ME. This was six years after the NICE guidelines were published, proving that the NICE guidelines had not been useful and doctors were still uninformed about this disease.

Therefore, to leave the current outdated and unusable NICE guidelines for ME for another period, just sitting on the shelf with no updates reflecting the current poor education regarding ME and without any knowledge of the biomedical research performed/about to be performed, would effectively mean that no clinical guidelines for ME will have been reviewed for 15 years. That is unacceptable.

This would show not only contempt for the patients and families suffering from the effects of this disease – it would also show gross incompetence and negligence by NICE.

Patients are currently being misdiagnosed, mistreated and healthcare staff are being mis-informed and the current unsatisfactory status cannot be left for another generation.

GPs are left in a situation where their patients have rejected NICE, they do not understand enough about the disease, they are not familiar with the real effects and consequences of ME or of the possible research producing data.

49. The PACE trial demonstrably proved that CBT and GET (the primary treatment recommendations of the NICE guidelines) do not work.

Many articles have proven the PACE Trial to show that CBT and GET do not benefit ME patients and do not back up the original NICE guidelines’ recommendations.

NICE guidelines should be updated to reflect recent evidence that the recommended therapies in the existing guidelines (CBT and GET) do not lead to objective improvements in physical activity –
or they should be rewritten in the next couple of years as more biomedical research evidence is likely to be published - but certainly not based on FITNET and PACE.

<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.E Lochaber</td>
<td>No</td>
</tr>
<tr>
<td>ME Support Northern Ireland</td>
<td>No</td>
</tr>
<tr>
<td>Royal Free London NHS</td>
<td>Yes</td>
</tr>
</tbody>
</table>

The guideline trivialises myalgic encephalomyelitis. It is not fit for purpose. The Lancet has been using methods of reporting usually associated with the gutter press. NICE must consider the views of patients, and experts who are not associated with PACE. http://www.virology.ws/2015/11/13/an-open-letter-to-dr-richard-horton-and-the-lancet/ Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

The IOM 2015 report, ICC 2011 and recent paediatric primer 2017 highlight that the need for regular review and update due to emerging evidence regarding symptoms, symptom management and subsets of those affected by ME.

- The diagnostic criteria used in the current guidelines are too broad and not specific to the complexities of the condition as highlighted in the research based criteria above.
- The research regarding GET /CBT has been proven to be flawed and therefore should be removed from the current guidance.
- Quantitative Evidence for the cardinal feature of ME PEM is available and it supports the use of Pacing as strategy in self management.
- The prevalence of OI in ME is well documented. For the vast majority of those with ME/CFS, some form of orthostatic testing (whether tilt testing or 10 minutes of standing) is likely to be informative and to help determine whether treatment of orthostatic intolerance is warranted.
- The inference that patients have abnormal illness belief should be dispelled and the guideline should refocus on the assessment, treatment and management of this complex physiological illness.
- The misconception that there is no effective treatments when there is effective treatment for many of the symptoms.
We also take the opportunity to note that PROMs completed by patients who received CBT and/or GET in this department, with session numbers no less than 18, show an overall improvement of 60% in 60% on the SF-36.

<table>
<thead>
<tr>
<th>Stockport ME Group</th>
<th>No</th>
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Stockport ME Group feel strongly that the current guidelines are in urgent need of update for the reasons given below:-

A significant number of Stockport ME Group members have reported that, following Graded Exercise Therapy (GET) they suffered a deterioration in their overall health and well-being. In some cases, the consequences were moderate and, whilst GET had caused unnecessary pain, suffering and a deterioration in their health, within a few months they “recovered” to the point they were before carrying out GET therapy. In other cases, however, members have reported substantial long term and permanent harm following GET.

Harm caused by GET and to a lesser extent CBT has been reported more generally in the patient communities and this has also been represented in questionnaires and feedback gathered by national charities - ME Association and Action for ME (see for instance http://www.meassociation.org.uk/wp-content/uploads/2015-ME-Association-Illness-Management-Report-No-decisions-about-me-without-me-30.05.15.pdf ME Association Illness Management Report “No Decisions about me without me”). We believe that the failure to give this evidence sufficient weight by the surveillance is a significant error that puts patients at risk.

In addition to patient reports about harm from GET and to a lesser extent CBT, there are also a number of recent research articles that provide evidence that both highlight the potential for GET to cause harm and also for GET and CBT to be less effective than their proponents claim. See :-

Graham McPhee Cognitive behaviour therapy and objective assessments in chronic fatigue syndrome, Journal of Health Psychology June 2017

‘It’s time for an independent review of the PACE Trial methods and results’ | Dr Charles Shepherd, Journal of Health Psychology | 10 April 2017

“Do graded activity therapies cause harm in chronic fatigue syndrome?” Tom Kindlon, Journal of Health Psychology March 2017


Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
Among many other articles on this matter.

The current guidelines do not inform practitioners of patient experience or alternative scientific views on the effectiveness of GET and CBT. The current guidelines present only one perspective which fails to give patients the ability to make an informed choice on what treatments, if any, they would like to receive. We have seen an advanced draft of Action for ME’s Stakeholder Submission and they cover this issue more fully and effectively than we are able to.

In the Surveillance report at 1.6.2 the recommendations for CBT are significantly worrying to the Stockport ME Group. What is being recommended is not CBT the way it would be recommended for any life-long condition. Rather, in direct contradiction to 1.6.2.11 that “GET should only be delivered by a suitably trained GET therapist” it is recommending that CBT practitioners administer GET. Furthermore, it advises that any problems the patient experiences with GET be attributed not to GET itself but to “over vigilance to symptoms”. Also, the therapist is encouraged to use “refocusing/distraction techniques” to keep the patient carrying out GET and to ignore their symptoms. In our experience, ignoring ME/CFS symptoms has the potential to be very detrimental. Part of pacing, which is recommended by NICE, is listening to your body and when your body tells you to rest and stop - you do it. Yet the recommendations for CBT with GET fly in the face of this.

Locally we have an excellent CBT therapist through our Stockport NHS ME/CFS service (note this service was originally established by Stockport ME Group through Big Lottery Funding) but many other experiences of other services and practitioners that members have experienced have not been as promising. We acknowledge that CBT, carried out with a trained therapist can undoubtedly support a patient to adapt to life with ME/CFS and deal with any psychological issues that might aggravate their ME/CFS, but we would argue that recommending CBT in general as a primary treatment by NICE misrepresents the nature of ME/CFS (leading many people in the NHS and wider world thinking it is just in patients heads), can leave patients and their family with hard to meet expectations and undervalues the one truly effective treatment for ME that both the scientific and patient community agree on: pacing.

In the last decade, there has been significant research into the causes and treatment of ME and failure to update the guidelines sends an inaccurate message to NHS staff. It is saying that there is nothing new they need to know about the condition and that their existing beliefs and knowledge are accurate. Members of Stockport ME Group have frequently reported a failure to sufficiently explore alternative diagnoses before ME is diagnosed, they have also reported recommendations based on outdated understanding of the condition. Failing to update the guidelines will exacerbate the substantial problems that patients with ME/CFS experience in the NHS.
<table>
<thead>
<tr>
<th>Organisation</th>
<th>Response</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Ehlers-Danlos Support UK</td>
<td>No</td>
<td>We believe it is essential to specifically add information about ruling out the Ehlers-Danlos syndromes (EDS), especially hypermobile EDS (hEDS) and hypermobility spectrum disorders (HSD) in section 1.2.1.4. (Malfait et al, 2017. The 2017 international classification of the Ehlers-Danlos syndromes. <em>Am J Med Gen</em>175 (1): DOI: 10.1002/ajmg.c.31552)</td>
</tr>
<tr>
<td>The Young ME Sufferers Trust</td>
<td>No</td>
<td>The 2007 Guideline is now 10 years old. In the intervening years much has changed with respect to biomedical knowledge of ME/CFS, in particular in the USA. As a result of these discoveries including evidence from Professor Van Ness concerning dysfunction in the aerobic/anaerobic muscle metabolism with post-exertional deterioration, the US Centre for Disease Control has taken the serious step of removing its recommendation on graded exercise from its website. Whilst NICE is entitled to evaluate evidence for itself, it should not withhold such information from doctors, who follow the Guideline in the belief that they are doing right by their patients, and from patients themselves, who have the right to full information on the potential benefits and risks of treatments, so as to be able to give informed consent. The Young ME Sufferers Trust [Tymes Trust] is the only UK charity dedicated to children with ME, and their parents are entitled to such full information in order to give informed consent on behalf of their children. To effectively censor one side of the current evidence on this disease, and the serious step taken by the CDC, is to present a partial, rather than impartial view to unsuspecting parents and their doctors – surely an unethical stance that is already reflecting poorly on NICE and its reputation. Once the medical profession learns that NICE is now, in effect, actively promoting one side of the medical debate and suppressing the other, this cannot fail to have consequences.</td>
</tr>
<tr>
<td>University of Manchester – FINE Trial</td>
<td>Yes</td>
<td>No comments</td>
</tr>
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</table>

Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53
<table>
<thead>
<tr>
<th>Welsh Association of ME &amp; CFS Support</th>
<th>No</th>
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<tbody>
<tr>
<td>Thank you for the opportunity to comment on this surveillance consultation.</td>
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<tr>
<td>We do not agree with the proposal not to update the guidance in CG53 on CFS/ME.</td>
<td></td>
</tr>
<tr>
<td>We believe the NICE Guidance CG53 on CFS/ME omits guidelines on key issues, includes guidance that is potentially harmful and is misleading to both patients and clinicians. It is in need of urgent revision.</td>
<td></td>
</tr>
<tr>
<td>The decision not to review the guidelines has been taken on the basis that evidence in other trials supports the original PACE trial results. No consideration has been given to the flaws that are common to all these trials:</td>
<td></td>
</tr>
<tr>
<td>i) broad patient selection criteria, ignoring the possibility of subgroups requiring different management approaches and ignoring the wide range of severity experienced by patients, or the possible differences between children and adults or men and women – research has repeatedly been shown that different criteria identifies different groups of patients and reduces the usefulness of research results e.g. Baraniuk <a href="http://www.tandfonline.com/doi/abs/10.1080/21641846.2017.1353578?journalCode=rftg20">http://www.tandfonline.com/doi/abs/10.1080/21641846.2017.1353578?journalCode=rftg20</a> Johnston <a href="http://hqlo.biomedcentral.com/track/pdf/10.1186/1477-7525-12-64?site=hqlo.biomedcentral.com">http://hqlo.biomedcentral.com/track/pdf/10.1186/1477-7525-12-64?site=hqlo.biomedcentral.com</a> Nacul <a href="http://www.tandfonline.com/doi/full/10.1080/21641846.2017.1273863">http://www.tandfonline.com/doi/full/10.1080/21641846.2017.1273863</a>, &amp; Jason <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3658447/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3658447/</a>;</td>
<td></td>
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<tr>
<td>ii) measuring only subjective outcomes;</td>
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<tr>
<td>iii) the lack of double-blind, randomised, placebo-controlled trials, especially as some trials have actively sought to influence the results by promoting their approach as ‘the most effective therapies’;</td>
<td></td>
</tr>
<tr>
<td>iv) assumptions about the nature of the illness, the factors that sustain it and the suitability of exercise therapy which are contradicted by scientific research into the illness.</td>
<td></td>
</tr>
<tr>
<td>The PACE trial was set up to validate the evidence base for GET &amp; CBT, which was recommended for mild to moderately affected people with CFS/ME. <a href="https://www.nice.org.uk/guidance/cg53/chapter/4-Research-recommendations">https://www.nice.org.uk/guidance/cg53/chapter/4-Research-recommendations</a>. Its failure to replicate those results, without the goalposts being moved, should not be ignored, in spite of the authors’ continuing support of and justifications for it. It is not good research practice to change the</td>
<td></td>
</tr>
<tr>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
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way outcomes are measured part way through a trial, even if 2 oversight committees were involved, or for smaller earlier trials to over-ride the results of the later larger one. Rather the failure of the PACE trial should raise questions about the earlier studies.

A new Cochrane review will only be of value if a stricter assessment of the quality of research is carried out.

A recent study by the FITNET researcher Dr Crawley concluded that only 30% derived some benefit from specialist treatment in England for CFS (largely CBT and GET based) and only 5.7% considered themselves recovered. They concluded that ‘CFS/ME is a long term condition that persists for the majority of adult patients even after receiving specialist treatment’. This is an important comment by a CBT researcher and should influence considerations of how cost effective CBT and GET are when applied to all patients, without any attempt to assess whether it might be beneficial.

The guideline contains little to help healthcare and social care professionals to give ongoing care and management advice to patients who do not improve, who remain ill over a long period and who are severely affected. The guidelines do not recommend CBT or GET for the severely affected, but fails to provide adequate alternative guidance. The assumption that patients must be encouraged to do more and more regardless of how ill they are is rife within the NHS and Social services. Support can be withdrawn because there is no understanding that ME is a long term condition, that refusing support has a negative physical and mental effect, or that some people do not improve and need continuing palliative care. The guideline should include such information and direct professionals to appropriate guidance to caring for the severely ill.

The guideline should be clear that there is a difference between CBT that aims to change negative illness beliefs about ME and CFS, and CBT that aims to help you adapt and cope better with the limitations of the illness. The latter may have value as it provides support and better understanding but does not mitigate against some degree of improvement or recovery, where the former is simply offensive.

A number of other issues also need to be updated e.g. Pharmacological interventions (1.6.3.2). NICE recommend amitriptyline for pain but there is recent research which links this drug directly with an increase in developing dementia. This recommendation should be withdrawn immediately http://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2091745

A failure to update the guideline will simply drive a bigger wedge between the medical and the patient communities. Many already go without medical help due to the pressure they experience to receive inappropriate psychological therapy and/or physiotherapy. A failure to acknowledge patient experience and the flaws in research trials (PACE, FUTNET, GETSET, MAGENTA etc. have been
ridiculed all over the world), places the NICE guidelines in the same category. They will continue to fail to be a valuable and believable resource.

The Myalgic Encephalomyelitis Action Network (#MEAction) is an international grassroots network dedicated to working for health equality for patients with ME. #MEAction Network UK is the local affiliate operating in the United Kingdom. We are a patient voice in this consultation.

Our members are distressed about the proposal to not update the guidelines, as UK patients view an update to be an urgent necessity. Widespread patient concern is evidenced by the ME Association patient petition: “the current guidelines are not fit for purpose and require complete revision”\(^ {34} \) (14,757 signatures in less than two weeks).

In summary, the main NICE recommendations of cognitive behavioural therapy (CBT) and graded exercise therapy (GET) as treatments only make sense in the context of the causal CBT Model of CFS and ME (a psychosocial model), but we consider this hypothesis to have been refuted, so therefore the guidelines require updating for patients with ME (see 1h). The quality of evidence is lacking for us to feel safe in regards to the risk versus benefit of these treatments given the absence of theoretical justification (see 1b, 1c, 1d, 1e, 1g). In particular, graded exercise therapy is not considered by patients to be effective, acceptable or tolerable (1c, 1d, 1g). The body of research that these treatments are based on fails to meet our patient threshold of satisfactory scientific rigour which includes:

- Post Exertional Malaise (PEM) as a symptom in a recognised case definition (ME criteria such as the Canadian Consensus Criteria (CCC), or the International Consensus Criteria (ICC) and provisionally the CFS Fukuda Criteria, see 1a and 1i)
- Blinded trial and or objective outcomes (but never neither of these, see 1b)
- Satisfactory recording of harm (1d).

Instead we put forward some suggestions of patient-preference revisions for the new guidelines (see 1i, 1f, 1g). Evidence for our position on this is outlined below.

1a PEM and appropriate definition is key to effective treatment

Post Exertional Malaise (PEM), sometimes called Post Exertional Neuroimmune Exhaustion (PENE), is the key differentiating characteristic of ME (Institute of Medicine report, 2015; Jason et al., 2013; Maes, Twisk & Johnson, 2012). By definition, PEM is the loss of stamina/function and the post-exertion exacerbation of symptoms following even trivial amounts of mental or physical exertion, often with delayed onset.

\(^ {34} \)ME Association 2017, Petition: The NICE Guidelines for ME/CFS is UNfit for purpose and needs a complete revision viewed 17th July https://www.change.org/p/petition-the-nice-guideline-for-cfs-me-is-unfit-for-purpose-and-needs-a-complete-revision

Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
In studies that only require chronic fatigue in the case definition, and therefore not the ME and CFS specific symptom of PEM, it is likely that participants with other fatiguing conditions are included. This confuses the results leading to inflated outcomes. This requires serious reconsideration as there cannot be relevant actionable findings from trials which do not properly define the patient population. When NICE includes studies which solely rely on the symptom of chronic fatigue, as in the Oxford criteria, the resulting recommendations are likely to include advice which is unsuitable (and possibly unsafe) for ME patients.

A study published this week shows that "85% of Oxford-defined cases were inappropriately classified as CFS". "The Oxford criteria designated CFS in 25.5% of 2004 males and 19.9% of 1954 females…[in contrast] Fukuda criteria identified CFS in 2.3% of males and 1.8% of females." (Baraniuk, 2017). This calls into question the relevance of any studies using the Oxford criteria which have been used as evidence for the current NICE guidelines (such as Fulcher 1997, Powell 2001 and 2004; Wearden 1998) as well as the large PACE trial.

The US Centers for Disease Control and Prevention have recently set a precedent by downgrading studies which use the broad Oxford case definition criteria - in which PEM is not included. The result of this is that their treatment website page no longer mentions CBT or GET as suitable for ME (see https://www.cdc.gov/me-cfs/). In addition, the U.S. Agency for Healthcare Research and Quality found evidence for CBT and GET was negligible after removing Oxford criteria studies from its analyses (Smith et al 2015).

Also, exacerbation of symptoms after exertion cannot be optional in ME, as is implied by the current guidelines (section 1.6.2.16). We feel that PEM does not feature prominently enough in the current guidelines (section 1.2.1.2).

1b The evidence for the efficacy of GET & CBT is unsound
(Re: NICE guidelines Section 1.6.3 more specifically CBT 1.6.2.8 GET 1.6.2.11 and Review Question-05 of your Proposal)

We would like to make clear that our concerns about methodology extend beyond the PACE trial to include the entire body of GET/CBT research, where it relies on the flawed combination of unblinded randomisation and subjective outcomes (Helmfrid, 2016). We ask that such clinical trials be excluded or downgraded.

The apparent effects of CBT or GET in these studies can be explained solely by study design: an unblinded trial using self-reported measures. This is supported by the recent (Stouten 2017) paper which showed that "the more objective the outcome, the worse the result for CBT and GET".

This flaw particularly applies to studies using CBT as a treatment for ME due to the nature of this specialised form of treatment. While we have no objection to the use of talking therapies as a tool to process the adversity of living with chronic illness, the CBT that has been advocated for ME aims to challenge thought patterns about the disease itself (see 1h). Evidence is lacking that this type of CBT produces any improvement in patients' physical capabilities in objective measures, such as...
return to work (McPhee G 2017). We assert that this combination of unblinded and subjective measurement creates a dynamic of participants being trained to answer the questionnaires ‘better’ rather than ensuring that the patients actually get better. As (Stouten 2017) has stated, “Though patients think they are able to walk more after CBT, they fail to actually do so”.

1c Ineffective treatment cannot be cost-effective

For a treatment to be cost effective, it must demonstrate efficacy.

We consider the difference between the findings in the original PACE papers and the reanalyses to be substantially different. They cannot accurately be described as similar (as described on p3 of Surveillance Proposal Review). Alterations to the clinical protocol were made, which artificially presented GET and CBT as more beneficial than under the original protocol (Goldin, 2016). In contrast to the original analysis, which claimed that the majority of patients improve, after the PACE authors’ own reanalysis a majority of approximately 80% did not improve. This could more accurately be described as opposite rather than ‘similar’. Furthermore, the two year follow-up study also failed to show significant between group differences (Sharpe et al., 2015 cited in Geraghty forthcoming).

These unconvincing results are not confined to the methodologically flawed PACE trial; there is a pattern of long term, null between-groups results in other trials. The FINE trial, a nurse-led CBT based treatment for the more severely affected, housebound patients, found no benefit at one year follow-up, reporting that ‘there were no statistically significant differences in fatigue or physical functioning between patients allocated to pragmatic rehabilitation and those on treatment as usual’ (Wearden 2010).

The lack of sustained long term effects of CBT (and also GET) suggests issues with placebo effects, or demand characteristics influencing initial results, especially in combination with unblinded/subjective methodology (see section 1b).

Regardless of the relative costs of delivering CBT, GET, Pacing or medications, an ineffective treatment cannot be a good use of public money.

1d Reporting of Harm

One serious concern for our community is the issue of harm caused by GET and CBT. Both anecdotal evidence and patient surveys indicate that a proportion of patients have suffered significant deterioration after GET in particular, but also after CBT. The under-reporting of harms in the GET/CBT literature is of huge concern (Kindlon 2011). Although one recent trial has attempted to ameliorate this by measuring adverse events, the way in which these harms were measured is not sufficient, in our opinion.

We feel, as has been suggested by others, that patient surveys should be given more weight by NICE (Laws 2017). Greaves et al. (2012) found that patient surveys do usually correlate well with
conventional research outputs, so the discrepancy here does not automatically place the bias on patient survey sampling. The psychosocial trials also involve volunteer sample bias; this is not unique to patient surveys, and trials such as PACE are biased towards the mild end of the disease spectrum (and a likelihood of miscategorising psychiatric illness as CFS/ME due to a loose case definition, see 1a). Also “more than half of the ‘RCTs’ in the Cochrane review failed to describe randomisation procedures, thus similarly making it impossible to assess the extent to which selection bias may have occurred” (Laws, 2017).  

This table from Kindlon (2011) illustrates the scale of the issue:

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Sample Size</th>
<th>Harms (N)</th>
<th>Mean rate of harms (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graded Exercise Therapy (GET) (or similar terms)</td>
<td>4338</td>
<td>2223</td>
<td>51.24%</td>
</tr>
<tr>
<td>Cognitive Behavioural Therapy (CBT)</td>
<td>1808</td>
<td>360</td>
<td>19.91%</td>
</tr>
<tr>
<td>Pacing (or similar terms)</td>
<td>5894</td>
<td>152</td>
<td>2.58%</td>
</tr>
</tbody>
</table>

*This includes any degree of harm e.g. both "somewhat worse" and "a lot worse" from the ME Association
*Taken from [75,78-80,82-85]; 2Taken from [80,81,83-85]; 3Taken from [79,80,83-85]

Patient surveys indicate that deterioration can be substantial with "21% more patients reporting being more severely afflicted after GET", for example their illness going from moderate to severe (Geraghty, forthcoming). In real life terms this is experienced as long term relapse (including becoming housebound, bedbound or starting to need a wheelchair) and the risk is intolerable in the face of so little potential benefit.

"CBT and GET with one of the leading proponents of the treatment landed me in a hospital bed, physically iller than I had ever been and psychologically scarred. [Over 20] years later I am still severely affected by ME." (Patient voice 1)

There is a substantial discrepancy between the reporting of harm in clinical trials and deterioration in patient surveys. At the very least, this calls into question the reporting of harm during the relevant clinical trials. There may be issues with participants blaming themselves as dysfunctional if they experience harm with CBT/GET, due to the nature of the content (Kindlon, 2017; Geraghty, forthcoming), as well as more standard therapeutic relationship issues. Participants may prefer to drop out rather than report harm. Participant drop out rate is 50% higher for CBT than usual care, perhaps indicating psychological distress or physical harm (Laws, 2017). There is also some indication that participants of such trials do not actually increase activity, they fail to comply, but there is usually no objective measure of adherence in these trials to show this (Kindlon, 2017 and Helmfrid, 2016).
We request that this issue of harm reporting is more thoroughly investigated rather than dismissing patient reports.

**1e Biomedical evidence and exercise induced harm**

This table from an overview of the Canadian Consensus Criteria shows how the nature of our response to exercise can often be in the opposite direction to healthy controls:

<table>
<thead>
<tr>
<th>Response to Exercise</th>
<th>Healthy People</th>
<th>ME/CFS Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sense of well-being</td>
<td>Invigorating, anti-depressant effect</td>
<td>Feel malaise, fatigue a worsening of symptoms</td>
</tr>
<tr>
<td>Resting heart rate</td>
<td>Normal</td>
<td>Elevated&lt;sup&gt;13,14&lt;/sup&gt;</td>
</tr>
<tr>
<td>Heart rate at maximum workload</td>
<td>Elevated</td>
<td>Reduced heart rate&lt;sup&gt;13,14&lt;/sup&gt;</td>
</tr>
<tr>
<td>Maximum oxygen uptake</td>
<td>Elevated</td>
<td>Approximately ½ of se controls&lt;sup&gt;13&lt;/sup&gt;</td>
</tr>
<tr>
<td>Age-predicted target heart rate</td>
<td>Can achieve it</td>
<td>Often cannot achieve it should not be forced&lt;sup&gt;13&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>Increased</td>
<td>Sub-optimal level&lt;sup&gt;13,14&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cerebral blood flow</td>
<td>Increased</td>
<td>Decreased&lt;sup&gt;15,16&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cerebral oxygen</td>
<td>Increased</td>
<td>Decreased&lt;sup&gt;15&lt;/sup&gt;</td>
</tr>
<tr>
<td>Body temperature</td>
<td>Increased</td>
<td>Decreased&lt;sup&gt;17&lt;/sup&gt;</td>
</tr>
<tr>
<td>Respiration</td>
<td>Increased</td>
<td>Breathing irregularities of breath&lt;sup&gt;17&lt;/sup&gt;, shallow breath</td>
</tr>
<tr>
<td>Cognitive processing</td>
<td>Normal, more alert</td>
<td>Impaired&lt;sup&gt;18&lt;/sup&gt;</td>
</tr>
<tr>
<td>Recovery period</td>
<td>Short</td>
<td>Often 24 hours but can or weeks&lt;sup&gt;1,12,19&lt;/sup&gt;</td>
</tr>
<tr>
<td>Oxygen delivery to the muscles</td>
<td>Increased</td>
<td>Impaired&lt;sup&gt;13&lt;/sup&gt;</td>
</tr>
<tr>
<td>Gait kinematics</td>
<td>Normal</td>
<td>Gait abnormalities&lt;sup&gt;20&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Table from an Invest in ME overview of the Canadian Consensus

A recent meta-synthesis found that acute exercise increased fatigue over 7 relevant clinical trials, particularly after 4 hours (Loy et al, 2016).

"Acute exercise exacerbated symptoms, impaired cognitive performance and affected brain function in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome patients. These converging results, linking symptom exacerbation with brain function, provide objective evidence of the detrimental neurophysiological effects of post-exertion malaise." (Cook et al 2017)
However, this does not just apply to intense, acute exercise, there are also problems with low-level exercise. “Bioenergetic muscle dysfunction is evident in CFS/ME, with a tendency towards an over utilisation of the lactate dehydrogenase pathway following low-level exercise, in addition to slowed acid clearance after exercise.” (Rutherford et al 2016)

Biological abnormalities lie behind our difficulty with exercise. This is likely to be why we experience harm after exercise, and combined with the complementary consistent evidence of deterioration in patient surveys, is good reason to end graded exercise as viable ‘treatment’ for ME. Please see more evidence of this in under our comments 3b.

1f There is no clear evidence that rest should be discouraged

We disagree with the current wording of CG53 where warnings about rest are given (section 1.4.2.4). There is no evidence demonstrating rest is harmful for people with ME. From our lived experience, proper rest is often the most beneficial activity. “Patient survey data consistently indicate that rest makes just 1 per cent of patients worse and is helpful to more than 85 per cent of patients” (Action for ME, 2008: 13; Action for ME, 2014: 19; Action for ME, 2001 cited in 2008: 13 which was then cited in Kirke 2017). It is therefore confusing to be given warnings of rest, but not warnings about GET.

We are particularly concerned about the lack of evidence for guidelines relating to Severe ME (eg 1.9.3.1, 1.6.2.22). Very little research has been done into patients with severe ME (Strassheim et al 2017). We are alarmed at the recommendations for “Graded activity” (section 1.9.3) given there is no evidence that this is beneficial and has the potential to cause harm and permanent bodily damage to patients with ME. The FINE trial found this type of intervention to be unsuccessful.

There is an urgent need for updated recommendations for the severely affected.

1g Patient preferences

It is important that any treatment recommended in the new guidelines combines: acceptance and tolerance by patients; efficacy; consistency with the evidence base; and sound theoretical underpinnings (e.g. Laws, 2017). In all of these areas we have a clear preference for Pacing (Kirke, 2017) and Energy Envelope Theory (Jason et al 2013) above the GET/CBT paradigm treatments. Patient surveys report these techniques to be more beneficial and less likely to be associated with deterioration than CBT/GET.

A forthcoming analysis examines over 18,000 patient responses to surveys on management of ME symptoms from 2000-2015: Pacing showed the largest improvement at 82% and was also the most frequently used technique (n=8762). CBT was most likely to result in no change (47% no change, total n=3251). GET was most likely to result in deterioration (57%, total n=4652) (Geraghty, forthcoming).

The same pattern is illustrated in this figure (Kirke, 2017 Figure 1)
Pacing is an adaptable approach that is able to encompass almost all levels of severity, apart from the most severe (Geraghty, forthcoming). It encourages us to stay within our current activity limits which can be achieved without triggering delayed PEM (see also Jason et al, 2013 on the Energy Envelope Theory). We have a ceiling of possible activity, depending on the current severity of our biological limitations. Under Pacing, we can sometimes increase activity, if our underlying health improves.

Pacing "is overwhelmingly favoured by patients (84% finding it appropriate/partly appropriate) and has a moderate impact on reducing the degree of illness severity." (Geraghty, forthcoming). Our preference for Pacing is not just based on our lived experience of this being the ‘best fit’ activity management. It also complements the research evidence that our energy is limited at a cellular level and exertion causes us unusual biological problems (Cook et al, 2017, Rutherford et al, 2016;
Naviaux, 2016; Twisk, 2015; Vermeulen 2014; Nacul, 2011; VanNess, 2010; Light 2009 see Q3) because it respects these limits rather than ignoring them.

In a small study, 82% of patients improved with Pacing and the improvement was sustained at 12 months follow up (Goudsmit et al 2009), in direct contrast with PACE CBT/GET in which 80% did not improve and long term follow up was null. It should be noted that ‘Adaptive Pacing Therapy’, as assessed within the PACE trial, was not the self management ‘pacing’ as it is understood by most patients, but was an operationalised therapy designed to fit within the therapist reliant design of the PACE trial (Jason, 2017).

1h Causal CBT Model refuted

The theoretical basis of CBT and GET as treatment for ME has effectively been refuted. For NICE to fail to hold a full review at this time would demonstrate dismissal of the scientific method, which is an essential foundation for evidence-based medicine. The empirical principle is also a feature within CBT itself, for economic and ethical reasons, the CBT ethos states that treatment should be both effective and founded on well-established theories.

Whilst CG53 does not explicitly attribute any causal mechanism for CFS and ME, the main recommended treatment regimes of CBT and GET themselves necessarily imply that NICE supports the model that the illness is caused by illness beliefs and de-conditioning known as the CBT Model. It is important to understand that Cognitive Behaviour Therapy is not a monolithic structure but includes within it different approaches, models and disagreements (Westbrook, 2006). The regimes of CBT/GET used in most treatment trials for ME are not generic but are explicitly founded on these premises, which is known as the CBT Model of CFS/ME:

“The interventions with cognitive behavioral therapy and graded exercise therapy are based on a hypothesis that the disease is perpetuated by avoidance behavior and that symptoms are caused by a lack of fitness. Although the Oxford school [CBT Model, PACE trial proponent researchers] have not described any underlying mechanisms, nor presented any evidence for the presumed causation, they refer to their hypotheses either as theories or models. This gives the impression of scientific support, which in fact does not exist.” (Helmfrid, 2016)

However, it is possible to imagine how this specific theoretical hypothesis can be effectively be refuted, so it is testable and falsifiable under the established Scientific Method (e.g. Popper 1963). Falsification would involve demonstrating that physical dysfunction in ME is not related to deconditioning; illness beliefs are not associated with activity levels and the treatments resulting from the model are ineffective or harmful. A competing model should also ideally be shown to better fit the data. We can demonstrate that each of these conditions apply:

1h.i Deconditioning: studies such as Vermeulen (2014) show that the problem in ME is not deconditioning. “The high increase of the cardiac output relative to the increase of oxygen uptake argues against deconditioning as a cause for physical impairment in these patients.” (Vermeulen, 2014). Various 2-day CPET studies show a peculiar second day response, evidencing PEM
Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomylitis (or encephalopathy) (2007) NICE guideline CG53

(Institute of Medicine, 2015) rather than deconditioning. Many biomedical studies evidence bioenergetic difficulties incompatible with the concept of deconditioning as the cause (see 1e and 2b). Also, people who are deconditioned (perhaps from hospital admission) do not describe the experience of ME.

1h.ii Illness beliefs: a very recent study of 990 participants (defined under several case definitions) found that the theory did not fit the data, and was an especially poor fit for those who met more stringent case definitions (Sunnquist 2016, and under review, which also supports the findings of Song and Jason, 2005). The Sunnquist study concludes:

"Findings suggest that individuals’ activity level is unrelated to perceptions about illness etiology; rather, activity level is an indicator of general illness severity, along with impairment and fatigue. These findings are inconsistent with cognitive behavioral theories of [ME and] CFS that presume that individuals’ symptoms stem from deconditioning and maladaptive illness beliefs. As these theories lack empirical support, and patients continue to express concerns about the efficacy of cognitive behavioral and graded exercise treatments, caution should be exercised in prescribing these treatments to patients. Furthermore, future research efforts may better serve individuals with ME and CFS by working toward developing alternative treatments." (Sunnquist 2016 p48)

There are other failures of explanation such as:

"The hypotheses do not explain why some pathogens do not trigger ME/CFS. The same perpetuating cognitive factors should be present after any infection." (Helmfrid, 2016)

1h.iii Efficacy of treatments: as we've demonstrated more extensively in sections 1b, 1c, 1d, and 1e, the treatments proceeding from the CBT Model hypothesis of ME do not lead to successful outcomes in trials (results are null or show unconvincingly small effects). Most patients do not benefit and a sizeable proportion deteriorate after these treatments.

There is also a lack of face validity to the treatments coming out of this hypothesis, which is perhaps explained by the irrelevance of the theory. It is widespread patient opinion that CBT and GET as ‘treatments’ for ME contrast sharply with our lived experience of what helps or hinders our disease. It misses something important of the essence of what it is like to live with ME. For patients this was recently encapsulated by activity diaries in the GETSET trial patient guide which were atypical, unusually mild and did not show normal PEM timing35. There is also a potentially biased affiliation of this hypothesis to a political agenda associated with disability and return to work, which is perhaps not in patients’ best interests (Faulkner, 2016).

1h.iv Competing model supported:

The competing biomedical model of ME is a better fit for the data and accepted by the World Health Organisation. Although we accept that more research is needed in this area, the biomedical

35 http://www.wolfson.qmul.ac.uk/images/pdfs/getset/GET%20guide%20booklet%20version%201%2022062010.pdf
research fits together in a way that the causal CBT Model does not. Examples of this are presented throughout this document (see 2b and 3b). For example, in the past year several studies have agreed that there is a hypometabolic issue (see 3b ii). Although we do not yet know the results of the blinded rituximab trials (expected this year) previous results were impressive and, with the delayed benefit shown, point to an immunological defect (see 2ai 3b.iii) This does not contradict the hypometabolic hypothesis and is complementary to it. The pieces of evidence for the biomedical jigsaw are coming together rapidly.

Therefore, we consider the CBT model hypothesis about the nature of ME to have been falsified under the standard procedures of normal science (Popper, 1963). This is a fundamental issue in regards to the principle of scientific rigour which NICE supports. We ask that NICE update the related treatment guidelines for CBT and GET accordingly.

1i Requests for updates:

People with ME have no confidence that CBT and GET are either safe or effective as treatment for ME.

- We ask that CBT based on the causal CBT Model for CFS and ME is excluded from the guidelines (see 1b, 1c and 1h). Generic talking therapies to process the adversity of chronic illness are acceptable to patients, but given the background context, the difference should be made explicit in the new guidelines.

- We hope that PEM as a mandatory symptom will be seen as a normal expectation for research and resulting guidelines in the future. For this review, we ask that evidence is disregarded if it combines the flaws of not including PEM in the case definition, unblinded randomisation and subjective outputs, and any studies using the discredited Oxford criteria.

- Mild ME: Following the 2015 case Montgomery v Lanarkshire Health Board the law now requires that “reasonable care to ensure that the patient is aware of any material risks involved in any recommended treatment, and of any reasonable alternative or variant treatments”. If GET is not removed from the guidelines for people with mild ME, then we feel that there must be a warning to ensure that patients are aware of the risks as per 2015 law. It is the strong opinion of patients informed of the evidence and debate that other reasonable patients who are not yet informed (perhaps due to new diagnosis) would be likely to attach significance to the risk of deterioration from recommendation to exercise as treatment for ME.

- Moderate ME: Recommendations of graded exercise (section 1.6.2.13) (or graded activity) should be suspended until concerns about methodological flaws in clinical trials and
Concern for patient safety have been more adequately addressed. An urgent update is necessary to avoid unnecessary, long term harm.

Severe ME: We also ask that the unsuitability of GET for Severe ME is strongly emphasised in updated guidelines. It is the experience of patients that even those with Severe ME can be under pressure to comply with GET. We have similar concerns about the use of Graded Activity for Severe ME and wish to see the lack of evidence for this reconsidered and warnings about rest removed. Any recommendations for "Graded activity" or activity management (section 1.9.3.1) should be revised, given that so little is known about Severe ME and the potential for these treatments to cause harm. We ask that you consult with charities such as Stonebird and 25% Severe ME who are experts in caring for people with severe ME and revise the guidelines according to their recommendations.

We have divided references into key references, which is the main evidence we wish to draw your attention to, and additional references

Key References Q 1


<table>
<thead>
<tr>
<th>Royal College of Physicians</th>
<th>We would like to endorse the responses submitted by the Association of British Neurologists and Royal College of Psychiatrists</th>
</tr>
</thead>
</table>


Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including...
Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

<table>
<thead>
<tr>
<th>RCGP</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The guideline could be improved for primary care with more focus on the mental health aspects, which are hardly mentioned. The model is very bio-medical and should be amended to give more weight to the psychological and social elements.</td>
<td></td>
</tr>
<tr>
<td>• The current guidance does not adequately guide the General Practitioner to consider several relatively common medical conditions which can masquerade as CFS/ME, each having chronic fatigue as a major component of their presentation. Patients suffer the double jeopardy of a generally low level of awareness of these conditions amongst the medical professions (1). If identified, each of these conditions has its own management approach, which will, understandably, differ from patients who in fact have CFS/ME. It remains important to explore and exclude other diagnoses before a diagnosis of CFS/ME is made.</td>
<td></td>
</tr>
<tr>
<td>• Primary care clinicians may have a difficult task in NOT increasing and commencing long-term medications of no proven value (especially of addiction) and having a high consultation rate for little therapeutic improvement.</td>
<td></td>
</tr>
<tr>
<td>• 1.2.2.3 The tests listed need to be updated with consideration of HgbA1c or fasting glucose.</td>
<td></td>
</tr>
<tr>
<td>• 1.6.3.1 Referral to a pain clinic in reality is likely to end up with gabapentin and narcotic prescription which are unlikely to help.</td>
<td></td>
</tr>
<tr>
<td>• 1.6.3.3 Melatonin. Suggesting referral as not licenced may not help, as the reality is someone will then advise the GP to prescribe it. The GMC expect GPs to carefully consider any treatment that they prescribe, and expect GPs to be able to justify their decisions and actions when prescribing, administering and managing medicines regardless of whether they are licensed or unlicensed.</td>
<td></td>
</tr>
<tr>
<td>• Since the publication of NICE guideline CG53 10 years ago, there has been further published evidence to consider, including two MRC-funded studies (FINE and PACE):</td>
<td></td>
</tr>
</tbody>
</table>
### Stakeholder Consultation Comments Table

<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Comment</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regional Public Health Agency for Northern Ireland</td>
<td>Yes – at this time</td>
<td>Despite widespread criticisms of the PACE trial, NICE’s consultation document states that, even without its inclusion in the evidence review, the remaining published evidence points in the direction of symptom management as currently described in the guideline. The suggestion to ask Cochrane to revisit its systematic review including the PACE trial on the other hand appears bizarre in this context- what benefit could possibly come from doing this with a discredited trial?</td>
</tr>
<tr>
<td>False Allegations Support Organisation with Parents Protecting Children UK</td>
<td>No</td>
<td>I believe that recent increased medical awareness of hereditary collagen deficiency conditions such as Ehlers Danlos Syndrome and Marfan Syndrome suggest that a significant number of people previously thought to have viral myalgic encephalopathy illnesses are actually presenting with symptoms of Postural Orthostatic Tachycardia Syndrome caused by underlying collagen deficiency. I think that it is extremely urgent to review diagnostic practice to differentiate one condition from the other and therefore provide the best treatment for both groups. I believe that those reviewing the situation regarding ME / CFS should review website material and consult with EDS UK, EDS.COM AND THE HMSA and look at the new 2017 diagnostic criteria for the various types of collagen deficiency conditions to determine which patients formerly thought to have ME / CFS are presenting with symptoms of Postural Orthostatic Tachycardia Syndrome as a result of EDS or a related collagen deficiency condition.</td>
</tr>
</tbody>
</table>

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Concerns about the quality of CG53 and its impact in practice are longstanding, and a matter of record.

For example, in June 2014 Professor Mark Baker, then Director of the Centre for Clinical Practice at NICE, met with the Forward-ME Group of ME organisations, convened by the Countess of Mar. The minutes of this meeting indicate that a range of concerns were presented: [www.forward-me.org.uk/25th%20June%202014.htm](http://www.forward-me.org.uk/25th%20June%202014.htm)

In March 2007, at which point a draft of CG53 had been circulated for comment but the final version as yet unpublished, the LocalME list-owner contributed to a submission to a Health Select Committee Inquiry into aspects of the work on NICE. This submission addressed three of the Select Committee Inquiry’s questions:

- why NICE’s decisions are increasingly being challenged;
- whether public confidence in the Institute is waning, and if so why;
- NICE’s evaluation process, and whether any particular groups are disadvantaged by the process.

The final version of the guidance emerged later that year. The concerns raised in the memorandum to the Health Select Committee remained pertinent.

Points made to the Health Select Committee with reference to CG53 included:

1. **DIAGNOSTIC GUIDANCE** - The Institute’s guidance conflates M.E. - a neurological illness with a unique and distinctive clinical presentation - with chronic fatigue due to mental health problems. Management approaches which may help the latter group of patients are contra-indicated in respect of those with M.E. This basic flaw renders the guidelines unsuitable for their purpose.

2. **COMPOSITION OF GUIDELINE DEVELOPMENT GROUP (GDG)** - Few, if any, of the GDG had clinical experience of the illness they were advising upon. Authoritative medical professionals and researchers with in-depth experience and understanding of the neurological disorder M.E. were absent, while representatives with a belief in a ‘biopsychosocial’ model - which does not stand up to critical scrutiny - were many.

3. **ELIGIBILITY AND ASSESSMENT OF EVIDENCE** A narrow view is taken as to what constitutes admissible evidence, with the potential for a broad range of relevant information to be disregarded. This can lead, as with the guideline on ‘CFS/ME’, to false conclusions and inappropriate and dangerous guidance.

GET and CBT as a management strategy for CFS and ME is presented by NICE on the basis of what is perceived as ‘best evidence’. However, NICE is ignoring the fact that many scientists have questioned and demonstrated that, on closer inspection, the research is not as rigorous as is necessary and findings are not sufficient to support the original hypotheses. We feel this is a

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Please note that the aim of surveillance is to check that published guidelines are current and decide whether updates are needed. To do this, all surveillance reviews rely on assessing 2 elements that influence the decision to update a published guideline as outlined in the guidelines manual:

- Intelligence gathering on the perceived relevance of the guideline, which may include responses to questionnaires or external enquiries about the guideline recommendations
- Abstracts of primary or secondary evidence that has been published since the end of the search period for the guideline

It is the role of the developers to consider the full text studies when they are conducting full systematic reviews for the guideline update.
Graded Exercise ‘Therapy’ (GET) is still included as a management strategy when NICE has been made aware that patients report that it worsens their symptoms.


We are appalled that NICE plans to continue to recommend GET despite overwhelming patient feedback including from our own members that Graded Exercise has caused serious harm to many ME patients.

Patients need to be listened to, including those who have become severely affected after attempting graded exercise. Findings from a membership survey conducted by the 25% ME Group, which specifically supports those who are severely affected, show that the incidence of adverse impact was high, with 82% of those who had undergone graded exercise reporting that it had made them worse. It was also noted that some patients were not severely affected before trying GET.

REF: Severely Affected ME (Myalgic Encephalomyelitis) analysis report on questionnaire; 25% ME Group 2004. NB: Their most recent published information is from summer 2016 and is in keeping with the prior survey, with 86% made worse (The Quarterly, Issue 41, p25: http://www.25megroup.org/Information/Newsletter/issue%2041/PDF%20ISSUE%2041.pdf)

The Surveillance document cites a 2017 Cochrane review of 8 studies as a reason to continue to recommend Graded Exercise Therapy (GET).

However, although Clinical Guideline 53 states that Post Exertional Malaise (PEM) is a key clinical feature required for diagnosis (page 165 section 1.2.1), NONE of the 8 studies reviewed by Cochrane made it a requirement that PEM should be present. 5 used the Oxford criteria, which do not require it at all:


and the remaining 3 the 1994 CDC criteria, for which PEM is only optional:

Fukada et al. The Chronic Fatigue Syndrome: a comprehensive approach to its definition and study’ Annals of Internal Medicine 1994; 121: pp953-959

These studies are all, therefore, on a heterogeneous group and to apply the findings in guidelines for patients with PEM is unsafe.

Indeed, the Cochrane review itself concludes, under the Heading - What does the evidence from the review tell us? "limited information makes it difficult to draw firm conclusions about the safety of exercise therapy."

It also advises, under the Heading - Quality of the Evidence "However, the number of potential heterogeneity factors is high and the number of available trials is low; therefore we were limited in our ability to explore heterogeneity in a sensible way at the aggregate level."
We are sure that NICE will agree that the quality of the evidence and what the evidence tells us are both of relevance in the context of this surveillance review. However, by looking only at the abstracts of evidence published since CG53, it may be that this information has been missed. If this is at all indicative, we are of the view that this is a shoddy approach towards recommending a treatment in a clinical guideline.

In any case, it is clear that the 2017 Cochrance review cannot be cited as providing straightforward and conclusive reinforcement of CG53’s recommendations.

The Surveillance document rightly refers to the PACE trial and notes that controversy surrounds this trial. However it fails to mention that it has been highly criticized by many scientists, both from the UK and abroad.

Doctors and scientists who understand the illness need to be listened to.

101 international scientists and medics are here asking for retraction of a PACE trial paper that purports to refer to ‘recovery’:

In our view, the PACE research publications have effectively been discredited.

Even at best, the PACE trial shows that CBT and GET are not as efficacious as the researchers thought, so it does not support the promotion of those management strategies in a NICE guideline.

Recent research backs our perspective, as it illustrates an illness that is not the same as the condition that PACE (and other behavioural research) authors are referring to, since it cannot be accounted for by imputed physiological effects of ‘deconditioning’ through inactivity.

For example, research from Ronald Davis (Professor of Biochemistry and Genetics) and colleagues at Stanford University USA, including leading infectious disease specialist Professor Jose Montoya, who was awarded a 2016 Top Doctor Award - dedicated to selecting and honoring those healthcare practitioners who have demonstrated clinical excellence while delivering the highest standards of patient care.


Brief biography of Dr Montoya at http://www.pamf.org/serology/montoya.html

At the International Association for CFS/ME Conference in Fort Lauderdale last year, among more than 100 papers that further contribute to the evidence-base Dr Jose Montoya presented findings from a study involving 192 patients and 392 healthy but sedentary controls. He had found significant elevations for 17 specific cytokines, 13 of them pro-inflammatory, that correlated with symptom severity in the serum of ME/CFS patients compared with controls. Montoya said these findings “likely substantiate many of the symptoms experienced by patients and the immune nature of the disease”.

http://iacfsme.org/Conferences/2016-Fort-Lauderdale/Agenda
An overview of Stanford’s research work on immune system abnormalities (as of autumn 2014) can be found at:

Other Stanford publications include this a small but robust study using different types of brain imaging, which found three distinct types of abnormality:

Right Arcuate Fasciculus Abnormality in Chronic Fatigue Syndrome Michael M. Zeineh et al.
Published online October 30 2014
Department of Radiology, Lucas Center for Imaging, Stanford University School of Medicine: http://bit.ly/1yLUTDA

Even if NICE take the view that the above research is inconclusive, it is incumbent to advise our health professionals in line with a ‘first, do no harm’ approach. Asking a person to gradually increase exercise - or other form of activity - when the cause of their condition has not been conclusively established may hold the potential for harm. For example, a person with Polymyalgia Rheumatica needs steroid treatment before being advised to try GET.

The potential exists that exercise is contra-indicated in people with an unknown physiological disease if the underlying mechanism of the disease is not corrected. GET is a dangerous treatment for a patient with unidentified autoimmune disease and NICE in view of a substantial body of biomedical evidence - including evidence that directly contraindicates exercise - is wrong to encourage the medical profession to recommend it in the case of ‘CFS/ME’. (As far as we are aware, NICE has been made aware of the biomedical evidence we are alluding to. If not, please ask and we will furnish some details.)

The WHO classify myalgic encephalomyelitis as a neurological disorder (code G93.3), and index ‘the chronic fatigue syndrome’ to this classification. A classification with which the Department of Health concurs.

CBT/GET are therefore no more suited as a primary treatment for ME/CFS than they would be for cancer, multiple sclerosis etc. They may possibly have some value as coping aids but they are not a treatment.

CBT as currently researched and administered for ME and CFS patients is based on deconditioning and fear of exercise and is designed to change patients’ beliefs about their illness to encourage them to undertake graded exercise.

It is not, therefore, used as in other chronic physical illnesses like Cancer, Multiple Sclerosis to help patients adjust and cope with their illness.

The Quick Reference Guide is the resource used by GPs, and states that one of the key priorities is:
The health care professional should provide information about the range of interventions and management strategies as detailed in this guidance (such as the benefits, risks and likely side effects). [page 4]
Most Health professionals will be unaware of the following

1. the controversy surrounding research into the use of CBT and GET for patients diagnosed with CFS/ME.
2. that while NICE carry out a detailed research review process, this is rigidly blinkered, and does not grapple with the questions being raised by concerned patients and scientists.
3. That research studies into CBT and GET have been criticized by large numbers of scientists.
4. That GET has been the cause of worsening symptoms according to a vast body of patient reports.

We consider that health professionals and patients have the right to know of the reports of harm and any controversy regarding the management strategies being recommended by NICE.

At present, they are unable to accurately provide information about the range of interventions and management strategies as detailed in this guidance, in terms of the benefits, risks and likely side effects.

ME and CFS are seen by many NHS UK healthcare providers and commissioners as somatoform illness, despite the biomedical evidence to the contrary and the fact that the WHO classify myalgic encephalomyelitis as a neurological disorder under G93.3, a classification with which the Department of Health concurs.

There is widespread confusion with ‘fatigue syndrome’ - a mental/behavioural disorder (WHO ICD code F48.0).

The guideline does nothing to dispel this and it is time NICE took the time to consider why this is happening and who benefits from such a serious factual error.

In view of the above, Myalgic Encephalomyelitis becomes ‘lost’ in this Guideline, including in relation to those who are severely affected.

The existence of people presenting with M.E. in its severest forms almost seems to muddy the waters.

The section on severely affected patients can only be found towards the end of the full guideline (over 300 pages into the document), where it is advised: *this is not intended as a definitive guide to the specialist CFS/ME care needed for this patient group, and further reading is recommended.*

**REF 50:** Crowhurst G. *Supporting people with severe myalgic encephalomyelitis.* Nursing Standard 1921; (21).

Many of us contributing to this response have first hand experience of severe ME and it is not something patients and carers can ignore. It is a form of living hell. These patients need more help from NICE and the NHS.
<table>
<thead>
<tr>
<th>ME-Letterforce</th>
<th>No</th>
</tr>
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<tbody>
<tr>
<td><strong>Q1 comment 1</strong></td>
<td></td>
</tr>
<tr>
<td><em>This submission is not complete due to the very short consultation period</em></td>
<td></td>
</tr>
<tr>
<td>Our group recommends that NICE acknowledges the unusual circumstances in the UK regarding ME and CFS, i.e. that research into CFS and ME in the UK has been dominated by researchers who do not treat patients using a bio-medical model, and who do not have the trust of ME patients.</td>
<td></td>
</tr>
<tr>
<td>The ME Association and other ME patient groups including over 15000 people who signed the MEA petition find the current Guideline “not fit for purpose” and this was echoed by Professor Mark Baker at a Forward ME meeting in July 2014.</td>
<td></td>
</tr>
<tr>
<td>Our group are in full agreement and recommend that there is a complete review of the guideline in consultation with patient groups.</td>
<td></td>
</tr>
<tr>
<td><strong>Q1 Comment 2</strong></td>
<td></td>
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<tr>
<td>Our group recommends that NICE takes note of international research, and removes from both the current Guideline and from any further consideration research and trials carried out on the Oxford criteria for CFS, or not requiring Post Exertional Malaise as an essential key symptom, as required by NICE for diagnosis.</td>
<td></td>
</tr>
</tbody>
</table>

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Please note that the aim of surveillance is to check that published guidelines are current and decide whether updates are needed. To do this, all surveillance reviews rely on assessing 2 elements that influence the decision to update a published guideline as outlined in the guidelines manual:

- Intelligence gathering on the perceived relevance of the guideline, which may include responses to questionnaires or external enquiries about the guideline recommendations
- Abstracts of primary or secondary evidence that has been published since the end of the search period for the guideline

The most severely affected ME patients are unable to attend GP surgery or hospital - even by ambulance. Many such patients are currently receiving no healthcare at all, not even a GP home visit for monitoring purposes.

The guideline should recommend that patients with ME who are housebound be entitled to home visits by their general practitioner, and if necessary specialists in other areas of medicine, including for identification and treatment of concurrent illnesses.

The core defining feature of this illness is adverse impact of activity.

In terms of access to healthcare, GPs should therefore be made aware that patients may relapse and be too ill to attend in future, even if they managed to get to the surgery at some point previously. As a forum for Local Groups, we hear of too many local group members denied a home visit after relapsing, and of people relapsing as a direct result of the effort of getting themselves to the doctor’s surgery, having been denied a home visit.
In 2014 the USA NIH said the Oxford criteria is “flawed” and that continuing to use this “may cause harm” as it selects a broader population than more stringent criteria. [ii], [iii]

Q1 Comment 3

Our group recommends that NICE ceases to recommend CBT, GET, and GE in the light of increasing biomedical research and the failure of both the FINE and the PACE trial to show these to be effective as a treatment or strategy, and to recommend Pacing and rest instead, as patient evidence overwhelmingly shows these are the most helpful and, importantly, do no harm.

NB The CBT as recommended in conjunction with GET according to P White “was done on the basis of the fear avoidance theory of chronic fatigue syndrome”, rather than helping them adjust to a chronic illness as in eg cancer or MS

P.White “Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial” Lancet 2011 www.sciencedirect.com/science/article/pii/S0140673611600962

Our group notes that NICE argue in the Surveillance Review that even if PACE were downgraded there are still other earlier trials on similar interventions that the current Guideline evaluated.

Our group recommends that these earlier RCT’s and evidence be re-evaluated reading the whole paper not just the abstracts, removing all trials using the Oxford criteria, or any lacking Post Exertional Malaise as a required symptom, and any exercise or CBT trial that did not use a physical outcome measure such as an Actometer.

Q1 Comment 4

NICE needs to consider the composition of the GDG and include Topic experts and advisers knowledgeable about the international biomedical research into ME.

Previously it has relied on those who believe ME is a somatoform disorder. It is unreasonable for ME patients to have Guidelines for their care and treatment produced by those who hold this controversial view when there is a vast body of experts who disagree.

Q1 Comment 5

Diagnosis of ME – “International Consensus Criteria”

It is the role of the developers to consider the full text studies when they are conducting full systematic reviews for the guideline update.
Our group recommends NICE updates the section on Diagnosis to stress that the cardinal feature should be post exertional symptoms and with a better description such as that contained in Table 1 from the International Consensus document.

Q1 Comment 6

Diagnosis and testing – IOM report

Our group recommends that the current NICE Guideline be updated in line with the USA. The Institute of Medicine report “Beyond Myalgic Encephalomyelitis / Chronic Fatigue Syndrome – redefining an illness” sections on symptoms to include

a. Orthostatic intolerance
b. Immune dysfunction
c. Sensitivity to external stimuli (eg food, drugs, chemicals)

Also their recommendations for testing

EG

a. Recommend that severely affected patients may need to lie down while they are being interviewed.
b. Use two cardiopulmonary exercise tests (CPETs) separated by 24 hours (if patient agrees and is well enough)
c. Use formal neuropsychological testing, to observe slowed information processing, etc
d. Use a standing test or tilt test to evaluate for postural tachycardia syndrome, neurally mediated hypotension, and orthostatic hypotension.

Suffolk Youth & Parent Support Group1 & Norfolk & Suffolk Service Design and Service Implementation Group2.

RE: NICE guideline on CG53 Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (or encephalopathy) 3: diagnosis and management: Surveillance consultation

I received the following notice last week via the NICE stakeholder, ME Association, “Bad news to the MEA from NICE: no review considered necessary. 4 To Surveillance Team; you state; “The clinical guideline for CG53 Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy); diagnosis and management has been checked by NICE for the need for update. Registered stakeholders for the guideline are invited to comment on the provisional decision via this website. Organisations not registered as stakeholders are not able to comment, we recommend that you register as a stakeholder or you contact the registered stakeholder organisation that most closely

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will
represents your interests and pass your comments to them. Note that the provisional review decision presented here does not constitute NICE's formal decision on this guideline. The decision is provisional and may change after consultation."

Consultation dates: 10 July 2017 (9am) to 24 July 2017 (9am)

I have had to challenge the NICE Consultation period 10th-21st July and secure an extension; and have issued an FOI- to secure material information to inform my response. (which will not be made available within the necessary timeframe).

The provisional decision issued and now under consideration by NICE: may endanger compliance with the following NICE Terms of Reference 5 in the footnote below.

Having looked at the NICE website, I can see no evidence that the NICE process of review is in the public interest and complies with the transparency and openness required by the public who have a right to interrogate the NICE decision making and question y NICE guidance fitness for purpose.

General references

References from Suffolk Youth & Parent Support Group1 & Norfolk & Suffolk Service Design and Service Implementation Group2. Colchester MESH Essex:

1 http://suffolkmeandyou.blogspot.co.uk/2016/05/
2 http://nandsme.blogspot.co.uk/
3 Myalgic encephalopathy is not a recognised and validated condition and this name should be removed. Capitals should be used to identify ME and CFS. :Chronic Fatigue Syndrome/Myalgic Encephalomyelitis
5 https://www.nice.org.uk/Media/Default/About/Who-we-are/20140910-smt-tors-final.pdf

ATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE Senior Management

TeamStanding Orders and Terms of Reference

Terms of Reference Overview 1. constructing effective relationships with partner organisations and maintaining good communications with the public , the NHS, social care and local government and with the life sciences industries * identifying and mitigating the risks faced by the Institute.

6The Montgomery case has changed the way in which guidance now needs to be given. NICE can no longer rely on only the best available evidence in their opinion, they have a duty to identify all

be passed onto developers for consideration during the update of the guideline.
risks and benefits.
https://www.supremecourt.uk/decided-cases/docs/UKSC_2013_0136_Judgment.pdf
8 Source: UK House of Lords Date: July 19, 2017UR
http://www.parliament.uk/business/publications/written-questions-answers-statements/written-question/Lords/2017-07-10/HL637/
Ref: http://www.me-net.combidom.com/meweb/web1.4.html#westminster
9NIHCE draft guideline 'Intermediate care (including reablement)'
https://www.nice.org.uk/guidance/GID-SCWAVE0709/documents/draft-guideline
Question made during correspondence with NICE Team- "The Institute responded to my comments on behalf of*** Group at guideline scope stage Regaining Independence Guideline Scope Consultation: Scoping exercise with response from developers's
‘I anticipate that this will be an important issue for the Guideline Committee to consider’. Can you direct me to any point in the draft that is indicative of the Guideline Committee having considered this ‘important issue’?"
Contacts- Danielle Conroy Guideline co- ord 0160 41604008
Nick Staples, the project manager was out of his office 020 7045 2076
10 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 people with ME’s needs and safety. This can 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’ I the core principle for personal choice.”
http://www.meresearch.org.uk/information/publications/misdiagnosis-on-a-grand-scale/
12 NICE Enquiry (our ref EH82669) 11/07/17
13 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 people with ME’s needs and safety. This can 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.


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**Do you agree with the proposal to remove the guideline from the static list?**

<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Overall response</th>
<th>Comments</th>
<th>NICE response</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Infection Association</td>
<td>Yes</td>
<td>No comments</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or...</td>
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</table>
Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

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<tr>
<th>The Pernicious Anaemia Society</th>
<th>No</th>
<th>See above</th>
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<tbody>
<tr>
<td>VIRAS</td>
<td>No</td>
<td>No comments</td>
</tr>
<tr>
<td>ME Research UK</td>
<td>Yes</td>
<td>No comment</td>
</tr>
</tbody>
</table>

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

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<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Yes/No</th>
<th>Comments</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Royal Liverpool University Hospital, CFS/ME services</td>
<td>No</td>
<td>Not until there is significant new evidence of treatment, however if it is I/we would be very keen to be involved in the new guidelines as we are one of the biggest CFS services in the UK.</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
<tr>
<td>PoTS UK</td>
<td>Yes</td>
<td>No comments</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
<tr>
<td>Royal College of Paediatrics</td>
<td>Yes</td>
<td>There will be new evidence.</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
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<tr>
<td>Stakeholder</td>
<td>Response</td>
<td>Comment</td>
<td>Additional Information</td>
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<td>-----------------------------------------</td>
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<td>------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>North London ME Network</td>
<td>Yes</td>
<td>No comment</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
<tr>
<td>Association of British Neurologists</td>
<td>Yes</td>
<td>We note that NICE is planning to wait for an updated Cochrane Review of Cognitive Behavioural Therapy which we agree with</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
</tbody>
</table>
| **FORWARD-ME** | **Yes** | In 2007, NICE guidelines for the management of CFS/ME reflected a global consensus among researchers and health authorities about the nature and optimal management of the condition. In 2017, however, that is no longer the case. Given the unanimous reversal of opinion towards biological management of CFS/ME by US health authorities, it is ethically concerning that NICE could entertain the possibility of not only maintaining the guideline as it stands, but keeping it on the static list.

First, to allow for these possibilities is to fail to respect NICE’s commitment to evidence-based practice. While policy makers at NICE have every right to a professional evaluation of current research that is opposed to the evaluation made by their counterparts in the US, the US interpretation of the research is itself evidence of which patients, physicians and mental health providers in the UK must be informed.

Second, to allow for these possibilities is to fail to respect NICE’s commitment to ethical practice as specified in the Social Value Judgements document. While we respect NICE’s concern to avoid questions of aetiology, that concern in no way frees NICE, or the NHS, from the ethical obligation to inform patients and providers of a substantial difference in orientation to this condition by respected health authorities elsewhere. |

| **Patient and Client Council** | **Yes** | We expect a review as new evidence emerges. |

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

| **Inclusion London** | **No** | We believe that the guidelines should be on the active list so they can be reviewed every two years. |

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53
<table>
<thead>
<tr>
<th>Mast Cell Action</th>
<th>Yes</th>
<th>No Comments</th>
<th>Mast Cell Action</th>
<th>Yes</th>
<th>No Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Royal College of Psychiatrists</td>
<td>Yes</td>
<td>We support the view that the NICE guideline on chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) should be removed from the static list. This is because there is important ongoing research in the area that will be published in the next 3-5 years thus requiring active surveillance. We support the request from NICE for an updated Cochrane review to include PACE data which may influence the outcome of future surveillance.</td>
<td>Royal College of Psychiatrists</td>
<td>Yes</td>
<td>We support the view that the NICE guideline on chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) should be removed from the static list. This is because there is important ongoing research in the area that will be published in the next 3-5 years thus requiring active surveillance. We support the request from NICE for an updated Cochrane review to include PACE data which may influence the outcome of future surveillance.</td>
</tr>
<tr>
<td>The ME Association</td>
<td>Yes</td>
<td>There are serious omissions and lack of detail in numerous parts of the current NICE guideline covering clinical assessment, diagnosis and management. Our recommendations for improvement were made in the comprehensive submission that we submitted in 2013 when we opposed the proposal to place the NICE guideline in the NICE static list.</td>
<td>The ME Association</td>
<td>Yes</td>
<td>There are serious omissions and lack of detail in numerous parts of the current NICE guideline covering clinical assessment, diagnosis and management. Our recommendations for improvement were made in the comprehensive submission that we submitted in 2013 when we opposed the proposal to place the NICE guideline in the NICE static list.</td>
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Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53
Website link to MEA recommendations re NICE static list consultation:

Having attended a meeting with Professor Mark Baker from NICE at the House of Lords on 25th June 2014, we were left with the clear impression that Professor Baker understood and accepted the concerns of the ME patient community about defects in the guideline. Consequently, we find it very difficult to understand why NICE decided to reinforce their inactivity over the guideline by placing it on the static list only a few months earlier in September 2013.

These are two relevant extracts from the Minutes for this meeting:

2.2 Turning to the ME/CFS Guideline specifically, the Professor said that it did not meet our needs and it did not meet theirs (NICE's) either. The pressure for guidance started in about 2002 when the then CMO, Sir Liam Donaldson, wanted the subject “put to bed” in the form of advice to doctors that ME/CFS was a real illness and what they should do about it. It did serve a purpose because it was the only bit of guidance in the NHS on ME/CFS, but it was limited in its scope. It was designed to get patients seen and helped, but it assumed there were specialists who knew what to do – and there were not.

2.4 In summary, Professor Baker said:
   · He sympathised with the position we were in with the Guideline
   · The Guideline failed to address the real issues in ME/CFS
   · It does not promote innovation
   · It had a disappointing impact on specialist care and commissioning issues.

Complete Minutes for this meeting can be found here:
http://www.forward-me.org.uk/25th%20June%202014.htm

decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
<p>| | |</p>
<table>
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<tbody>
<tr>
<td>We must, however, return to two key issues that are of major concern to the ME/CFS patient community. These relate to:</td>
<td></td>
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<tr>
<td>(a) guidance on clinical assessment and diagnosis of ME/CFS and</td>
<td></td>
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<tr>
<td>(b) the failure of NICE to provide any meaningful guidance on management of people with severe ME/CFS.</td>
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<tr>
<td>Both issues were recently raised at a meeting at the House of Lords between members of the Forward ME Group of ME/CFS charities and two senior representatives from the Royal College of General Practitioners.</td>
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<tr>
<td>Minutes for this meeting can be found on the Forward ME Group website: <a href="http://www.forward-me.org.uk">http://www.forward-me.org.uk</a></td>
<td></td>
</tr>
<tr>
<td>Delays in diagnosis, resulting in no clear guidance, or even harmful guidance on management, creates a very distressing and unsatisfactory situation for patients.</td>
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<tr>
<td>Both NICE and the Chief Medical Officer’s Working Group report on ME/CFS have issued clear guidance on the timeline for making a diagnosis. The NICE guideline states:</td>
<td></td>
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<tr>
<td>A diagnosis should be made after other possible diagnoses have been excluded and the symptoms have persisted for 4 months in an adult or 3 months in a child or young person and that this should be made or confirmed by a paediatrician.</td>
<td></td>
</tr>
<tr>
<td>Despite the NICE guidance being in place for almost 10 years, recent patient evidence collected by the ME Association indicates that less than 20% of people are diagnosed within 6 months of symptoms occurring. Over 60% are waiting a year or more.</td>
<td></td>
</tr>
<tr>
<td>At the other end of the spectrum, a GP with special interest in ME/CFS sent in written evidence to the RCGP meeting relating to a GP trainee who had been chastised by her trainer for even making a diagnosis of ME/CFS.</td>
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</tr>
<tr>
<td>In addition, what has become known as the NICE guideline diagnostic criteria for ME/CFS is far too broad. This is in direct contrast to the much more selective criteria that has been proposed by the Institute of Medicine in America. Use of the NICE diagnostic criteria increases the possibility that people who do not meet one of the stricter research or clinical diagnostic criteria for ME or CFS can be diagnosed as having ME/CFS without proper consideration being given to other possible explanations for having ME/CFS like</td>
<td></td>
</tr>
</tbody>
</table>

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Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

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Misdiagnosis is therefore another significant concern to The MEA. In support of this position, one research study reported that around 40% of people referred to a specialist ME/CFS service in Newcastle did not even have a diagnosis of ME/CFS on further assessment.

Reference:


Around 25% of people with ME/CFS are severely affected – being wheelchair, house, or bed-bound. This group faces a number of serious problems that are not being addressed in the current guideline.

First is the lack of any meaningful guidance on clinical assessment of people with severe ME/CFS.

Second is the failure to refer to serious neurological symptoms such as diplopia, blackouts, atypical convulsions, loss of speech, and loss of swallowing necessitating nasogastric feeding – all of which are referred to in section 4.2.1.1 of the 2002 Chief Medical Officer’s Working Group report on ME/CFS. The only reference to management of severe ME/CFS in the CG53 Quick Reference guidance is on page 17 where it recommends the use of telephone or email based management based on the principles of CBT and GET. This recommendation has not been welcomed or used by people with severe ME/CFS.

Third is the almost complete lack of any form of domiciliary care or assessment being provided by hospital-based referral services for people with severe ME/CFS. When added to the fact that it has become increasingly difficult for people with severe ME/CFS to obtain a home visit from a GP, many are left with no form of on-going medical care at all.
McDermott et al surveyed all of the 49 English NHS specialist CFS/ME adult services in England, in 2013. This involved a cross-sectional survey conducted by email questionnaire.

All 49 services replied (100%). 33% (16/49) of specialist CFS/ME services provided no service for housebound patients. 55% (27/49) services did treat patients with severe CFS/ME and their interventions followed the NICE guidelines. The remaining services (12%, 6/49) offered occasional or minimal support where funding allowed. There was only one NHS unit providing specialist inpatient CFS/ME provision in England.

Reference:

Fourth is the way in which lack of proper medical care results in people with severe ME/CFS having great difficulty in accessing social care. This situation resulted in an Inquiry by the All Party Parliamentary Group on ME.

Reference:
Social care and ME/CFS – interim report prepared for the APPG on ME:

Problems relating to late diagnosis and misdiagnosis, along with the difficulties in accessing both medical and social care are two key issues that must be re-visited by NICE. The only way to do so is through a proper review and update of the 2007 guideline.

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<table>
<thead>
<tr>
<th>Action for ME</th>
<th>Yes</th>
</tr>
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<tbody>
<tr>
<td>Action for M.E. agrees with the proposal to remove the guideline from the static list.</td>
<td></td>
</tr>
<tr>
<td>There are a number of ongoing trials that are expected to conclude in the coming years that warrant more frequent review of the guideline.</td>
<td></td>
</tr>
<tr>
<td>Trials into pharmacological treatments include ongoing research on HyQyia, an immunoglobulin [<a href="http://bit.ly/2gQ44oh">http://bit.ly/2gQ44oh</a> accessed 21 July 2017] and on the</td>
<td></td>
</tr>
</tbody>
</table>

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

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immunosuppressant cyclophosphamide [https://www.clinicaltrials.gov/ct2/show/NCT02444091 accessed 21 July 2017]. Other research that has concluded called for further investigation of the antiviral valganciclovir [Montoya et al 2013, Randomized clinical trial to evaluate the efficacy and safety of valganciclovir in a subset of patients with chronic fatigue syndrome, Journal of Medical Virology 85(12)]. There is also a Norwegian phase III trial into the immunosuppressant Rituximab [Fluge et al 2015, B-Lymphocyte Depletion in Myalgic Encephalopathy/ Chronic Fatigue Syndrome. An Open-Label Phase II Study with Rituximab Maintenance Treatment, PLoS ONE 10(7)] taking place as of May 2017. These are just a few examples of a broad field of research listed on NHS Choices from the WHO International Clinical Trials Registry Platform [NHS Choices, Chronic fatigue syndrome (CFS/M.E.): Clinical trials, http://www.nhs.uk/Conditions/Chronic-fatigue-syndrome/Pages/clinical-trial.aspx, accessed 21 July 2017] which may impact on the NICE recommendations, and which ought to be considered in upcoming reviews.

The NICE proposal also mentions that the data from the PACE trial is currently under dispute. Given that this data is used in support of the guideline’s recommendations, and that there are continued re-analyses of this data and comment on the conduct of the trial, the guideline must also be in a position to be updated promptly in case the results of the trial are determined not to be valid.

<table>
<thead>
<tr>
<th>British Association for CFS/ME</th>
<th>Yes</th>
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<tbody>
<tr>
<td>We cite the GETSET trial (Clarke et al. Lancet 2017; epub), FatiGo publications, and other research cited above that was published too recently for the surveillance review. BACME will be undertaking a survey of our members within the coming year. We aim to consult on diagnostic and therapeutic practices and will submit those findings for surveillance.</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
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<tr>
<th>Healthwatch Kirklees</th>
<th>Yes</th>
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<tbody>
<tr>
<td>It is possible that the ME/CFS community in Britain has suffered years of health inequalities, which need to be addressed. In the UK over 250,000 people (2.6% of adult population) are suffering with no effective treatments and minimal resources being put into research. The pressures on the NHS are significant with 19,985 estimated newly diagnosed cases in the UK each year. (2007 report by the National Institute for Health</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have</td>
</tr>
</tbody>
</table>
and Clinical Excellence NICE.) In 2012, 46% of GPs report that ME/CFS is the illness group for which they have the most difficulty in making referrals and that 22% of GPs reported an increase in patients reporting ME/CFS in 2011. (The Aviva Health of the Nation Index. 2012). The NHS uses a bio psycho-social approach to ME/CFS which treats the illness as a somatic/psychological illness. The patients in Kirklees and Calderdale with ME feel this is scientifically inaccurate. Professor Anthony Komaroff, one of the world’s foremost experts on ME/CFS from Harvard Medical School, has noted that the American National Academy of Sciences/Institute of Health reviewed 9,000 peer-reviewed studies into the illness in 2015. This landmark report stated that ME/CFS is a neurological illness that is biological in nature. In a webinar for the Solve ME/CFS charity on 10 November 2016, Professor Komaroff commented: “Low-grade brain inflammation causes symptoms of ME/CFS. This involves a connection between the brain, the immune system and possibly in some people the gut. The good news. I think we can now address the controversy: that this illness is not something that people are imagining. That this is not a primary psychological disorder. We now have abundant evidence that this illness involves the body, the brain, the autonomic nervous system, and involves the immune system and specifically energy metabolism and oxidative and nitrosative stress.”

The 25% ME Group

| Yes |

But emphatically not for the reason specified, particularly the example of ‘important ongoing research’ cited. The description of this study - ‘fatigue in teenagers on the internet’ - is quaint. Its relevance to teenagers with M.E. is dubious.

ESSENTIAL FEATURE OF ANY CLINICAL GUIDELINE TO BE APPLIED TO M.E. PATIENTS ON THE NHS:

Diagnosis, information, and support

1. Recognise that the clinical profile of M.E. is unique and does not mimic any other illness or condition.
2. Equip health professionals to recognise this clinical profile. (Particularly important since diagnosis is made clinically, rather than via a diagnostic test.)
3. Aim for clarity as to key feature and what underlies them: i.e. group according to specific areas of pathogenesis (i.e. as per Carruthers’ et al. Clinical Case Definition 2003) rather than giving the appearance of a ‘laundry list of unrelated symptoms’.
4. Relatedly, make links with research to illuminate clinical presentation, thereby avoiding the implication that research is something that happens in an ivory tower and doesn’t yet have implications for clinical practice. For example: (i) Significantly higher levels of IL-2-R and T8-R are found in patients with CFS compared to controls. This is consistent with the presence of a chronic viral illness decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Thank you for your response.

We note your concerns about the FITNET-NHS trial. However, this was just an example of ongoing research identified through the surveillance review and not the only ongoing evidence we are aware of on this topic.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
in CFS patients. There was a correlation between the values of soluble receptors and the severity of the illness. (ii) The objective postural cardiac output abnormalities correlate with the degree of reactive fatigue and overall severity of ME/CFS. [references available]

5. Recognise that getting the diagnosis wrong can have profound consequences, particularly if people who have M.E. are advised to undertake greater activity (however gradual) based on the premise that they have chronic fatigue due to physiological de-conditioning.

BEHAVIOURAL INTERVENTIONS:

1. Recognise that there is no research trial evidence on which recommendations for rehabilitative approaches specifically relating to the care of M.E. patients might be based. None of the research trials reporting benefit from graded exercise and/or cognitive behavioural therapy recruited participants according to a case definition specific to ME. Nor is there evidence of benefit from any other source – quite the contrary.

2. Recognise that physiological response to exercise has been found to be abnormal.

3. Take seriously patient reports indicating deterioration thereafter.

CG53 is illogical and inconsistent. The definition of ‘exercise’ in CG53 is not the same as the definition used in the studies on which it relies. (Neither is it the same as the definition that ‘Cochrane’ cite in their literature search in recent review.) So recommendations for graded exercise in CG53 are not truly based on the reported outcomes of the trials.

This applies equally to CBT, in so far as the same type of activity modification is advocated in the CBT trials (i.e. ‘CBT’ = exercise plus an ‘explanation’ of why exercise ‘will help’). The patient group selected for participation in the trials is not the same as the patient group defined in CG53 (no trial, to our knowledge, has yet used ‘NICE’ criteria to recruit). The numbers involved are so small that the aggregate data is insufficiently robust for this method to hold water (would not normally pass muster with regard to any other disorder). However this is then applied to said patients (and a whole lot more, as diagnostic practice on the ground is very poor indeed, also caveats on application are not recognised). With doctors being expected to warn of risk that the CG53 considers do not exist.

**CG 53 and the surveillance review purport to be rigorous but this claim does not bear scrutiny, despite the elaborate process involved.**

| Blue Ribbon for the | Yes | Yes for all the reasons stated in question 1, which I will not repeat here, this Guideline on ME/CFS needs updating urgently; this guideline is not fit for purpose for the patient | Thank you for your response. |
| Awareness of Myalgic Encephalomyelitis (BRAME) | population, or the supposed values of NICE to promote quality healthcare – which is currently not the case for people with ME and CFS. We feared that these guidelines would be used to further perpetuate the erroneous biopsychosocial model, resulting in the only management techniques being offered to be those which so many patients, in so many different studies, prove to be either unhelpful or harmful. This has come to fruition; once biomedical clinics have become biopsychosocial, the patient population are complaining about the way they are being treated and yet the answer is always – we are following NICE. NICE are bioethically supposed to provide impartial advice, and where there is disagreement, both sides of the argument should be provided, with no preference given to one or the other – a technique used in the CMO Working Group Report (2001). Instead NICE has, in many cases, due to its reduced research scope, ignored much research evidence and yet appears to have based its decisions, to basically prop up its guidelines, on a highly disputed research trial, which the authors themselves admitted did not study people with ME/CFS, and changed the way that the results were interpreted as to provide the results they expected to achieve. NICE are supposed to provide best practice – not support practices the patient population shows to be unhelpful/harmful. They are supposed to lead the way, acknowledging where research, and patient evidence, have shown that their original recommendations are wrong, and saying we will not accept this; we will ensure that the patients are treated with respect and receive the correct management. NICE is supposed to be a leading light; not something to cast shade and push a patient population even further into the darkness. The patient population, carers, researchers and healthcare professionals are begging you to become that leading light, to stand up for them and say we got it wrong, but we will now get it right – this will then show that NICE is a strong institution to be respected. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline. |
| Hope 4 ME & Fibro Northern Ireland | Yes | We agree that the guideline needs to be removed from the static list, however, we do not agree with the reason that the review panel have chosen for proposing this action. The “FITNET” study\textsuperscript{36} identified in the surveillance review as, “important ongoing research” has caused consternation within the ME community and most especially amongst parents of children with ME. Some of these parents are members of our charity, and have voiced their considerable concerns to us. Thank you for your response. We note your concerns about the FITNET-NHS trial. However, this was just an example of ongoing research identified through the surveillance review and not the only ongoing evidence we are aware of on this topic. |

\textsuperscript{36} FITNET study: http://www.isrctn.com/ISRCTN18020851
David Tuller has explained many of the problems with the FITNET study on Virology Blog\(^{37}\) noting that it is an unblinded study relying on subjective outcomes, with weak subject selection criteria (no post exertional malaise required), which operates on the premise that no ongoing disease process is present.

This hardly seems like a gold standard trial worthy of the description of “important research", and for which a NICE guideline should be removed from the static list in anticipation of its results.

Further problems with the FITNET study were noted in David Tuller’s follow up article\(^{38}\) where he introduces the matter stating, “I guess people get upset when researchers cite shoddy “evidence” from poorly designed trials to justify foisting psychological treatments on kids with a physiological disease.”

We take the view that the FITNET study is not worthy of consideration in updating CG53, and as such it is not a valid reason to remove CG53 from the static list.

However, there is sufficient evidence that the multiple studies supporting GET and CBT should be regarded as scientifically flawed. This is an ongoing issue, but it is our view that science will eventually prevail and papers such as the PACE Trial and its spin-offs will be retracted. We are not alone with this view: an open letter\(^{39}\) addressed to Richard Horton and The Lancet calls for a retraction of the PACE paper, and a petition from ME Action\(^{40}\) signed by over 12000 has also called for retraction.

A challenge like this to the science behind GET and CBT, along with the reported harms in the MEA survey\(^{41}\), and the massive patient concern over the inclusion of these therapies in CG53 as demonstrated by the current MEA petition\(^{42}\) calling for a review of CG53, should be sufficient reason to for immediate review, and certainly for the removal of CG53 from the NICE static list.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

\(^{40}\) ME Action petition: [https://my.meaaction.net/petitions/pace-trial-needs-review-now](https://my.meaaction.net/petitions/pace-trial-needs-review-now)
\(^{41}\) ME Association Survey - as ref 1 above
\(^{42}\) ME Association Petition – as ref 4 above
Biomedical research is however in progress and this type of research is likely to produce better outcomes for patients in the future. The studies linked in the IOM report (that lists some 9000 biomedical studies on ME) should not be discounted by the review panel, but rather highlighted as potential optimism for the future.

Yet, we were surprised that the review panel seemed only to consider papers supporting the psycho-social premise for ME, and so would again like to call for an independent investigation into the makeup of the review panel, and the topic expert team for CG53.

<table>
<thead>
<tr>
<th>Invest in ME</th>
<th>Yes</th>
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<tbody>
<tr>
<td>1. Yes. But not because of the dubious and cynical reasons given by NICE. It is good that the guideline will be off the static list but the reasons stated make it even clearer that the guidelines probably need a complete rewrite that exclude research based on Oxford Criteria and all references to the PACE Trial.</td>
<td></td>
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<tr>
<td>2. You have used two reasons for taking it off the static list. One is PACE – something you forever claim never influenced the original guidelines but now say it does – despite all of the unbiased and informed academic world documenting the flaws in that study and recommending that it should be dismissed completely. The other is FITNET – another contrived establishment set up to produce policy-based evidence which has not real use in the real world. Yet NICE quite bluntly – and negligently – avoid mentioning the Phase III multi-centre, placebo controlled rituximab trial in Norway.</td>
<td></td>
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<tr>
<td>3. The reason NICE have made the Surveillance proposal consultation is to avoid having to examine the results of a possibly positive rituximab trial. In your world where you try to avoid doing anything it will be quite convenient to keep this away from being reviewed for another five years so that nothing happens. If this is true it shows that NICE is a very suspect organisation that needs to be investigated.</td>
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Thank you for your response.

We note your concerns about the FITNET-NHS trial. However, this was just an example of ongoing research identified through the surveillance review and not the only ongoing evidence we are aware of on this topic. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

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43 IOM report – as ref 8 above
<table>
<thead>
<tr>
<th>Name</th>
<th>Response</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>ME Lochaber</td>
<td>Yes</td>
<td>NICE guidelines consider only psycho-social studies. The PACE trial is flawed, and cited in university courses as an example of ‘bad science’. These failures must be accepted as rendering PACE and GETSET unfit for purpose. <a href="http://journals.sagepub.com/doi/10.1177/1359105317714486">http://journals.sagepub.com/doi/10.1177/1359105317714486</a></td>
</tr>
<tr>
<td>ME Support Northern Ireland</td>
<td>Yes</td>
<td>This guideline should be removed from the static list due to the potential of current valid research identifying biomarkers and treatment. The IACFS/ME conference in Florida in 2016 and Invest in ME in London, 2017 have brought about an explosion of research in ME/CFS therefore “static” limits the opportunity to incorporate new evidence into NICE Guidelines</td>
</tr>
<tr>
<td>Royal Free London NHS Foundation Trust</td>
<td>Yes</td>
<td>As above. We also cite the GETSET trial (Clarke et al. Lancet 2017; epub), FatiGo publications, and note other research publications too recent for the surveillance review. Further, in this department, an audit (and subsequent abstract submitted to the CMRC conference 2017) of the prevalence of Joint Hypermobility Syndrome (JHS) presenting at this clinic was 25% - such prevalence represents a substantial comorbidity, and raises the possibility that JHS or related aetiology is the primary disease, at least in a proportion of patients. Research has shown that adults with JHS benefit from exercises promoting proprioception, balance reactions and plyometrics (Sahin et al, 2008), suggesting that graded exercise therapy provision in a patient with fatigue may need to encompass these</td>
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</table>

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Yes/No</th>
<th>Comment</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stockport ME Group</td>
<td>Yes</td>
<td>No comment</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
<tr>
<td>The Ehlers-Danlos Support UK</td>
<td>Yes</td>
<td>No comment</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
<tr>
<td>The Young ME Sufferers Trust</td>
<td>Yes</td>
<td></td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
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The Young ME Sufferers Trust [Tymes Trust] believes that it is essential to remove the guideline from the static list. In July 2014 a peer-reviewed paper by our Executive Director Jane Colby on 'False Allegations of Child Abuse in Cases of Childhood Myalgic Encephalomyelitis (ME)' was published (http://www.argumentcritique.com/publications.html) (and republished with permission at http://www.tymestrust.org/pdfs/falseallegations.pdf).
At that time there were 121 families on our list who had faced or were facing such suspicions/allegations. This number has now risen to 194, with 6 new cases in the last week. We stress that to date, not one of these families has been found guilty of anything, indicating a virtual epidemic of misunderstanding amongst medical professionals, who are diagnosing FII, MSBP and PRS, later found to be incorrect. These cases arise because the child does not recover having had CBT and GET, or because the family declines it.

NICE now has the opportunity to highlight prominently that there is now profound medical disagreement on the efficacy and safety of its hitherto recommended treatments. If it fails in this vitally needed task, we see no abatement in the current distress and trauma suffered by innocent families and their sick children, if they are unfortunate enough to contract ME.

<table>
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<tr>
<th>University of Manchester – FINE Trial</th>
<th>Yes</th>
<th>No comment</th>
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| Welsh Association of ME & CFS Support | Yes | If the reason for being removed from the static list is because there is ‘important ongoing research in this area’, then we agree. The trials into rituximab (https://clinicaltrials.gov/ct2/show/NCT02229942) and cyclophosphamide (EudraCT Number: 2014-004029-41) are important examples of trials which could make a life changing difference to many of the people with ME in the UK.

We do not consider the trial mentioned - 'UK trial of internet-based cognitive behavioural therapy in children and young adults’ – as important research into CFS or ME. On the contrary the FITNET-NHS trial is a waste of time and money as it shares many of the same flaws as the PACE trial, including lack of objective measures. The leaflet accompanying the trial claims that CBT will aim to ‘change negative thinking’. There is no evidence that negative thinking causes or perpetuates ME or CFS in any of the
|
| Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
| Thank you for your response. We note your concerns about the FITNET-NHS trial. However, this was just an example of ongoing research identified through the surveillance review and not the only ongoing evidence we are aware of on this topic.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

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subgroups of patients. No attempt will be made to identify individuals with this specific problem it is simply assumed that all subgroups of people falling under the broad heading of CFS suffer from negative thinking. This trial appears to be attempting to replicate results from a similar FITNET trial in the Netherlands where no difference was found between the active and control groups at long-term follow-up (http://pediatrics.aappublications.org/content/early/2013/05/08/peds.2012-2007), which is consistent with every other trial of CBT. The trial has been criticised by many professional researchers around the world e.g. ‘the height of clinical trial amateurism’ by Dr Bruce Levin of Columbia University and it’s ‘more meaningless research based on flawed assumptions and bad studies’ by Prof David Tuller of University of California, Berkeley.

WAMES wishes to see the research into dysfunction in the body’s systems (neuro, immune, endocrine etc.) play a more important role in determining the NICE guidelines. We do not believe it makes sense to promote a management approach, simply because it has been more widely researched than others, when i) there is research about the role of exercise in the dysfunctional ME body that contradicts the assumptions of such a management approach; ii) the research does not use objective measures.

We agree with the proposal to move the guidelines from the static to active list. However, the research issues we raised in 1a and 1b also apply to the FITNET trial and Cochrane review mentioned in the Surveillance review, and should be taken into account when these are published.

Due to UK research funding not being commensurate with the disease burden, we ask that NICE be open to all international, well-designed studies. This is an advancing and expanding area of research, despite a dearth of funding. There is a lot of interesting research going on into ME and CFS, including research which might lead to potential biomarkers or treatment for patients. There are currently 20 active clinical studies related to ME and CFS in the clinicaltrials.gov registry and 10 in the EU Clinical Trials register. Below we have highlighted a number of upcoming studies that we would like NICE to consider. It is essential that the guidelines are moved to the active list and updated in light of the findings of these studies.

2a Upcoming research into treatment and biomarker
2a.1 Rituximab (RituxME trial)
Consultant Øystein Fluge and Professor Olav Mella at the Department of Oncology and Medical Physics at Haukeland University Hospital in Norway are researching whether B-lymphocyte depletion can be effective in ME treatment. Currently, Fluge and Mella are...
running a national, randomized, double-blinded and placebo-controlled multicentre phase III study with the monoclonal antibody Rituximab on patients with ME. The estimated completion date of the trial is September 2017. Rituximab is a monoclonal anti-CD20 antibody and is a licensed product for non-Hodgkins Lymphoma, chronic lymphocytic leukaemia, rheumatoid arthritis and granulomatosis. It has been shown to effectively deplete B-lymphocytes in rheumatoid arthritis and non-Hodgkins Lymphoma (reviewed in Donner, 2010). Fluge and Mella have conducted several human trials investigating the effect of Rituximab on patients with ME. These studies found that in a subset of patients, fatigue scores improved following 6-10 months of treatment. Three studies on Rituximab clinical trials in ME patients have been published (Fluge and Mella 2009, 2011, 2105). In addition to supporting the potential use of Rituximab to treat ME, these findings suggest a possible role for B cells in ME. Further work by researchers at University College London has shown that ME is indeed associated with an altered B cell phenotype (Mensah et al 2016). Fluge and Mella present the hypothesis that the delayed response to treatment suggests that ME is an autoimmune disease and that autoantibodies may be gradually removed preceding a clinical response (Fluge and Mella 2011).

ME Research UK has funded research looking into a way to predict which ME patients will benefit from Rituximab, by looking at immune signatures. This work is being conducted Professor David Patrick at the School of population and Public Health, University of British Columbia, in collaboration with Drs. Fluge and Mella.

Currently, the UK charity Invest in ME is funding an ongoing Rituximab clinical trial in the UK, at University College London, where the principal investigator is Dr. Jo Cambridge. The charity is being advised on the trial by Professor Jonathan Edwards, one of the pioneers of the use of Rituximab in rheumatoid arthritis at University College London. Consultant Øystein Fluge and Professor Olav Mella are also collaborators on the trial.

2a.ii Cyclophosphamide (CycloME trial)
Drs. Fluge and Mella at Haukeland University Hospital in Norway are also conducting a phase II clinical trial investigating the effect of cyclophosphamide treatment in patients with moderate to severe ME. Cyclophosphamide is a DNA replication inhibitor used to treat cancer and autoimmune diseases. The trial completion date is July 2017 (ClinicalTrials.gov).

2a.iii Immunoglobulin therapy
Immunoglobulin therapy is an effective treatment in a number of diseases including primary immunodeficiency, autoimmune diseases and HIV/AIDS. Charité
Universitätsmedizin Berlin is currently running a proof of concept study in 15 patients to assess the effect of subcutaneous immunoglobulin infusions (HyQvia formulation from Shire Pharmaceuticals) on patients with ME/CFS. This study is estimated to be completed in 2018 (EU Clinical Trials register). Studies in the 1990s reported mixed results; however, patient definitions were redefined in 2015 and further research is warranted. This treatment is not widely available to ME patients in the UK.

2a.iv Ongoing biomarker studies
We feel these studies are important to NICE as they may identify biomarkers and diagnostic tests which would be important for updating section 1.3 of the guidelines. Recent work identified activin B as a novel serum biomarker for ME/CFS (Lidbury 2017), and numerous studies have identified immunological disturbances that are potential biomarkers (e.g. (Brenu 2011)). In addition, there are at least a couple of these studies ongoing at the moment:
- The National Center for Neuroimmunology and Emerging Disease at Griffith University in Australia were recently awarded a grant from the Stafford Fox Foundation for biomarker discovery in ME/CFS. They aim to produce a diagnostic test for ME/CFS by 2021 (Griffith University 2017).
- The Open Medicine Foundation is running a collaborative biomarker discovery project (ME Severely Ill Big Data Study) focused on severely ill patients, involving a wide spectrum of high throughput approaches (combining proteomics, RNA sequencing, metabolomics), clinical tests and monitoring (Open Medicine Foundation 2017).

2b Funded research projects on ME/CFS by funding body
We have included this section to highlight that most national and international researchers, from a variety of medical disciplines, do not agree with the causal CBT Model or with using CBT/GET as a treatment (see 1h). These researchers are all investigating other causes and treatments and we feel the guidelines should take into account their recent and ongoing work. The future research highlighted in the 10 year surveillance systematic review exclusively supported the causal CBT model of ME, which is popular with a few UK proponents but is not supported by biomedical evidence (see 1h). We also feel that NICE should keep up to date with research looking into the cause of ME, as this is relevant to assessing the relevance of treatments.

2b.i UK Medical Research Council
The MRC are funding a number of biomedical research projects on ME. Highlights include: Professor Anne McArdle at the University of Liverpool was the recipient of a grant to study the function of mitochondria and cytokine production in the skeletal muscle of patients with ME/CFS; Professor Julia Newton at Newcastle University was granted funding to investigate the pathogenesis of dysfunction of the autonomic system in ME/CFS and how this relates to cognitive impairment. In addition, Dr Carmine Pariante at King’s College London has received funding to establish an immunological model for ME and CFS.

2b.ii NIH
There are 43 active grants in the NIH reporter supporting biomedical research into ME. The NIH in the United States is currently conducting an exploratory cross-sectional intramural study to learn more about the cause of ME/CFS, estimated to be completed in September 2018 (ClinicalTrials.gov). Following a workshop on ME, NIH issued a call to action in 2015 for increased research effort. Proposals for a recent NIH funding opportunity are currently under review and will result in three new ME/CFS Collaborative Research Centers as well as a Data Management and Management Center. The NIH also issued 7 supplemental grants to expand ME research in existing grants.

2b.iii Research Council of Norway
The Research Council of Norway has awarded funding to several researchers for biomedical research into ME/CFS (Forskningsgradet.no). Of particular note, the University of Oslo received funding for genetic studies in ME to investigate the potential involvement of the immune system and reveal biomarkers. The University of Bergen was awarded a grant for study of defective energy metabolism in ME/CFS, and the University Hospital of North Norway, Harstad, was granted funding for research into fecal microbiota transplants in ME/CFS.

2b.iv Solve ME/CFS
Solve ME/CFS is currently funding several seed projects related to ME/CFS. Their research includes looking into possible viral causes, exercise physiology, immunology and neuro-imaging. They are also funding research into repurposing drugs which have been shelved or are used for other diseases. These drugs have already passed a significant number of safety tests ensuring they are safe. This should significantly reduce the time it takes for them to be available, if they prove beneficial to ME patients.

2b.v UK ME/CFS Biobank
The UK ME/CFS Biobank was established at the London School of Tropical Medicine and Hygiene in 2011 (Lacerda et al 2017). A large dataset of clinical samples has been obtained to enable comprehensive phenotyping of ME/CFS patients.

| Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53 | 123 of 209 |
In conclusion, we agree with the decision to remove the guidelines from the static to active list. However, we are concerned about the emphasis on updating the guidelines purely on the basis of UK psychiatric research, especially since this is based on a refuted model and treatment that has caused widespread harm to patients. Both nationally and internationally, exciting research is being done into the cause and potential treatment of ME, in a variety of academic disciplines. It is of utmost importance that this research is considered in any future update.

We have divided references into key references, which is the main evidence we wish to draw your attention to, and additional references

Key evidence Q2


<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Comments</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Royal College of Physicians</td>
<td>We would like to endorse the responses submitted by the Association of British Neurologists and Royal College of Psychiatrists</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
<tr>
<td>RCGP</td>
<td>Yes • Usually Clinical guidelines placed on the static list will be reviewed every 5 years to determine if they should remain on the static list. This contrasts with the usual 2 yearly routine surveillance for active guidelines.</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
<tr>
<td>Regional Public Health Agency for Northern Ireland</td>
<td>Yes- with a view to review in future As evidence regarding the physiological nature of ME continues to emerge and trials to treat it medically are under way, the focus of interventions is likely to change in future, namely towards a more causative as opposed to symptomatic approach.</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic...</td>
</tr>
<tr>
<td>Stakeholder</td>
<td>Comments</td>
<td></td>
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<tr>
<td>-------------</td>
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<td></td>
</tr>
<tr>
<td>False Allegations Support Organisation with Parents Protecting Children UK</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Local ME</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>ME-Letterforce</td>
<td>Yes, but not for the reasons</td>
<td></td>
</tr>
</tbody>
</table>

**Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53**

The potentially harmful effects of GET stipulated by patients and some healthcare providers in particular might become more plausible and lead to even more qualified and cautious recommendations regarding its indications especially in relation to increasing activity levels.

Fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

I don't really understand the issue about lists but I don't think that anything is currently static in relation to understanding awareness and diagnosis of collagen deficiency conditions - there have been very recent changes in diagnostic categories for collagen deficiency conditions and I'm sure that diagnosis of ME/CFS should be looked at in the light of this new and emerging information.

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

No Comment

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Our group is shocked that the Surveillance document reveals that NICE has not looked seriously at the considerable body of international biomedical research, Please note that the aim of surveillance is to check that published guidelines are current and decide whether updates are needed. To do this, all surveillance reviews
<table>
<thead>
<tr>
<th>given by</th>
<th>but only given weighting to papers based on the psychiatric or deconditioning model.</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICE</td>
<td>There have been major revisions on recommendations on the name, diagnostic criteria and treatment of ME from the USA.</td>
</tr>
</tbody>
</table>


We can see that there are some references to the USA research in the Proposal section and through Appendix A but that even when considered, this has not resulted in the Topic Expert recommending guideline updates.

Papers have been published with valid criticism of treatments recommended by in the existing Guideline particularly those based on a faulty model of de-conditioning.

https://www.researchgate.net/publication/312464313_Can_patients_with_chronic_fatigue_syndrome_really_recover_after_graded_exercise_or_cognitive behavioural_therapy_A_critical_commentary_and_preliminary_re-analysis_of_the_PACE_trial

Q2 Comment 2

We recommend that NICE evaluate all important papers identified in their entirety and not just abstracts. It has been shown that some researchers exaggerate the effect on patients in a way positive of their methods. Only a thorough examination of entire papers will reveal the errors and omissions.

Furthermore, NICE needs to read in their entire responses to papers which criticise the methods used and high-light the flaws and errors.

It is the role of the developers to consider the full text studies when they are conducting full systematic reviews for the guideline update.

We note your concerns about the FITNET-NHS trial.
However, this was just an example of ongoing research identified through the surveillance review and not the only ongoing evidence we are aware of on this topic.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
It is not enough as NICE did in the Surveillance document to include that the authors of a particular study have responded if the response failed to address the errors or flaws.

**Q2 Comment 3**

Furthermore, we are disturbed that the Cochrane review on Exercise therapy 2017 was overseen by the editorial group Cochrane Common Mental Disorders Group although ME is classified as a neurological illness G93.3

Cochrane has previously missed flaws in the PACE trial highlighted internationally.

We recommend that future reviews should be conducted by appropriate biomedical experts and if Cochrane is asked to do it they should assemble an editorial group of biomedical experts in ME and CFS.

**Q2 Comment 4**

NICE needs to recognise that there is a lot of confusion between chronic fatigue, CFS and ME and that exercise that is safe for CF and some kinds of CFS is dangerous for ME patients with Post exertional malaise.

With the guiding principle of first do no harm, we need to find what level of exertion is safe for people with ME before it is recommended since there have been so many patient reports of very serious harm.

Our group was not given enough time by NICE to produce a detailed response to the Surveillance document, but the following papers back up the removal of recommendations of exercise therapy.

These papers are taken from the ME-Research database document [viii]

2. Exercise capacity and immune function in male and female patients with chronic fatigue syndrome (CFS). In Vivo. 2005 MarApr;19(2):387-90

Q2 Comment 5

Our group recommends that NICE should warn against exercise and exertion in patients as that has been shown to cause harm, and instead advise pacing and rest. We need research to show what level of exertion people with ME can tolerate and until we have evidence of this we need to do no further harm

Our Group contains long term ME patients who have been harmed through exercise programs.

ME patient Tom Kindlon wrote in his paper “Reporting of Harms Associated with Graded Exercise Therapy and Cognitive Behavioural Therapy in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome”

“It is hoped that this paper will lead to a greater focus on the reporting of harms in ME/CFS, not just those that might be associated with GET or CBT, but from any posited treatment. Interventions should not be presumed to be harmless when there exists evidence of potential harm and there have not been well-planned systematic methods to track and assess harms both within and outside trials. Potential strategies to improve reporting of harms are summarized in Table 3. ME/CFS research should at least conform to standards being recommended for the majority of medical research while taking into account the unique features of the disease, such as its relapsing-remitting nature. Moreover, in the ME/CFS field, comparisons are often not made just within the classes of pharmacologic interventions and non-pharmacologic interventions but also between pharmacologic and non-pharmacologic treatments (38). False conclusions could be reached that a non-pharmacologic intervention is “safer”
than a pharmacologic agent if harms related data was collected more rigorously for the latter (87).[ix]

**Q2 Comment 6**

Our group recommends that the following papers and reports be considered for the new Guideline with a high weighting of evidence

Due to the time restraints placed on out group by NICE there are many other papers we would like to be read in their entirety and given a high weighting of evidence

ME Association ‘purple book’ for clinicians


CDC website on CFS - [https://www.cdc.gov/me-cfs/index.html](https://www.cdc.gov/me-cfs/index.html)

**Q2 Comment 7**

Our group recommends that the following unpublished research be considered for the new Guideline.
1. Myalgic Encephalomyelitis Chronic Fatigue at the National Institutes of Health
2. ME/CFS: Activity Patterns and Autonomic Dysfunction
3. Coenzyme Q10 Plus NADH Supplementation in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis
4. Oral Melatonin Plus Zinc Supplementation in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME)
6. The temporal relationship of the effects of repeated exercise on physiological variables in individuals with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME)
7. Valganciclovir (Valcyte) for Chronic Fatigue Syndrome Patients Who Have Elevated Antibody Titers Against Human Herpes Virus 6 (HHV-6)and Epstein-Barr Virus (EBV)
8. Drug Intervention in Chronic Fatigue Syndrome KTS-1-2008

Due to the time restraint placed on this submission the list is incomplete

**Q2 Comment 8**

Our group recommends that this paper (highlighted in the Surveillance proposal) not be considered for future guidelines

“How effective is FITNET-NHS for children and young adults with CFS/ME?”
We are alarmed that evaluated this highly because

1. A previous similar study in the Netherlands failed to show a positive effect
2. There are no physical outcomes measured employed such as an actometer
3. There is an emphasis on fatigue and not the cardinal ME symptom of post exertional worsening

The study acknowledges “There is a small risk that the study may recruit children that do not have CFS/ME but instead have other disorders that present with fatigue." This may be a larger risk then the study designers admit given that they will use NICE criteria which require updating to bring them up to international standards.

| Suffolk Youth & Parent Support Group1 & Norfolk & Suffolk Service Design and Service Implementation Group2. | Yes | A review of CG53 needs to be done, to achieve compliance with and to meet the requirements of the 2012 Health and Social Care Act & the 2003 Standards for Better Health which in turn inform the Care Quality Commission Core Requirements of which 3 of the 5 core requirements used in inspections are relevant. The NICE pathway process on the NICE website for CFS and ME Guidance which is under review, appears to be incomplete, limited and inadequate (see my annotations of your “patient experience flowchart” on page (of my response)). Most importantly, the 2007 NICE guidance and review process appears inconsistent with the requirements currently placed on health care providers (many of whom follow the 2007 NICE Guidance, in principle, to determine provision). We suggest that the 2007 guidance is now inconsistent with and potentially at odds with the requirements and aims of the Health & Social Care Act 2012. It is non compliant with the 2003 “Standards for Better Health” -Aims and specific Standards. decision not to review may lead to noncompliant with the current legislative approach and relevant Standards for Health which govern service provision. |}

Do you have any comments on areas excluded from the scope of the guideline?

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Overall response</th>
<th>Comments</th>
<th>NICE response</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Infection Association</td>
<td>No</td>
<td>No comments</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
<tr>
<td>The Pernicious Anaemia Society</td>
<td>Yes</td>
<td>The test used to ascertain the B12 status of patient is so unreliable that it leads to patients who have Pernicious Anaemia being told that they have ME as there is a discordance between the serum B12 test and the patient’s symptoms. 17% of members of the PA Society were initially told that their symptoms were due to ME and not Pernicious Anaemia. This is a very important topic that needs thorough investigation as left undiagnosed a B12 deficiency masquerading as ME can and does lead to irreversible nerve damage.</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
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<tr>
<td>Organisation</td>
<td>Response</td>
<td>Comments</td>
<td>Feedback</td>
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<td>-----------------------------------------------</td>
<td>----------</td>
</tr>
<tr>
<td>VIRAS</td>
<td>Yes</td>
<td>See equality issues below</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
<tr>
<td>ME Research UK</td>
<td>No</td>
<td>No comments</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
<tr>
<td>Royal Liverpool University Hospital, CFS/ME services</td>
<td>No</td>
<td>No comments</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
<tr>
<td>PoTS UK</td>
<td>No answer</td>
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</table>

We strongly believe that screening for PoTS should be included in assessment of people with CFS/ME. Studies have shown that up to 30% of patients with CFS/ME have PoTS (Hoad et al 2006 QJMed). We have shown that almost 29% of patients with PoTS have been given a diagnosis if CFS/ME (Kavi et al 2016, BJ Cardiol). Fatigue is the most common symptom of PoTS (91%). It takes a mean of 7 years for patients with PoTS to be diagnosed and meantime 50% are mislabelled with a psychiatric/psychological explanation for their symptoms.

I have been able to extract data from our 2015 survey of PoTS patients and analyse those who have been diagnosed with PoTS and CFS/ME (286 patients). At presentation to a healthcare professional, over 90% of CFS/ME+PoTS patients had lightheadness and over 80% had palpitations. 25% of these patients had to wait over 5 years to obtain their PoTS diagnosis after first presenting to a healthcare professional and over 50% were advised these symptoms were ‘in their head’.

PoTS has many more treatment options than CFS/ME, and many PoTS patients are able to return to school, employment and enjoy and improved quality of life once correctly diagnosed and treated. We anticipate this will reduce the financial cost of such patients upon the NHS (as many undergo multiple referrals, and unnecessary investigations before diagnosis) and on the UK welfare system.

We would suggest that the assessment of CFS/ME patients should include enquiry about orthostatic intolerance and palpitations. Appropriate patients should then undergo an active stand test, which in many cases is sufficient to diagnose PoTS (and orthostatic hypotension which also occurs in CFS/ME). Where appropriate, a tilt test will help to exclude other conditions.

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
| Royal College of Paediatrics and Child Health | Yes | We are aware there is new evidence regarding effective management for CFS/ME in young people which will be published very soon, and is highly likely to lead to a change in recommendations. This is an important and but long document. Does it distinguish between adults and children. In children it is often called postviral fatigue and has a better prognosis. |
| North London ME Network | No | No comments |

Current NICE CFS/ME Guidance states that patients should not undergo a routine tilt table test and we agree with this statement. However, an active stand test for those with orthostatic intolerance is a cheap and quick test and would identify patients who may benefit from more timely diagnosis and treatments not currently available to them.

I would be happy to provide information or advice on this issue.

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
### Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

<table>
<thead>
<tr>
<th>Association of British Neurologists</th>
<th>No</th>
<th>No comments</th>
</tr>
</thead>
</table>

| FORWARD-ME | Yes | The surveillance report considers and resolves the question of whether the guideline should be changed to align with the conclusions in the US about diagnosis and management of CFS/ME. Our request, however, is not that the guideline be revised to reflect a change of opinion in the UK, but rather that it is revised to present a truthful, neutral picture of the difference of opinion between UK and US health authorities about the nature and management of this condition.

For this reason, the surveillance report fails to address, or even consider, the heart of the matter, the question of whether the guideline as it stands is ethical with respect to (1) informed consent, and (2) the obligation never to obstruct access to biological medical care for any patient group that faces a significant possibility of biological need.

We request that either the guideline be revised to include vital information now excluded, or that NICE develops a new surveillance report that directly addresses these ethical considerations in a way that reflects the organisation’s commitments to the ethical practices described in the Social Value Judgements document. |

| Patient and Client Council | Yes | Patients would like to see less emphasis on treatment perceived as psychological therapy like CBT and a more biopsychosocial approach taking account of emerging biomedical evidence for the physiological origins of ME. |

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
<table>
<thead>
<tr>
<th>Name</th>
<th>Question</th>
<th>Answer</th>
<th>Feedback</th>
</tr>
</thead>
</table>
| Inclusion London      | No answer| We support the ME Association petition demands in the particular:  
  - We want a complete and proper review of the existing guideline with full stakeholder input and for it to include recognition of published and emerging international research evidence and medical opinion  
  - We want NICE to amend the current guideline to appropriately recognise CFS/ME as a neurological disease – in accordance with the position taken by the UK Govt. and Dept. of Health – and give more regard to characteristic physical symptoms  
  - We want NICE to remove Graded Exercise Therapy as the recommended treatment for patients who are moderately affected and to place an appropriate health warning against general use of this therapy in CFS/ME specialist clinics.  
| Mast Cell Action      | No       | MCAS was coded into ICD 10 in 2017. There is a vast amount of published literature on the presentation diagnosis and treatment of this condition.  
  Chronic fatigue is a common symptom reported in the patient community and based on our patient community a not uncommon misdiagnosis. 83% of patients report fatigue as a symptom according to one study Afrin, L. B., Butterfield, J., Raithel, M. & Molderings. Often seen, rarely recognized: mast cell activation disease – a guide to diagnosis and therapeutic options. Ann. Med. 48, 190–201 (2016)  
  Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline. |

Recently the Protein Reference Unit is Sheffield Introduced tests to support the diagnosis of mcas “We are pleased to be able to offer the following range of mast cell activation markers: • Tryptase (serum or plasma) • Urine Methylhistamine • Urine Prostaglandin F2 alpha • Urine Prostaglandin D2 • Urine Prostaglandin DM

If you look at the literature on MCAS you will note the relative lack of knowledge of this condition in the UK with almost no published literature by UK doctors, and in countries such as Germany where they have significant research and clinics dealing with MCAS many doctors believe it is significantly misdiagnosed and under diagnosed.

Many patients respond well to low cost medication, particularly children. Without treatment many patients simply go in circles seeing specialists with a waste of resources to little benefit, eventually hitting a buffer.

Due to its often unusual symptoms patients struggle to be taken seriously, and often parents of children are told their children’s reactions and symptoms are “simply impossible” with no appreciation of the severity and impact of the symptoms on the child’s life. Parents in desperation spend fortunes in private clinics.

Increased awareness of this condition and its clinical presentation are key and could save the NHS money and improve care.

Royal College of Psychiatrists  | No  | No comments |
|-------------------------------|-----|-------------|

Thank you for your response.
Following further consideration of new evidence and information from stakeholders, alongside the evidence.
<table>
<thead>
<tr>
<th>The ME Association</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) The NICE expert group appears to have ignored or dismissed the fact that outside the UK, especially in America, there has been a very significant shift in official guidance on management of ME/CFS away from the use of CBT and GET.</td>
<td></td>
</tr>
</tbody>
</table>

In America, guidance on management issued by the highly respected Centres for Disease Control (CDC) has now dropped all reference to their previous recommendations relating to CBT and GET. As a result, the CDC is now producing a far more balanced, comprehensive and pragmatic overview of management of ME/CFS. This approach is welcomed by the US patient community, whereas the ‘one size fits all’ approach involving CBT and GET in guidance produced by NICE, is opposed by the UK patient community.

Link to new CDC guidance: [https://www.cdc.gov/me-cfs/treatment/index.html](https://www.cdc.gov/me-cfs/treatment/index.html)

In a letter dated May 2017, sent to 85,000 doctors by Dr Howard Zucker, Commissioner at the New York Health Department, revised guidance relating to the use CBT and GET in ME/CFS is summarised as follows:

In the past, cognitive behavior therapy (CBT) and a graded exercise therapy (GET) were recommended as treatments. However, these recommendations were based on studies that included patients with other fatiguing conditions. Because of the hallmark intolerance to exertion of ME/CFS, exercise may actually worsen the health of those living with this disease. Currently, there are no FDA approved treatments for ME/CFS.

Link [https://drive.google.com/file/d/0B37JHmPXER6JZkZRd0hlalA2bUE/view](https://drive.google.com/file/d/0B37JHmPXER6JZkZRd0hlalA2bUE/view)

With regard to the ethical position of the situation facing NICE, we cannot stress too highly that the significant change in direction taking place in America regarding the use of CBT and GET does necessitate a revision of the NICE guideline. This should reflect the fact that there is now a serious debate surrounding the use of these two treatments taking identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
place amongst both patients and health professionals. This is the case regardless of whether the UK medical establishment agrees or disagrees with the US position.

As organisations responsible for the nation’s health care, NICE and the Department of Health have a duty to protect every patients right to receive safe and appropriate care. They should therefore be producing recommendations on treatments that are acceptable, effective and safe – as well as providing up to date information that can be presented and discussed with patients as part of the long established principle of informed consent.

The new position taken in the US establishes that there is growing and convincing evidence to support the view that people with ME/CFS have a serious and debilitating biomedical condition involving neurological, immunological and energy producing impairments. This is a condition that does therefore require a biomedical approach management. The change in position in America has profound ramifications in relation to a revision of the NICE guideline and cannot be ignored.

b) Patient evidence on the acceptability, efficacy and safety of CBT, GET and Pacing appears to have either been dismissed or ignored by the expert group. This is in sharp contrast to the Chief Medical Officer’s Working Group Report on ME/CFS. The CMO report recognized the importance of taking patient evidence into equal account where there are strong and differing opinions on the value of CBT, GET and Pacing.

Extensive patient led research carried by The MEA, and other ME/CFS charities, has consistently found that the majority of people find CBT to be of no value. Over 50% report that GET has made their condition worse.

The MEA carried out the largest ever survey of patient reports on the use of CBT, GET and Pacing. This was followed up with a detailed report containing qualitative and quantitative patient evidence. A paper carrying these results, which has been subjected to peer review, has been accepted for publication in the *Journal of Health Psychology*. A summary of the MEA report, along with a link to the full report, can be found here:

http://www.meassociation.org.uk/2015/05/23959/

c) The expert group has not given proper attention to the widespread and serious criticisms of the methodology and presentation of results from the PACE trial from academics, clinicians and patients.
<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Action</th>
<th>Notes</th>
</tr>
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<tbody>
<tr>
<td>Action for ME</td>
<td>No</td>
<td>No comment</td>
</tr>
</tbody>
</table>

This criticism includes a letter to the editor of *Psychological Medicine* from over 100 clinicians, medical researchers, epidemiologists and statisticians, calling for the retraction of the PACE trial recovery paper and the re-analysis of the recovery data by Wilshire et al who concluded:

*The claim that patients can recover as a result of CBT and GET is not justified by the data, and is highly misleading to clinicians and patients considering these treatments.*

References:

Letter to the editor of *Psychological Medicine*:


Re-analysis of PACE trial recovery data:


Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
<table>
<thead>
<tr>
<th>British Association for CFS/ME</th>
<th>Yes</th>
<th>Issues with diagnostic criteria, no mention of aetiology, subgroups, and comorbidities as discussed above. These are relevant to diagnosis and management.</th>
</tr>
</thead>
</table>
| Healthwatch Kirklees           | Yes | **NICE guidelines - Complementary therapies/lack of community services for ME Patients**

In its 2007 quick reference guide NICE states that the use of complementary therapies is, "Not recommended: there is not enough evidence they are effective." The Kirklees and Calderdale residents with ME feel that NICE and the Medical Research Council are unwilling to support any research into the efficacy of complimentary therapies for ME patients. Yet it is reported that so many people with the illness including themselves find these complementary therapies useful for symptom control. In our 2015 survey carried out with Kirklees and Calderdale Independent ME group we found the following results with regard to the use of complimentary therapies:

- 40% found that gentle yoga/meditation to be very helpful,
- 18.5% found acupuncture/acupressure to be very helpful.

This is in sharp contrast to the results for the use of psychiatry as a treatment to help patients manage their illness. 18.75% of respondents said that psychiatric interventions had made their illness less manageable, while 0% found psychiatric interventions to be helpful.

It is worth pointing out that the Centres for Disease Control and Prevention in the United States acknowledges the positive benefits that complementary therapies have upon the symptoms of some ME/CFS patients:

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
"Complementary therapies, like acupuncture, meditation, gentle massage, deep breathing, relaxation therapy, yoga, or tai chi, might be helpful to increase energy and decrease pain."

Kirklees and Calderdale Independent ME Support Group calls upon NICE to update its guidelines with regard to the use of complimentary therapies. Therapies such as meditation, yoga, massage, and acupressure/acupuncture should be provided by the NHS for ME patients. We further call upon NICE, in its updated guidelines, to acknowledge the lack of community services for people with ME/CFS.

Our comments relate to the Institute’s interpretation of the scope, as well as to the scope itself as set out in CG53.

The Institute’s response to comments on CG53 when in draft form repeatedly state that The guideline does not address the management of individual symptoms. (Neither is there an attempt to discuss cause - which is also deemed beyond the scope.)

Yet producing a guideline on symptoms is exactly what CG53 presents - albeit a very partial one. That symptom is fatigue. And the extracts cited in the present consultation paper from Cochrane review show that impact on ‘fatigue’ is what CBT and exercise (purport to) have modified.

So there is inconsistency here.

NB: Fatigue is a symptom, and not by any means the unique defining symptom of M.E./strictly defined CFS.

There is no balance in the guidelines, the tone and language perpetuate the erroneous belief that people with ME or CFS are ill because they believe they are ill and are deconditioned – despite the multitude of research papers to the contrary. The real illness can only be found in one section – the patient experience section. Bioethically, at the very least both sides of the viewpoint, as to the nature and management of these conditions, should be provided.

There is no mention in the guidelines of the ICD10 G93.3 classification of ME and CFS as neurological conditions. ME has been classified as such since 1969. This is vitally needed to inform healthcare professionals, and help to counteract the misconceptions which have sadly surrounded these serious long term neurological conditions.

There is now, as discussed in question 1, the International Consensus Criteria and Guidelines (2011/2012), which should certainly now be included within the guidelines, as
they provide accurate diagnostic and research criteria, as well as management advice for medical professionals.

The guidelines need to make it clear that there is no such thing as the NICE criteria – see question 1 again.

For those with long term conditions, including ME and CFS, healthcare and management are supposed to be 'no decision about me without me', along with mutual respect, shared decision making, hcp/patient partnership, and acknowledging the patient expert, and yet, NICE continually overlooks the patient, and their vital evidence and experience.

The guidelines need to provide a more balanced view, providing the biomedical view and approach and giving respect and credence to the patient experience and evidence – particularly for the severely affected and children/young people for whom there is little to no research evidence, therefore patient evidence is vital.

As we stated at the time, the scope for the review of research was flawed, what we said then, still stands today: “We strongly question the review search for evidence on ME/CFS, as we do not feel that all relevant evidence was picked up in this search. For example, GET research papers showing positive results were selected, but those which examined the negative bio-medical effects of exercise were not.”

There is a strong feeling that the patient, carers and hcps who believe in the biomedical approach were disregarded – something we again raised at the time in our response “There has been a total disregard, yet again, for a balanced view of surveys produced by patient groups, and of patient evidence as a whole. This is especially relevant for the severely affected and children/young people, for whom there are very little or no research evidence, apart from that found from within patient community itself.”

There was also the question of bias in regard to research and patient evidence, which we raised: “Many of our respondents feel that given that information from the patients/patient groups is treated with such contempt, and that the Guideline authors believe it is ‘subject to bias’, how can we have confidence our comments on this draft will be treated with respect and accorded credibility? As it is obvious that the patients’ experience/voice has not been observed or listened to in the
compilation of this draft. Given that research papers, particularly those written by psychiatrists on behavioural management programmes, are done with the preconceived bias that it is a somatic disorder, from which patients can exercise/think themselves better, and to produce the desired results they have used the flawed Oxford criteria, why have these not been charged with being ‘subject to bias’? Why only prejudice against the patient population?”

There is a wealth of evidence showing that CBT, GET and exercise are unhelpful/harmful for people with ME and CFS. This evidence should be given equal credence and reflected in the guidelines to provide both hcp’s and patients with all the information so that they can make an informed decision. Please also remember that countries, including the USA have started stating that CBT and GET should not be recommended as treatments for ME and CFS.

There are a multitude of research papers supporting the biomedical view, which need to be explored, including this one which has just come out of Australia which found significant impairments in cellular function, and cellular receptors in people with ME/CFS https://biolres.biomedcentral.com/articles/10.1186/s40659-016-0087-2

Hope 4 ME & Fibro Northern Ireland

As recorded in both the above sections, we have noticed considerable bias to towards the psycho-social approach for the treatment of ME reflected within the review panel decision making process. We feel that this bias should not be tolerated by NICE.

The following organisations have rejected the notion that ME is a behavioural, or mental health issue:

- The World Health Organisation[^44] recognises ME as a neurological (ie physiological) disorder.
- The Department of Health recognised ME as an organic disease, in November 1987[^45]
- The Royal College of General Practitioners has agreed to stop classifying ME as a mental health disorder[^46]

[^44]: World Health Organisation. ICD10 section G93.3
[^45]: Hansard: 27th November 1987:353
The Royal College of Paediatrics and Child Health also recognises ME is not a mental health issue. And NICE itself recently confirmed in a letter to Greg Crowhurst, that it does not regard ME as a mental disorder.

However it was recently brought to our attention that Improving Access to Psychological Therapies (IAPT) is managing the CG53 NICE guideline for CFS/ME on behalf of NHS England! This does not make sense.

The anomaly clearly demonstrates the lack of clarity from NICE about the nature of the disease “CFS/ME”. Certainly, the other conditions listed beside CFS/ME on the IAPT page would suggest that IAPT and NICE regard ME as a behavioural or mental health condition. This is totally unacceptable, and also in complete opposition to NICE’s assertion to Greg Crowhurst that NICE does not regard ME as a mental health condition.

No wonder then, that the review panel and topic experts considered only the psycho-social approach to ME. If, by remit, these individuals are “improving access to psychological therapies” then it should be obvious that they will disregard all biomedical evidence towards the understanding of ME. NICE should be very concerned about this situation.

This substantial bias surely challenges the integrity of the whole NICE brand? We suggest that NICE needs to address this concern as a matter of urgency.

We call for an urgent independent investigation into the makeup of the NICE review panel for CG53.

We further call for a review of the topic expert team working on the CG53 guideline. Are they also biased towards the psycho-social approach? Are they perhaps using their “expert” status to influence the review panel into making choices favouring a behavioural approach to ME?

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48 NICE confirmation to Greg Crowhurst that ME is not a mental disorder: [http://stonebird.co.uk/NICE/index.htm](http://stonebird.co.uk/NICE/index.htm)

49 Improving Access to Psychological Care (IAPT) [https://www.nice.org.uk/about/what-we-do/our-programmes/nice-advice/iapt#conditions](https://www.nice.org.uk/about/what-we-do/our-programmes/nice-advice/iapt#conditions)

50 NICE letter to Greg Crowhurst – as ref 44 above.

Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53
| Invest in ME | Yes
---|---
| **Appendix C:** stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53 148 of 209
| **Appendix C**
*We find this situation so unsatisfactory that we now call for both the topic expert team and the review panel for CG53 to be disbanded.*

We call for CG53 to be removed from the management of IAPT, and for a new team of topic experts and guideline reviewers to be selected from amongst scientists and medical professionals who are free from the influence of the behavioural or mental health approaches to ME.

CG53 must not be left in the charge of individuals who deny the physiological abnormalities that drive the disease process in ME.

Only once this has happened, will ME patients start to regain confidence in a health service that is currently failing to meet their needs.

| **Taxonomy**
---|---
| *We pointed this out when we reviewed the original NICE guidelines, and in the 2010 response to the consultation process.*

NICE have not listened or taken any action and continue to maintain and perpetuate the terminological mess around ME.

The name is myalgic encephalomyelitis – not encephalopathy.

As we noted in our response to the NICE guidelines the terminology may be crucial in dealing with ME, especially as GPs, paediatricians, other healthcare personnel and the media use different terms.

Dr. B. Saraceno of the WHO clarified the classification in writing on October 16, 2001 - “Post-viral fatigue syndrome remains under the diseases of nervous system as G93.3. Benign myalgic encephalomyelitis is included within this category.”

Benign myalgic encephalomyelitis (ME) and post viral fatigue syndrome (PVFS) are classified under WHO classification ICD 10 G93.3 and chronic fatigue syndrome (CFS) is listed in the tabular index.

We would prefer to use the term ME for the illness but also recognise that ME/CFS is used widely, as in the Canadian Consensus Criteria. CFS/ME is used in the NICE documents.

Thank you for your response.

Note that, in line with the [guidelines manual](#), Committee members and topic experts for the published guideline are surveyed for their opinions on the relevance of the published guideline, recent developments in the topic area and their knowledge of any new important evidence since publication of the guideline. In some circumstances (for example, when a significant period of time has passed since the guideline was published), members of the relevant Quality Standards Advisory Committee, or others with expertise, may be surveyed. This intelligence is considered alongside the new evidence identified through the surveillance review. However, the decision to update or not update a guideline remains with NICE’s Guidance Executive. This is the case for all surveillance review topics.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including
The UK government supports this definition of ME as a neurological illness and therefore subscribes and endorses the name of myalgic encephalomyelitis. Myalgic encephalomyelitis must be used by NICE to describe ME.

The original NICE standards on terminology were extremely poor and unprofessional and this continues.

It is a cynical move to attempt to try to make ME into something far more nebulous.

As we have stated CBT and GET must be dropped as recommendations for treatment of ME.

The NHS is currently wasting a huge amount of funds in giving these failed therapies to ME patients which are either useless, or deleterious to the health of ME patients. More importantly these therapies are rejected by patients and, at a time where the NHS needs all the funding it can get, there is no sense in wasting resources or funds like this.

We need to do things differently.

NICE’s remit - “Our aim is to drive and enable excellence across the health and social care system”

What does NICE plan for the future?

Patients are already against the existing NICE guidelines and demand change – is your proposal to leave it in such an unsatisfactory state of affairs – with misinformed healthcare staff pitted against patients?

It is not helpful to include yet more flawed research using broad criteria.

Of course, this all keeps people occupied – another delaying tactic of government agencies.

On the NICE website it is stated that NICE guidelines help health and social care professionals to:
1. prevent ill health
2. promote and protect good health
3. improve the quality of care and services
4. adapt and provide health and social care services.

Feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

A new committee will be recruited to take forward the update of the guideline. The resulting Committee should, as far as practically possible, reflect the range of stakeholders and groups whose activities, services or care will be covered by the guideline. All Committee members are recruited in accordance with NICE’s policy and procedure for recruitment and selection to advisory bodies and topic expert groups. Positions are advertised on the NICE website and other appropriate places (for example, NICE Twitter, social media and websites of stakeholders, Medical Royal Colleges and professional organisations), and relevant stakeholders are notified.
These guidelines and the predetermined NICE decision not to review them mean that, for ME patients, none of these are met.

NICE will now be guilty of maintaining ill health, is responsible for not promoting and protecting good health, is doing nothing to improve the quality of care and services, and is in no way adapting or providing health and social care services.

The NICE board and CEO are complicit in this and any harm done to ME patients by continuing to promote CBT and GET as therapies for ME will necessitate that the NICE board should be made accountable, especially as NICE have been forewarned of the dangers.

The USA IOM report conducted a full literature review for its report in 2015. Yet NICE did not see fit to build upon that and use it.

Instead it used its own selected, unidentified “Topic Experts” to cherry-pick research abstracts to satisfy an agenda to bias the ME guidelines.

To leave the current outdated and unusable NICE guidelines for ME for a number of years with no updates reflecting the current poor education regarding ME and without any knowledge of the biomedical research performed/about to be performed, would effectively mean that no clinical guidelines for ME will have been brought up to date for up to 17 years.

That would be unacceptable.

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<tr>
<th>M.E Lochaber</th>
<th>Yes</th>
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</table>
| All research must be considered. Focusing on the psychosocial model, while ignoring recent significant findings in MEcfs research is a betrayal of patients, and casts doubt over the integrity of NICE.  [
https://m.box.com/shared_item/https%3A%2F%2Fapp.box.com%2Fs%2F9s4coexxtys5bnz33i6gyggygu67ex5o](https://m.box.com/shared_item/https%3A%2F%2Fapp.box.com%2Fs%2F9s4coexxtys5bnz33i6gyggygu67ex5o)

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will
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<thead>
<tr>
<th>Stakeholder</th>
<th>Response</th>
<th>Comments</th>
</tr>
</thead>
</table>
| ME Support Northern Ireland | No response | - PAEDIATRIC S while symptoms may overlap with adults, paediatrics should be afforded a separate section within the guidelines to reflect the unique multifactor challenges prevalent in children and young people affected by this ME. 
- The needs of children and young people with ME/CFS should be more thoroughly addressed to enable schools and education professionals to recognize the challenges of this disability in their students and address their need for accommodations and support. |
| Royal Free London NHS Foundation Trust | Yes | The 10 year surveillance summary on the barriers to diagnosis and management, the topic expert feedback, and the impact statement that then agreed there is some evidence of inequity in accessing specialist services, issues with provision and uptake of service, to be outside the scope of the surveillance process. Quality (appropriately trained health care professionals, at the least) of provision of care, dealt with in the impact statement, is inextricably linked to equal access to quality care. And while it may be beyond the scope of the surveillance process, that does not preclude guidance for inclusion in royal collegiate training. |
| Stockport ME Group | No | No comment |

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
The Ehlers-Danlos Support UK

We believe it is essential that more information is added to the guideline throughout to recognise and highlight that chronic fatigue is commonly associated with (EDS), especially hypermobile EDS and HSD.


While section 1.2.1.4 includes investigating signs of ‘connective tissue diseases’ this is too broad in scope and does not sufficiently recognise the published association of chronic fatigue EDS and HSD as referenced above.

EDS and HSD symptoms can be improved with a correct diagnosis and a tailored management plan and many patients are able to remain in school or employment and enjoy a full life. We anticipate this will reduce the financial cost of these patients upon the NHS (as many undergo multiple referrals, and unnecessary investigations before diagnosis) and on the UK welfare system.

Unless NICE includes within the guidance specific advice to exclude these conditions, an opportunity will be missed to reach a correct alternative diagnosis and provide correct treatment for a large subset of patients who will otherwise be diagnosed with CFS.

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
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<tr>
<th>Trust / Organization</th>
<th>Response</th>
<th>Comment</th>
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| The Young ME Sufferers Trust | Yes | We understand that identifying a cause for ME/CFS, or ME and CFS separately, is not the remit of NICE, although the WHO classification is neurological ICD10 G93.3. However, given that, as a consequence of NICE’s treatment recommendations, children are routinely referred to mental health services rather than for further biomedical assessment and treatment such as symptom amelioration, the overall perception and widely held view amongst medical practitioners is that ME/CFS is a mental health disorder. This has resulted in the common expectation that mental health treatment will enable an apparently severely sick child to get back promptly to full-time school attendance (despite the term ‘chronic’ being part of a CFS designation). When they are unable to, suspicions of the family like those we have already detailed above inevitably arise.

We therefore request that NICE places the WHO classification prominently, and updates its guideline to include the US interpretation of current research so as to give a properly balanced and impartial picture of the current position. |
| University of Manchester – FINE Trial | No | No comment |
| Welsh Association of ME & CFS Support | Yes | When research into an illness is in the early stages and there is so little good quality research currently available into drugs and therapies for ME and CFS, it does not make sense to ignore the evidence of patients or the clues to pathogenesis being uncovered by scientific researchers. More effort should be given to assessing the research into management approaches in the context of what scientists are uncovering about the multisystem dysfunction in the body, the role of exercise in altering the way body systems function and the importance of the post exertional response affecting symptoms. |

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
<table>
<thead>
<tr>
<th>MEAction</th>
<th>Yes</th>
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<tr>
<td>The lack of benefit and experience of harm that patients report should also be given greater weight.</td>
<td></td>
</tr>
<tr>
<td>We consider there to be a number of omissions in the guidelines. We summarise a few of the main omissions below and would welcome the opportunity to explore this issue fully when there is a full review of the guidelines.</td>
<td></td>
</tr>
<tr>
<td><strong>3a Key Omissions</strong></td>
<td></td>
</tr>
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</table>
| **3a.i POTS and Orthostatic Intolerance**  
Postural Orthostatic Tachycardia Syndrome is a common comorbidity with ME and CFS, as has been shown in recent research. Okamoto et al (2012) found the majority of POTS participants also had CFS symptoms. About a third of people with ME meet POTS diagnostic criteria (Hoad et al, 2008). It could be the case that there is a common cause, as both conditions show similar issues with autoantibodies (Loebel et al, 2016), as yet this is uncertain, but it is established that a substantial comorbidity exists. “The presence of POTS marks a distinct clinical group of CFS patients, with phenotypic features differentiating them from those without POTS.” (Lewis et al, 2013).  
Many patients miss a useful diagnosis of POTS for years because tests for POTS and other Orthostatic Intolerance issues are not recommended by the NICE guidelines at the point of ME diagnosis (section 1.3). This needs to be revised.  
POTS has a number of reasonably effective treatments which could be used for patients with ME in this phenotype group. These include increasing salt, compression tights, off label drugs such as beta blockers, ivabradine, midodrine, fludrocortisone. An approach to this is covered well in the recent Paediatric Primer (Rowe et al, 2017). We ask that the guideline’s section 1.4 be updated to suggest these as potential treatments. |
| **3a.ii Gut dysbiosis**  
Intestinal dysfunction is a common symptom of ME, and up to 90% of patients report abdominal discomfort. Recent publications have identified shifts in the gut microbiota in people with ME compared to healthy controls (Fremont 2013), and further work has identified reduced microbial diversity in patients with ME compared to controls (Giloteaux L et al 2016, Nagy-Szakai D et al 2017). Following exercise, the gut microbiota of ME patients is also altered (Shukla SK et al 2015), implicating the gut |

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
microbiome in worsening of symptoms following exercise, a major feature of ME presentation. There is evidence for increased translocation of intestinal bacteria to the blood in these patients review by (Morris G et al 2016) which may be a source of inflammation in ME. These studies have led to ongoing research investigating the impact of faecal transplants on ME/CFS symptoms.

Given the prominence of gut dysfunction in ME, we ask that further advice for this is given (rather than the brief mention of exclusion diets in section 1.4.1.5 of the guidelines).

3b. Recent Important Areas of International Research

In this section we have included recent research from international researchers which we feel are relevant to any decision made on the care and treatment of people with ME. We feel that the conclusions of recent and influential publications such as the The Institute of Medicine (IOM) report [(now The National Academy of Medicine, NAM)] of the National Academy of Science (US) published in 2015 should be not be so easily dismissed by the reviewers: it details over 9000 articles related to ME/CFS and is the most comprehensive review to date.

3b.i ME as a neurological disease

A large number of publications have identified distinct neurological changes observed in patients with ME. Grey matter is reduced in patients with ME/CFS (de Lange FP et al 2005). In 2015, brain images of patients with ME/CFS identified numerous differences in brain structure compared to healthy controls (Zeineh et al 2015). Natelson et al surveyed brain and spinal fluid in patients with ME/CFS, with or without psychiatric comorbidity (Natelson B et al 2017). No differences in outcome between ME patients with or without psychiatric comorbidity were observed. This research provides further evidence for the presence of neurological abnormalities in ME regardless of psychiatric status. Along with numerous previous studies showing that exercise exacerbates ME symptoms, a recent study assessed patient symptoms and brain responses following exercise showed that neurophysiological symptoms in ME patients worsen as a result of physical exertion (Cook et al 2017), linking exercise to cognitive impairment in ME patients.

There are currently 88 published studies in peer-reviewed journals that demonstrate ME is a neurological disease and until the specific cause is found it would be appropriate to classify it as such. ME is classified under the diseases of the nervous system by the
World Health Organisation in its International Classification of Diseases. Based on this evidence, it would be most appropriate for NICE to classify ME as a neurological condition in the guidelines. We would be happy to provide full references of these studies if required.

3b.ii Metabolic shift in ME
Survey of serum metabolites has identified shifted metabolism in patients with ME. A chemical signature of ME was identified from serum metabolites and the direction of shifted metabolism was the opposite to that of metabolic syndrome; in contrast, ME resembles a hypometabolic state (Naviaux RK et al 2016). The observation of a metabolic shift was corroborated by two further metabolomic studies (Fluge O et al 2016 and Germain A et al 2017), the former implicating insufficient ATP levels and excessive lactate production following exertion in clinical disease presentation. Increased intramuscular acidosis occurs in ME patients following physical exertion, likely due to reduced anaerobic threshold (Jones DE et al 2012). In ME patients, elevated lactate is also observed in the cerebrospinal fluid (Mathew SJ, et al 2009). Furthermore, exposing muscle cells to serum from ME patients results in defective metabolism and increased lactate production (Fluge et al 2016). Together, these findings provide a mechanistic link between energy expenditure and exacerbation of ME symptoms, thus contraindicating the use of exercise therapy (e.g. graded exercise therapy or physiotherapy) in improving ME symptoms.

3b.iii Immunological disturbances in ME
In recent work on adolescents suffering from ME, differential expression of genes related to B cell differentiation and survival was observed (Nguyen CB et al 2017). Numerous studies have identified altered immunological responses in patients with ME. Distinct plasma and cerebrospinal fluid cytokine patterns have been observed in ME patients (Peterson D et al 2015, Hornig et al 2016), and these patterns fluctuate with illness duration (Russell L et al 2016, Hornig et al 2015; Hardcastle SL et al 2015 ), suggesting that ME is not a static illness. Furthermore, cytokine levels in subsets of patients associate with classical or atypical disease presentation (Hornig M et al 2017). Impaired natural killer cell function has been known to be associated with ME for over 20 years (Whiteside TL and Friberg D 1998, Ojo-Amaize EA et al 1994).

3c Treatments excluded from guidelines
We would also like the review board to consider the following evidence for treatment which has so far been excluded from the guidelines.

3c.i Ampligen / Rintatolimod
Ampligen has been approved for treatment of ME in Canada since 1997 and in 2016 was approved for people with ME in Argentina. In two clinical trials, treatment with Ampligen resulted in an increase in exercise tolerance (Strayer et al. 1994, 2012). Based on these studies, an NIH working group wrote that Ampligen may benefit patients with ME (Smith 2015). In 2016, the manufacturer established an Early Access Program for Ampligen for ME/CFS patients in the EU and Turkey.

3c.ii Valganciclovir
Valganciclovir is an antiviral drug. A randomized clinical trial demonstrated an improvement in mental fatigue score, fatigue severity and cognitive function in patients treated with valganciclovir compared to placebo (Montoya et. al 2013), following an initial encouraging prospective unblinded study (Watt et. al 2012). Anecdotal evidence suggests that this treatment is effective in a subset of patients but further research is warranted.

These are just a few of the areas which we feel are excluded from the guidelines. We identified POTS and gut dysfunction as key targets for guideline revision. We believe it to be important to include current international research in your consideration of the general nature of ME, as we think any decision into diagnosis and treatment of people with ME should be made in the light of the best available evidence.

We have divided references into key references, which is the main evidence we wish to draw your attention to, and additional references

Key evidence Q3


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<th>Reference</th>
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Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53


Royal College of Physicians

We would like to endorse the responses submitted by the Association of British Neurologists and Royal College of Psychiatrists

Thank you for your response.

Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53
Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

| Regional Public Health Agency for | Yes | The aetiology of CFS/ME is likely to become better understood and should be described in a future guideline revision in as far as it explains and underpins effective medical interventions. | Thank you for your response. |

| RCGP | Yes | • See question 1: There is new evidence since the publication of the guideline.  
• Consideration of screening for Postural tachycardia syndrome (PoTS) to be included in assessment of people with CFS/ME. Studies have shown that up to 30% of patients with CFS/ME have PoTS (2). Almost 29% of patients with PoTS have been given a diagnosis if CFS/ME (3). Fatigue is the most common symptom of PoTS (91%). It takes a mean of 7 years for patients with PoTS to be diagnosed and in the meantime 50% are mislabelled with a psychiatric/psychological explanation for their symptoms.  
• PoTS has many more treatment options than CFS/ME, and many PoTS patients are able to return to school, employment and enjoy an improved quality of life once correctly diagnosed and treated. This may reduce the financial cost of such patients upon the NHS (as many undergo multiple referrals, and unnecessary investigations before diagnosis) and on the UK welfare system.  
• The assessment of CFS/ME patients could include enquiry about orthostatic intolerance and palpitations.  
• Current NICE CFS/ME Guidance states that patients should not undergo a routine tilt table, however, an active stand test for those with orthostatic intolerance is a cheap and quick test and could identify patients who may benefit from more timely diagnosis and treatments not currently available to them.  


Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
<table>
<thead>
<tr>
<th>Country</th>
<th>Stakeholder</th>
<th>Comments</th>
</tr>
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<tbody>
<tr>
<td>Northern Ireland</td>
<td>False Allegations Support Organisation with Parents Protecting Children UK</td>
<td>Yes</td>
</tr>
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</table>

At False Allegations Support Organisation and at Parents Protecting Children UK we get many requests for help from families in which one or more children have been diagnosed with ME / CFS and where Educational and Social Care practitioners don't understand the child's needs. There are interminable arguments about the value of or harm done by various treatment regimes based on exercise or 'mind over matter' type psychological treatments. As a family this is an issue we have faced first hand.

I now look back with a very different perspective and have found that sharing some of our experiences has prompted turning points for other families too.

What I say here isn't true for all families where one or more member is thought to have ME / CFS - it's more likely (for genetic reasons) to be true if there are several family members with problems than a single individual.

I can't understand why thinking about this issue in public circles is so compartmentalised and bound up with apparent vested interests - surely the absolute priority should be getting it right for each and every individual or family.

I hope that sharing our experience will lead to reconsideration and change.

I am the mother of two young adults who as children were diagnosed with ME / CFS and whose subsequent treatment and education were based on the assumption that this debilitating illness was the correct diagnosis.

When my son was a teenager I had a chance social encounter with the GP journalist Dr XXXXXX, he felt that what I was saying about my son's ME / CFS didn't quite ring true for him, he told me of state of the art research being undertaken by Professor XXXXXXX XXXXXXX at XXXXXXX. It took some time for my son to get a referral and a diagnosis of Postural Orthostatic Tachycardia Syndrome. On the basis of revised treatment and practice he eventually got to university and graduated with first class honours. If it hadn't been for my chance meeting with Dr XXXXXX, this would have not been possible.

My daughter is younger and presented differently, she was fatigued and clumsy. She collapsed under academic pressure between GCSE and A Level. She was really quite unwell with a series of short hospital admissions. By chance I mentioned her sad predicament to one of my son's cardiovascular doctors during his routine appointment. Dr XXXXXXX immediately suggested that my daughter should be tested for orthostatic intolerance which could account for many of her difficulties.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
On my daughter's next visit to an unrelated hospital department, I mentioned this conversation to her consultant and the proverbial penny dropped. He gathered a small group of students around him and sent for a blood pressure monitor and a pulse oximeter. He gave his students a demonstration of how to check for orthostatic tolerance. My daughter was then referred to the

It transpired that for 12 years whilst everyone had thought she had ME / CFS she had been struggling with undiagnosed Ehlers Danlos Syndrome and consequent problems including postural orthostatic tachycardia syndrome. Dr XXXXXX at the XXXXXX provided helpful medication but told her that if she wanted to go to university she had to start with physical exercise. She built up her stamina by swimming, she went to university and this year graduated with first class honours. She's now about to join the NHS as a graduate trainee XXXXX rather than a perpetual patient. This only happened because of a chance comment. I think there is a lot of confusion regarding differential diagnosis of ME / CFS or of the effects of PoTS and EDS.

I think that one of the main reasons for the incessant arguments about PACE & CBT for ME / CFS is very simply that those people who have EDS & PoTS will most probably improve on exercise programmes which stimulate cardiovascular function and thereby reduce the strain on the autonomic nervous system; whereas those people with true viral myalgic encephalopathy need to rest and will most probably be made worse by intensive exercise programmes.

It seems to me VITAL that URGENT RESEARCH is needed out into differential diagnosis of the two conditions and that this would lead to the correct treatment plans and an end to the interminable arguments.

For advice on how ME / CFS can be misrepresented as PoTS and EDS, and on how to test for PoTS and EDS, I would refer you to Professor XXXXXX XXXXX and his associates Dr XXXXXX, Dr XXXXXX XXXXX and Dr XXXXXX XXXXX at the XXXXXX

I suggest that it ought to be possible for GPs with a BP monitor and pulse oximeter to undertake a simple test, to determine which of their patients with supposed ME / CFS may have orthostatic problems and should be referred for investigation, as this condition may benefit from practical advice (such as extra fluids & flight socks), exercise and possibly medication.

This would then mean that those with viral ME could be spared the problems of misunderstanding and potentially harmful therapies / exercise regimes.

Local ME

| No answer | No comment |

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE's guideline on Chronic
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<tr>
<th>ME-Letterforce</th>
<th>No Answer</th>
<th>Q3 Comment 1</th>
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<tr>
<td>The current Guideline did not include a section on severe ME. This has left approx. 25% of patients in limbo. This has not been entirely a bad thing as some have been able to avoid some of the harmful advice in the Guideline but many of these patients are without medical care and lie forgotten in their homes too often without the support or visits from a supportive GP.</td>
<td></td>
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<td>The current Guideline also did not include a section on patients who would not benefit from or have been harmed by the current recommendation.</td>
<td></td>
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<tr>
<td>Many people with ME cannot attend the current CFS clinics as there is no understanding of their disease, symptoms and advances in treatment. This has left them, as an example unable to use any doctors report for the DWP.</td>
<td></td>
<td></td>
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<tr>
<td>Our group recommends that NICE recognise that patient feedback is important and should use patient surveys as one of the highest forms of evidence.</td>
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</table>

| Suffolk Youth & Parent Support Group1 & Norfolk & Suffolk Service Design and Service Implementation Group2. | Yes | The surveillance report considers and says it resolves the question of whether the guideline should be changed to align with new conclusions in the US about the diagnosis and the management of ME/CFS. ME and CFS is an International problem and needs dealing with as such. There is a growing international consensus supported by patients, carers clinicians, medical researchers and some NHS commissioning teams with which NICE should align its guidance. Furthermore, recent case law will require that NICE show due diligence to assess the need to review their decision making against any new legal benchmarking. We request that either the guideline be revised to include the vital information now excluded, or that NICE develops a new surveillance report that directly addresses these ethical considerations in a way that reflects the organisation’s commitments to the ethical practices described in the NICE Social Value Judgments document. We draw your attention to the; |

Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

I am aware to date of the following:

Professor Mark Baker, NICE7

“2.1 The Chairman introduced Prof Baker who explained he had been in post for about two years. The Professor said he would start with an explanation of the process by which subjects come before NICE. Originally they had just responded to whoever wanted guidance. Then around 2005-6 a formal process of topic selection, with specialist panels, was set up. That process was changed around the end of 2010 when the main political parties preferred “standards” to guidelines in the NHS. In March 2012 a Library of Quality Standards Topics was established; it included a number of NICE guidelines but ME/CFS was not among them and he did not know why. It was not feasible to update or change guidelines not in the Library until at least 2017. The Library was now the responsibility of NHS England, not of the Department of Health.”

The Groups observations
1. That recommendations are made apparently by “topic experts”8 who are unknown to the public or anyone outside of NICE including interested politicians
2. That the “research” done and evidence base for these recommendations are unknown to the public or anyone outside of NICE, including interested politicians
3. That likewise, the “Surveillance Team” at NICE are unknown to the public or anyone outside of NICE including interested politicians; so their competency and possible conflicts of interests and declaration currently have not been released to public scrutiny.
4. That this is a selective and discriminatory and inconsistent approach by NICE who have released the footnoted information for other NICE consultations which, Norfolk and Suffolk Groups, we have contributed to recently as partner stakeholders together with other registered stakeholders. 9
5. The NICE Equality Impact Statement for CG53 should be available for public scrutiny.
6. UNCRPD10 compliance is required as well. The current guidance process is in our view, incompatible with the UK Conventions on Children, the disabled and women.

I would like to ask the following question of the Surveillance Team (in addition to my EH82739 Freedom of Information request- as I have received a notice that NICE seem to be too busy to oblige me with information: it is unfortunate that response to the FOI will not be available during the consultation period;
1. 2. The 2007 NICE Guidance and review process does not appear to have been assessed against the new legislative requirements enacted over the last 10 years . How can “no review needed” therefore be a recommendation?
3. Where is the evidence for the “no review needed”?
4. Who are the individuals within NICE who suggested this decision?
5. What factual data and evidence was used to arrive as this recommendation?
6. NICE Guidance CG53 was controversial in 2007:10 years on, it is none the less so.
7. Professor Mark Baker from the National Institute for Health and Clinical Excellence (NICE) As can be seen from the Minutes, Professor Baker accepts that the NICE guideline on ME/CFS is no longer meeting the needs of people with ME/CFS and it fails to take proper account of the wide variety of clinical presentations and disease pathways that come under the ME/CFS umbrella. Surely therefore, it beggars belief that this provisional review decision has been announced?
8. Do the topic experts and the Surveillance Team not agree that the suggestion of recommending “no review”, (this is added to the potential breach of Government protocol and guidance on public involvement and consultation I identified) once again could trigger and lead to a judicial review challenge by those aggrieved and harmed by the current guidance?
9. The review exercise to date does not appear to be underpinned by a fair, sensible or robust process. Surely NICE have a duty to engender public support or confidence in the guidance?

Do you have any comments on equalities issues?

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<tr>
<th>Stakeholder</th>
<th>Overall response</th>
<th>Comments</th>
<th>NICE response</th>
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<tbody>
<tr>
<td>British Infection Association</td>
<td>No</td>
<td>No comments</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.</td>
</tr>
<tr>
<td>The Pernicious Anaemia Society</td>
<td>No</td>
<td>No comments</td>
<td>Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have</td>
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In February 2004, NICE accepted its remit for CG53 from the Department of Health and the Welsh Assembly: “Remit: To prepare for the NHS in England and Wales, guidance on the assessment, diagnosis, management of adjustment and coping, symptom management, and the use of rehabilitation strategies geared towards optimising functioning and achieving greater independence for adults and children of CFS/ME.”

This remit, instructed the supposedly independent institution of NICE, to recommend the use of “rehabilitation strategies”. NICE obliged by recommending CBT and GET. In the process, it confirmed to any reasonable person, that M.E. and CFS are indeed, “in the patient’s head” and that patients are undisciplined and need to be told what to do because their actions and beliefs are causing their illness.

In its ‘Comments Form’, NICE graciously ask: “Do you have any comments on equalities issues?” In view of the fact that NICE accepted a highly discriminatory remit, which before the GDG was even started, was prejudiced against the interests of patients, and which would predictably be detrimental to their medical care, wellbeing and quality of life – Yes. There is an equality issue here because M.E. and CFS patients evidently are not ‘equal’ as far as NICE are concerned. Abundant evidence that recommendations in CG53 are false and misleading have been ignored by NICE themselves, making the institute unfit to pass judgement on its own prior and present conduct.

The remit that NICE accepted would have been rejected by any credible independent medical or scientific institution. It was loaded with competing interests that predetermined what the GDG should produce, but it did keep some NICE employees busy for some years and its final product did not inconvenience anyone important or ‘equal’. So it is hardly surprising that now that NICE have the opportunity to virtually rewrite their own remit by way of a review, and pass judgement on its own earlier work, it would rather ignore the fact that CG53 misleads patients, doctors and the public and clearly prefers to maintain these seriously flawed guidelines.

VIRAS | Yes
---|---

decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Thank you for your response.

Note that, in line with the guidelines manual, Committee members and topic experts for the published guideline are surveyed for their opinions on the relevance of the published guideline, recent developments in the topic area and their knowledge of any new important evidence since publication of the guideline. In some circumstances (for example, when a significant period of time has passed since the guideline was published), members of the relevant Quality Standards Advisory Committee, or others with expertise, may be surveyed. This intelligence is considered alongside the new evidence identified through the surveillance review. However, the decision to update or not update a guideline remains with NICE’s Guidance Executive. This is the case for all surveillance review topics.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

A new committee will be recruited to take forward the update of the guideline. The resulting Committee should,
This is despite the fact that the Centres for Disease Control and Prevention have removed all mention of CBT and GET from their pages for the public (Tuller, 2017. ME Association, 2017). And it is despite the fact that the PACE Trial, the FINE Trial, the GETSET trial and all similar efforts to establish GET and/or CBT as treatments, have provided incontrovertible evidence that these therapies are not treatments for M.E., or for CFS, or for ‘Oxford CFS’ and they provide no credible clinically significant benefit to patients.

VIRAS believe that pretending that these therapies can treat M.E. and CFS provides the public and some doctors with ‘evidence’ to support discrimination against patients and intentionally or not, even encourages abuse of patients as time-wasters and hypochondriacs. It protects the incomes, careers and reputations of the ‘wessely-school’, who created the illusion that CBT and GET are treatments for M.E. and CFS by: 1/ paper-pile publishing 2/ circular referencing, 3/ misrepresenting research data and 4/ the inveigling of every institution the old-boy network could access – to the extent that there is hardly an institution or individual in the field, which has not at some time or other either overtly or implicitly, supported wessely-school opinions. All these people, like NICE itself, now have a vested interest in maintaining the fantastical and disproved notion that M.E. and CFS can be rehabilitated with CBT and GET.

NICE Guideline CG53 is and always has been unfit for purpose, but NICE is not fit to conduct the review. The task must be assigned to a truly independent scientific body. NICE has demonstrated by its own conduct that they have bowed to, and continue to pander to the vested interests and undue influence of the wessely-school. The result is guidelines that have no credible scientific or medical basis influencing the medical care of thousands of seriously ill patients.

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will as far as practically possible, reflect the range of stakeholders and groups whose activities, services or care will be covered by the guideline. All Committee members are recruited in accordance with NICE’s policy and procedure for recruitment and selection to advisory bodies and topic expert groups. Positions are advertised on the NICE website and other appropriate places (for example, NICE Twitter, social media and websites of stakeholders, Medical Royal Colleges and professional organisations), and relevant stakeholders are notified.
<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Response</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Royal Liverpool University Hospital, CFS/ME services</td>
<td>No</td>
<td>No comments</td>
</tr>
<tr>
<td>Royal College of Paediatrics and Child Health</td>
<td>No</td>
<td>CFS/ME in children and young people is a very different condition to that seen in adults. For example, the controversial PACE study does not apply to CYP. We suggest that the next revision of the NICE guideline be split into two distinct documents, for adults and CYP, otherwise there is a risk of clinicians incorrectly extrapolating adult evidence to CYP.</td>
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<tr>
<td>Stakeholder</td>
<td>Response</td>
<td>Comments</td>
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<tr>
<td>North London ME Network</td>
<td>Yes</td>
<td>We are extremely concerned that our more disabled members have the least access to good medical care. When people are too sick to get to see their GP (or consultant, where there is one, and in some areas there is either no specialist or the wait is very long) then they can be left for years with no healthcare at all. It’s a disgrace that the most disabled patients with ME/CFS receive the poorest care. This is very different to the picture in most other illnesses.</td>
</tr>
<tr>
<td>Association of British Neurologists</td>
<td>No</td>
<td>No comments</td>
</tr>
<tr>
<td>FORWARD-ME</td>
<td>Yes</td>
<td>In the context of well-understood conditions of cancer, a significant possibility of need for biological medical care is immediately understood as sufficient to secure a right of access to that care. Based purely on the possibility of need, policy makers are clear that any patient group who might well suffer from cancer has a right to access to biological testing, treatment and support.</td>
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Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
Stigma about CFS/ME has made it difficult for policy makers to recognise the profound importance of their obligation to continue to protect that right in the context of this condition. Given the conclusion among US health authorities that CFS/ME is a biological condition for which patients require biological testing, treatment and support, a significant possibility of biological need is a scientific fact for this patient group.

Because the need for biological medical care is a possibility rather than a proven fact, it is unclear at this time whether policy makers have an obligation to proactively ensure that all patients in this group receive medical care. Still, the possibility of need is sufficient to establish that it is unethical for policy makers to knowingly obstruct access to biological testing, treatment and support for this patient group.

Because the current guideline directs patients squarely towards behavioural management, it clearly does obstruct patients’ access to biological testing, treatment and support. To avoid this ethical violation, we request that the guideline be revised to present a truthful, neutral picture of the current debate about the nature and management of CFS/ME.

Patients have expressed concern around current treatments and provide testament to what works and doesn’t work for them and consequent impacts. Unfortunately this individually lived experience does not lend itself to result in published studies that can be considered by NICE in reviews such as this other than that which we have published: http://www.patientclientcouncil.hscni.net/uploads/research/ME-CFS_Position_Statement.pdf

Thank you for your response.

It was disappointing that the consultation period was only 10 days. To enable Stakeholders to respond a longer consultation period is needed. Especially bearing in mind that some stakeholders are disabled and experience extreme fatigue, providing more time as a reasonable adjustment may be necessary (in line with the Equality Act http://www.legislation.gov.uk/ukpga/2010/15/section/20).

Thank you for your response.

<table>
<thead>
<tr>
<th>Patient and Client Council</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion London</td>
<td>No answer</td>
</tr>
</tbody>
</table>

Thank you for your response.

There is a 2-week consultation with stakeholders for all surveillance reviews that are no to update proposals, in line with the guidelines manual. Consultation dates and times are posted in advance on the guideline page on the NICE website, and stakeholders are reminded by email.
We recommend a minimum of 6 weeks for any consultation period with stakeholders, with an additional two weeks added if the consultation takes place at the time of a public holiday.

The 2-week consultation period is standard for surveillance reviews and there are no plans to extend this. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

| Mast Cell Action | Yes | MCAS has been slow to be accepted by UK doctors. Many patients spend a long time with a diagnosis that does not account for their symptoms and suffer tremendously, even when the doctor is aware of MCAS. A typical example would be a patient with a simple diagnosis of Urticaria, who can tolerate 10 foods, is highly reactive to external triggers, perfume etc such that they struggle in public places / school, and suffers episodes of acute abdominal pain and vomiting. We have “patient stories” that we would be happy to provide.
As a patient community we have no home or voice in the NHS or within any subspecialty. MCAS patients should be entitled to the same level of clinical and diagnostic care as other patients and importantly doctors that appreciate how disabling this condition can be. |
| Royal College of Psychiatrists | Yes | Outcomes are comparable and are similar in BME and white British groups (Ingham et al 2016). |

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
| The ME Association | Yes | The ME Association is a member of the Forward ME Group of charities. We will repeat the position that was agreed by the whole group in relation to equality issues in the group response to NICE. This is as follows:

*In the context of well-understood conditions such as cancer, a significant possibility of need for biological medical care is immediately understood as sufficient to secure a right of access to that care. Based purely on the possibility of need, policy makers are clear that any patient or patient group who might well suffer from cancer has a right to access biological testing, treatment and support.*

*Stigma about ME/CFS has made it difficult for policy makers to recognize the profound importance of their obligation to continue to protect that right in the context of this condition. Given the conclusion among US health authorities that ME/CFS is a biological condition for which patients do require biological testing, treatment and support, a significant possibility of biological need is a scientific fact for this patient group.*

*Because the need for biological medical care is a possibility rather than a proven fact, it is unclear at this time whether policy makers have an obligation to proactively ensure that all patients in this group receive biological medical care. Still, the possibility of need is sufficient to establish that it is unethical for policy makers to knowingly obstruct access to biological testing, treatment and support for this patient group.*

*Because the current guideline directs patient care squarely down the mental health track, it clearly does obstruct patients’ access to biological testing, treatment and support. To avoid this ethical violation, we request that the guideline be revised to present a truthful, neutral picture of current debate about the nature and optimal management of ME/CFS.*

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

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| Action for ME | Yes | According to the Equality Act 2010 Part 2 Chapter 1 Section 6, people are disabled if they have a physical or mental impairment that has a ‘substantial’ and ‘long-term’ negative effect on their ability to carry out normal daily activities. According to this definition, the vast majority of people with CFS/M.E., including those relatively mildly affected, are disabled.

The UN Convention on the Rights of Persons with Disabilities of which the UK is a signatory, requires (at article 25 d) that health professionals “provide care of the same

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or
<table>
<thead>
<tr>
<th>British Association for CFS/ME</th>
<th>Yes</th>
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<tr>
<td>We are concerned about unequal access to specialist service provision and local expertise variations in primary care. We are concerned that support may be less available or time-limited for those severely affected. The majority of CFS/ME patients are female and we are concerned that women’s health issues, including gynaecological and genitourinary symptoms, impact of menopause, sexual health and contraception, and sexual trauma and abuse are under-recognised, under-researched, and not well considered.</td>
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</table>

Thank you for your response. Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

We have outlined above our concerns that it is unethical not to provide clinicians and patients with a balanced current understanding of the evidence base for treatment and management approaches, and that failure to do so prevents informed consent. It is our view that to ensure compliance with article 25 d of the Convention, review and updating the guideline should not be delayed.

Action for M.E. frequently hears from patients who are not informed of treatments that could improve their symptoms. The guideline does not translate into the provision of appropriate symptom management in practice. The NHS England Accessible Information Standard [NHS England, Accessible Information: Specification, https://www.england.nhs.uk/wp-content/uploads/2015/07/access-info-spec-fin.pdf accessed 21 July 2017] outlines the need for all NHS care to ensure that people with a disability are supported to communicate effectively with health and care professionals. As people with CFS/M.E. can experience cognitive difficulties it must be considered how to ensure the full range of potential healthcare approaches is presented and communicated. If clinicians are not aware of the full and balanced picture of the international medical context, and therefore cannot communicate this clearly and accurately to patients, people with CFS/M.E. may not be aware of and therefore not able to access appropriate biological medical care.

On grounds of equality and human rights, as well as on grounds of effective healthcare, the NICE guideline must be reviewed and updated.

quality to persons with disabilities as to others, including on the basis of free and informed consent by, inter alia, raising awareness of the human rights, dignity, autonomy and needs of persons with disabilities through training and the promulgation of ethical standards for public and private health care.” [our emphasis]
**Healthwatch Kirklees**  
**Yes**

Healthwatch Kirklees have spoken to many people who have ME and have collected their stories to share with NHS England, MPs and Clinical Commissioning Groups. In Kirklees and Calderdale there isn’t a commissioned service available for people with ME. Approximately there are 1,200 people with ME in Kirklees alone and Healthwatch feel that this group of people are suffering because of little knowledge of the condition.

**Stigma**  
When speaking to patients with ME Healthwatch Kirklees found that many found that they faced stigma in the medical/clinical/media/public fields. It is a common complaint of ME/CFS patients we spoke to that GP's and hospital staff have a poor understanding of the illness. The Kirklees and Calderdale Independent ME Support Group feel that GP's fall into 3 categories when dealing with ME/CFS patients: a) supportive but admit they can do little B) insist that patients must get more exercise and engage with talking therapies C) do not believe ME/CFS is a real illness. In 2015, our survey revealed that many ME/CFS patients come across health professionals with little or no knowledge of the illness. For example,

- 60% of respondents found that information from the NHS regarding their illness was not accurate/helpful.
- 61% said that their GP was not knowledgeable about their illness.
- 55% said they would not trust their GP to provide them information about ME/CFS.
- 56% said that NHS doctors and nurses do not understand their illness.
- 80% found hospital doctors and nurses knowledge of ME/CFS to be overwhelmingly poor.

Some experienced quite negative attitudes from health professionals due to the stigma surrounding the illness. 28% of respondents said their GP sometimes talks to them with respect regarding their illness which rises to 33% for hospital doctors and nurses.

**Inequalities**  
In 2015 NHS England issued a document "Guidance for NHS commissioners on equality and health inequalities legal duties" "NHS England NHS England has a duty to have regard to the need to reduce inequalities between patients in access to services commissioned through its direct commissioning functions. This may involve:

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Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
Identifying health inequalities, evaluating how such inequalities might impact on people’s ability to access services, and commissioning for all of the population and all needs”.

This means CCGs and NHS England should understand the potential effect of policies and practices on people with characteristics that have been given protection under the Equality Act, especially in relation to their health outcomes and the experiences of patients, communities and the workforce. This will help the organisation to consider whether the policy or practice will be effective for all people.

It is common complaint from people with ME that there is a lack of specialist healthcare for their neurological illness. ME patients from Kirklees and Calderdale (which have a combined population of over 600,000 people) have to make the long journey to Seacroft Hospital on the outskirts of Leeds. For ME patients using public transport they use a train to get to Leeds and then a long walk across the city to the bus station then a 20 minute bus ride to Seacroft. Then once at the hospital they face a 15 minute walk across the hospital grounds to get to the ME clinic.

Most respondents in Kirklees and Calderdale pointed to the lack of community services to support them and many noted the poor quality treatment they received when treated as in-patients. Common problems that respondents noted ranged from travel/mobility issues and the benefits system to isolation/lack of social interaction. Respondents to the survey pointed to a variety of services that would be beneficial such as yoga, massage, meditation, transport to help access such services.

People with ME/CFS experience high levels of functional impairment across physical and mental domains, scoring lower overall on health-related quality of life tests than most other chronic health conditions including lung disease, depression, heart disease and diabetes. A study just published from DePaul University, USA in the journal Insights into biomedicine stated that: "The finding that ME and CFS group had more functional limitations and more serious symptoms than those with MS provides additional evidence to the seriousness of ME and CFS." (Jason et al, Differentiating Multiple Sclerosis from Myalgic Encephalomyelitis and Chronic Fatigue Syndrome.)

Healthwatch Kirklees have attached a link to a video case study we collected speaking to our local independent ME support group. (Please note this video is not to be shared any further than with the committee). https://youtu.be/8GIZDyVRkFs
| The 25% ME Group | Yes | There is some irony in this question, given that one of the points of information that the Institute declined to provide to practitioners and patients in CG53 is that ‘ME/CFS’ is a disease covered by the then Disability Discrimination Act (provisions since subsumed under the Equality Act 2010). This was deemed to be ‘beyond guideline scope’. There is a case to be made this guideline discriminates against people with M.E. because it treats this disorder as if it were another (i.e. fatigue syndrome). It is unethical to treat one disorder as if it were another. The result is application of some core recommendations on management that are at best irrelevant and at worst harmful. **Conclusion - please withdraw CG53, pending:**  
- a root and branch review of the range of relevant evidence, both pre and post publication of CG53 in 2007  
- a robust mechanism in clinical practice to allow health professionals to identify and screen out any and all patients who stand to be harmed by the intervention(s) recommended in the present guidance. NB: in our view, and it is a view we stand ready to substantiate, this applies to all those who have M.E.; it does not apply to all who are presently encompassed by the Oxford ‘fatigue’ criteria (on which the research studies concerned recruit). |

| Blue Ribbon for the Awareness of Myalgic Encephalomyelitis (BRAME) | Yes | Bioethically the NICE guidelines do not provide a balanced view. I cannot think of any other guideline which has garnered so much criticism and has been repeatedly asked to be rewritten, since even before it was published. Would NICE be promoting such a guideline that did not fit patient need, or could give such poor outcomes, if this was cancer, heart disease or diabetes? So why do patients with neurological ME or CFS, for which there is no cure, have to endure the overwhelming inequality of care and lack of biomedical care, to manage their condition, and instead be offered CBT and GET to think and/or exercise themselves better? Please look again at the results of the independent analyses of the PACE raw trial data, which I have commented on in question 2. This disparity of results must be reflected in the guidelines. How many other NICE guidelines recommend treatments for chronic health conditions, for which there is no cure, just CBT and GET, which the majority of patients find unhelpful and/or harmful, giving poor outcomes and QALY’s, and certainly not cost effective in this time of austerity? There is no equality with other guidelines. |

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
To give a balanced and neutral report on the facts and evidence about neurological Myalgic Encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS) then in tandem with asking Cochrane to do yet a further review of CBT and GET and the PACE trials, why is NICE not asking a well-respected researcher, agreed with the ME groups and population, to do a review of the biomedical research evidence. Only when this is done can the guideline be classed as being balanced and neutrally informative to health professionals. All sides of the debate should be discussed and reported to be ethically sound.

Given that any medical relationship is supposed to be a partnership between hcp and patient ie “no decision about me without me” – where is the partnership and equality in this document – the patient and their views and evidence are belittled and pushed to one side. The patient must once again come to the fore of these guidelines and provide balance and equality within, so that their voices are heard, and their evidence is not ignored.

Until the experts who were responsible for deciding whether the guidelines should be updated are revealed, we do not know whether there is an equality issue, ie whether you had an equal balance of experts who follow the biomedical approach to ME and CFS, and those who follow the biopsychosocial approach. Given the decision of ‘No Update’ we believe that there is probably an equality issue here!

It is unethical for policy makers to knowingly obstruct access to biological testing, treatment and support for people with ME or CFS. NICE cannot say that they have not had an overwhelming amount of biomedical research papers, and patient evidence/surveys making them fully aware of the latest evidence on the biomedical nature of the conditions, and the biomedical need of the patients, since the working group was formed in 2005, and continuously since then, to the present day. In what other conditions has NICE ignored or side-lined so much evidence?

Patients with neurological ME and CFS want NICE to revise, and produce a guideline, which truly reflects the reality of these complex and debilitating conditions, and to acknowledge the evidence of researchers, patients, and other respected global institutions, that CBT and GET are not appropriate treatments for ME and CFS, and for them to be able to have the biomedical healthcare they have sought, and fought for, for so long.
### Hope 4 ME & Fibro Northern Ireland

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<th>Stakeholder</th>
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The following commentary was prepared by Andy Hugh and Nancy Van Hoylandt:

There is a disparity between NICE and the CDC/IOM guidance. This could result in a breach of Human Rights if the NICE recommendation for no update goes forward. However, there is a possibility to bring about a resolution, should an appropriate review of the NICE guideline take place.

Currently the two guidelines have opposing views.

> “persons with disabilities have the right to the enjoyment of the highest attainable standard of health without discrimination on the basis of disability.”
> UNCRPD - Article 25: Health.

Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) is listed in the World Health Organisation classification of diseases, ICD-10, under report code G93.3 [51] as a Neurological Illness and there are proposals for its inclusion in ICD-11 [52] as a disease of the nervous system of viral causation. The United Kingdom as a member state of the World Health Organization (WHO), is expected to comply with the WHO Nomenclature Regulations 1967 [53].

### National Institute of Health and Care Excellence (NICE) Guidelines – UK

The National Institute for Health and Care Excellence (NICE) have guidance CG53 [54] from 2007, for the diagnosis and management of CFS/ME (Chronic Fatigue Syndrome/Myalgic Encephalomyelitis), states:

> “There is no one way of managing CFS/ME that helps everyone but there are several options to try (see Managing CFS/ME).” [55][56].

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

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[53] https://www.publications.parliament.uk/pa/ld201415/ldhansrd/text/141126w0001.htm
[54] https://www.nice.org.uk/guidance/cg53/chapter/1-guidance
[55] https://www.nice.org.uk/guidance/cg53/ifp/chapter/What-is-CFSME
[56] https://www.nice.org.uk/guidance/cg53/ifp/chapter/managing-cfsme
Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

and in their guideline it is stated:

“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.”

“1.6.2.4 Cognitive 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.”

So, NICE acknowledge that there is no treatment that helps everyone. This is an acknowledgement that ‘experimentation’ is necessary to find out if a NICE treatment recommendation will help or not. There is a distinct failure to recognise any impact on the patient should treatment fail.

NICE also acknowledge a right to refuse or withdraw from any component of care, however, in practice, paediatricians do not understand why a parent would refuse a treatment designed to help their child and this does result in false allegations of child abuse [57], numbers of which have risen dramatically over the last few months [58].

There is significant dispute as to whether one of the NICE treatment recommendations, Graded Exercise Therapy (GET) is therapeutic as will be seen later, however, the lack of acknowledgement by NICE of children’s rights to prevent experimental treatments being forced on them without the children or parents facing false allegations is a particular issue. Such breaches of human rights cause unnecessary suffering for both the child and the family as a whole; a situation that urgently needs addressing in the NICE guidance.

One key point to note is that NICE suggest that there is evidence of benefit from the use of their treatment options, yet, GET is clearly experimental because they admit it may not help and moreover, they do not cover the negative effects or possibility of harm when the therapies don’t work. The same is of course true for Cognitive Behavioural [57] http://www.tymestrust.org/pdfs/falseallegations.pdf [58] https://twitter.com/JaneCColby/status/886255772639916032
Therapy (CBT) in the way it is applied in practice. Trials such as FitNET-NHS use planned increases in mental exertion, which is clearly no different to GET. NICE recognise that mental, physical or emotional exertion affects patients.

NICE describes, in part, the implementation of Graded Exercise Therapy as follows:

1.6.2.13 People with mild or moderate CFS/ME should be offered GET that includes planned increases in the duration of physical activity. The intensity should then be increased when appropriate, leading to aerobic exercise (that is, exercise that increases the pulse rate).

So, the NICE message with respect to GET is that increases in exertion should be the goal and planned with an aim to exercise in the aerobic energy zone.

According to a number of studies of which a couple are referenced, there is a physical block in the metabolism of aerobic energy \(^59\)\(^60\) in those with CFS/ME and scientists warn of the abnormal response to exertion and that aerobic activities should be avoided \(^61\)\(^62\)\(^63\). It is clear that the NICE guidelines, have not taken into consideration the biomedical findings that demonstrate the potential for harm in the aerobic energy zone. NICE are clearly intent on ignoring and dismissing the plethora of harms from GET that have been reported, seemingly because they'll only recognise harms reported in trials.

NICE state \(^64\):

"From all sources, we considered 155 publications to be relevant to the guideline. Peer-reviewed study reports were assessed by abstract."

which is not so many publications given the IOM used approximately 9000 papers (see below) and yet NICE state:

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59 https://www.newscientist.com/article/2121162-metabolic-switch-may-bring-on-chronic-fatigue-syndrome/
60 https://www.youtube.com/watch?v=q_cnva7zyKM
61 https://www.facebook.com/griffithuniversity/videos/10154550816976005/?hc_location=ufi
62 https://www.youtube.com/watch?v=FXN6f53ba6k
63 https://www.youtube.com/watch?v=7BreGgEdMpA
64 https://www.nice.org.uk/guidance/cg53/documents/surveillance-review-proposal
“We did not find any evidence related to management of setbacks/relapses.”

At some time between August and October 2016, NICE made the following statement [65].

“In 2015 we were told about 3 US reports that indicated there are likely to be changes in diagnostic criteria that could have an impact on the guideline recommendations. We decided to start a check of whether the guideline needs updating, and plan to publish our decision in summer 2017. We have since been made aware of new information about the 2011 PACE trial, and we will also consider that in the check. Register as a stakeholder to be informed about the decision.”

Amongst those reports was a 372-page report from the Institute of Medicine (IOM) in the US, that was based on approximately 9000 biomedical papers [66].

**The Institute of Medicine (IOM) Report - US**

The Institute of Medicine were charged to do a thorough investigation into CFS/ME by the Department of Health and Human Services, the National Institutes of Health, the Agency for Healthcare Research and Quality, the Centers for Disease Control and Prevention, the Food and Drug Administration, and the Social Security Administration, to convene an expert committee to examine the evidence base for CFS/ME. In February 2015, the Institute of Medicine announced their report ‘Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness’ [67].

In their report, the IOM asserted quite firmly, that:

> “the committee recommends that the disorder described in this report be named “systemic exertion intolerance disease” (SEID). “Systemic exertion intolerance” captures the fact that exertion of any sort—physical, cognitive, emotional)—can adversely affect these patients in many organ systems and in many aspects of their lives. The committee intends for this name to convey the complexity and severity of this disorder. “exertion of

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| any sort (physical, cognitive, or emotional)—can adversely affect patients in multiple organ systems”

The NICE Guideline Development Group recommendation

Then in July 2017, NICE stated:

“Topic experts agreed with the conclusions of the surveillance team about the 3 US reports which were that no impact on the guideline was anticipated. They indicated that until and unless further research suggests otherwise, the NICE diagnostic criteria for CFS/ME remain valid.” [68]

and

“We have checked this guideline and are proposing not to update it. We are consulting on this proposal. Register as a stakeholder to be informed about the final decision.” [69]

Centers for Disease Control and Prevention (CDC) – US

Following the announcement of the report by the IOM in February 2015, the CDC made the following statement [70]:

“In 2011, CDC posted the CFS Toolkit on its website to provide an easy-to-use resource for clinical care. During recent months CDC scientists had been working with CFSAC and others to revise the CFS Toolkit. After publication of the IOM committee report, CDC decided to archive the CFS Toolkit and the brochure ‘Recognition and Management of CFS: A Resource Guide for Health Care Professionals’.”

In May 2017, a move in the US to officially remove GET as a recommended treatment first came from the New York Department of Health, who stated in a letter [71] to approximately 86,000 physicians:

[69] https://www.nice.org.uk/Guidance/CG53
[71] https://pbs.twimg.com/media/DA7LnGPW0AA3C66.jpg:large
“In the past, cognitive behavior therapy (CBT) and a graded exercise therapy (GET) were recommended as treatments. However, these recommendations were based on studies that included patients with other fatiguing conditions. Because of the hallmark intolerance to exertion of CFS/ME, exercise may actually worsen the health of those living with this disease. Currently, there are no FDA approved treatments for CFS/ME.”

In May 2017, the CDC also followed this with a statement [72] that said:

“Today, CDC recognizes the 25th anniversary of International Awareness Day for CFS/ME and Fibromyalgia. We continue to promote understanding of CFS/ME by:
Supporting one of the largest-ever studies of CFS/ME. Seven CFS/ME doctors are identifying major health problems and symptoms of patients with CFS/ME. This will help us develop better and easier ways to diagnose and treat CFS/ME. Early findings contributed to a 2015 report by the Institute of Medicine’s Committee on CFS/ME and have been recently published.“

More recently, on or around 8th July 2017, the CDC updated its website, having removed all references to GET [73] and made a statement [74] that demonstrates clearly that the CDC do not consider there to be any existing treatments for ME/CFS:

“There is no cure or approved treatment for myalgic encephalomyelitis/chronic fatigue syndrome (CFS/ME).”

On this date, the CDC also promoted the use of the IOM diagnostic criteria for the diagnosis of CFS/ME [75].

There are a number of disparities between the UK and US in the diagnosis and management of CFS/ME but I think the GET example is evidence enough to demonstrate that there are significant differences to warrant an acknowledgement in the NICE guidance that there is no consensus and a large disparity between authoritative members of the UN regarding treatment and management of CFS/ME and the harms

72 https://blogs.cdc.gov/publichealthmatters/2017/05/me-cfs/
73 https://www.cdc.gov/me-cfs/
74 https://www.cdc.gov/me-cfs/treatment/index.html
75 https://www.cdc.gov/me-cfs/symptoms-diagnosis/diagnosis.html
associated with treatment.

In particular, whilst the CDC/IOM identify the biological nature and needs of patients, the UK fails not only to include any reference to biological causation but to dismiss the IOM report out of hand. NICE favour a handful of very subjective and questionable RCT’s over 9000 biomedical papers.

This is clear psychiatric bias and discrimination against those with a physical illness and disability.

The pre-trial mass media promotion of the FitNET-NHS trial as a cure for 2/3rds of children is the latest continuation of mass media brainwashing of a plethora of professionals and the public. This can only serve to incite yet more prejudice against those with a physical disability, that responds very differently to exertion than most other illnesses. Exertion scientists warn, causes harm; that there’s a physical block in the metabolism of aerobic energy. Yet NICE guidance encourages planned increases aerobic exercise!

The inequality is exacerbated by psychiatric refusal to acknowledge cardinal symptoms or extreme symptoms that may exist. The weakening of diagnostic criteria (by omitting key features of ME) results in a cohort of sufferers that includes subjects that may not have CFS/ME. This makes researchers conclude that CFS/ME is less severe than a more accurately selected cohort might indicate. Indeed, it seems that sufferers with more with extreme symptoms are then denied a diagnosis, as it is claimed that CFS/ME cannot become so severe, and this results in the severe patients being denied appropriate care.

The continuation of the psychiatric bias in the UK directly denies patients their legal and legitimate rights to biomedical progress by putting a roadblock in the way of biomedical science and any possibility of a cure or treatments to alleviate patient’s suffering.

The following quotes clearly demonstrate the appalling prejudice that exists in the UK as observed by other major territories:

“In the UK, CFS is an exceedingly dangerous term.”, Dr Byron Hyde. [76]

“the protocols in England are totally barbaric!”, Prof. Ron Davis”. [77]

The UK urgently need to remove the importance of bio-psychosocial intervention and bias and embrace the plethora of biomedical science for its citizens in order to bring equality to patients.

Conclusion

Given that NICE are a public body with an exemplary function, it has a duty to protect the citizens of the UK and in particular people with disabilities.

The UK ratified the UNCRPD (08-06-2009) & UNCRPD Optional Protocol (07-08-2009) [78] meaning they will protect persons with disabilities, in this case people with ME/CFS. This document states: "States Parties recognize that persons with disabilities have the right to the enjoyment of the highest attainable standard of health without discrimination on the basis of disability.", UNCRPD - Article 25: Health [79]. By only making available coping strategies for people with ME/CFS and not acknowledging the current biomedical research available in the world, NICE withholds this right to the highest attainable standard of health.

If NICE does not recognize the opposing views on the benefits and risks of harm from GET and does not refrain from biased recommendations and from informing the public that there is no consensus on treatment they are bringing patients in danger and are in violation of Article 15 - Freedom from torture or cruel, inhuman or degrading treatment or punishment and Article 25 - Health [80] which says health services should be designed to minimize and prevent further disabilities, including among children and older persons.

As the NICE guidelines confirm treatment recommendations need free and informed consent of the person concerned, Article 3 in the NICE Charter on Human Rights [81], but in reality there are actual consequences.

<table>
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<th>Invest in ME</th>
<th>Yes</th>
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<td>1. By ignoring the recent IOM, NIH, AHRQ and CDC decisions to remove CBT and GET from their recommendations and stipulate that the Oxford criteria and research using those criteria need to be abandoned then NICE are negligent. Healthcare staff in this country will not be aware of the mounting evidence accumulated by the US organisations or their decisions if NICE ignore this recent evidence. This will therefore harm patients.</td>
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<tr>
<td>2. NICE has not given adequate time for a charity such as Invest in ME Research to respond. This is quite a cynical act by NICE. Knowing that patients have reduced capability to analyse, and charities such as Invest in ME Research who do not have salaried staff able to concentrate on only one thing, then NICE expect that they will have less to answer.</td>
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- NICE need to acknowledge that by necessity, coping with the illness may require extended periods of isolation; that the treatments recommended by NICE are experimental and may or may not cause harm and that adults and children alike should be free to refuse such experimental treatments without risk of false allegations being made against them; harms and false allegations that have to date, driven fear of the NHS and other professionals, into families who are faced by them.

- Also stated in Article 25 (d)(f) [82] persons with disabilities are entitled to the same standard of quality care as others. NICE therefore is obliged to incorporate awareness of rights of persons with disabilities so people with ME/CFS can access the same standard of quality care as to others. This asks for training and promulgation of ethical standards for public and private health care so patients can be treated with dignity, autonomy and have their needs taking seriously. Discriminatory denial of health care or health services without recognizing the risks of harm brought on by recommended treatment or false allegations is a violation of the rights of persons with disabilities.

- Therefore, NICE needs to review the current guidelines, not only in light of the international advances made in the scientific understanding of the disease, but also to ensure persons with disabilities are met with respect and dignity, and are protected from treatment that causes further harm.

- Note that, in line with the guidelines manual, Committee members and topic experts for the published guideline are surveyed for their opinions on the relevance of the published guideline, recent developments in the topic area and their knowledge of any new important evidence since

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This inequality deserves investigation as you certainly have given far more time to an anonymous group of “Topic Experts” – whom, it seems, are heavily biased toward the BPS view of ME.

As such this is discrimination.

3. The composition of your “Topic Expert” group cannot be determined. It is a group appointed by NICE to oversee NICE’s work. This surely is not correct and needs scrutiny by an independent body.

We do not trust NICE to investigate this themselves but feel we have to make this point.

The Surveillance proposal consultation document is clearly grossly biased toward a BPS view of ME and unrepresentative of patient views on the disease from which they, not NICE, suffer daily.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

A new committee will be recruited to take forward the update of the guideline. The resulting Committee should, as far as practically possible, reflect the range of stakeholders and groups whose activities, services or care will be covered by the guideline. All Committee members are recruited in accordance with NICE’s policy and procedure for recruitment and selection to advisory bodies and topic expert groups. Positions are advertised on the NICE website and other appropriate places (for example, NICE Twitter, social media and websites of stakeholders, Medical Royal Colleges and professional organisations), and relevant stakeholders are notified.

Thank you for your response.

M.E Lochaber

The PACE trial is responsible for suffering of patients. The credibility of researchers is compromised by conflicts of interest.
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<th>Stakeholder</th>
<th>Access to services</th>
<th>Notes</th>
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<tbody>
<tr>
<td>ME Support Northern Ireland</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Royal Free London NHS Foundation Trust</td>
<td>Yes</td>
<td>Access to services as above; we appreciate the impact of commissioning of services; however, given the majority of patients is female, disorders such as PCOS, vulvodynia, PMT, endometriosis, occurring more commonly in patients with fatigue, call for recommendations of a joint clinic, which in itself would reduce the number of referrals to individual clinics and replications of services. We appreciate that this is stated as being outside of the scope of the guideline.</td>
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Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.

Thank you for your response.

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Thank you for your response.
<table>
<thead>
<tr>
<th>Stakeholder Group</th>
<th>Response</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stockport ME Group</td>
<td>Yes</td>
<td>We do not feel that User led groups of patients who have ME/CFS were adequately engaged with prior to the Surveillance document being written. Had this been done then the full extent of problems with the current guidelines in terms of diagnosis and recommendations of CBT involving elements of GET and GET might have led to a recommendation to update the guidelines and it certainly would have led to patient experience being more significantly referenced and articulated in the surveillance. It would have also led to the Surveillance being opened to stakeholders with ME/CFS in a more accessible way. Asking for a jargon filled 56 page document to be responded to in a very tight time limit has meant that the engagement with stakeholders (ME groups representing people with ME/CFS) is too little and too late for sufficient patient involvement in the process. People with ME are experts on their own experience of the condition and given the lack of objective tests for both ME and the effectiveness of treatments for ME being used in the research of the condition, patient experience is particularly important. This consultation has been carried out in a way that has created significant barriers and problems to ensuring that patient experience is fully captured. The narrow time window did not enable Stockport ME Group to respond as fully as we would have been able to had the Stakeholder engagement process been more accessible.</td>
</tr>
<tr>
<td>The Ehlers-Danlos Support UK</td>
<td>No response</td>
<td>Medical awareness of the symptoms and potential impact of EDS and HSD remains shockingly low, especially in primary care. Data to be published shortly evidences an average wait of over 10 years for an accurate diagnosis in adults. This denies this group of patients access to the care and services they need and puts them at a distinct disadvantage compared to patients with better recognised conditions.</td>
</tr>
<tr>
<td>The Young ME Sufferers Trust</td>
<td>Yes</td>
<td>In 2013 Health Minister Earl Howe wrote in answer to patient group queries: “The Equality Act 2010 sets out the need to treat people equally who have a protected characteristic such as a disability.” He added: “ME/chronic fatigue syndrome (CFS) falls within the definition of disability.”</td>
</tr>
</tbody>
</table>

Thank you for your response. There is a 2-week consultation with stakeholders for all surveillance reviews that are not to update proposals, in line with the guidelines manual. Consultation dates and times are posted in advance on the guideline page on the NICE website, and stakeholders are reminded by email. The 2-week consultation period is standard for surveillance reviews and there are no plans to extend this.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
It was most helpful that NICE accepted our recommendation and referred in its 2007 guideline to the desirability of children with ME maintaining contact with ‘education’ in so far as is possible, rather than ‘school’. This was important because childhood ME can cause such a degree of illness and disability that it is the biggest cause of long term sickness absence from school (in staff as well as students) first revealed by Dowsett and Colby (Dowsett EG, Colby J. Long term sickness absence due to ME/CFS in UK schools Journal of Chronic Fatigue Syndrome, 1997; 3(2): 29-42). (Commentary by Dowsett http://www.tymestrust.org/pdfs/dowsettcolby.pdf)

Nevertheless, children disabled with ME commonly suffer discrimination because doctors are uninformed regarding educational rights, and about modern educational methods (already contracted by some education authorities) that enable interactive virtual education in their homes. Being interactive, this type of education mediates against isolation and, in our experience, results not only in educational qualifications but in a substantial number of children’s health improving, eventually recovering to an extent that sustainable return to school or college is achieved. A brief insertion by NICE highlighting the existence of such services would be immensely helpful.

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<tr>
<th>University of Manchester – FINE Trial</th>
<th>No</th>
<th>No comment</th>
</tr>
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<tbody>
<tr>
<td>Welsh Association of ME &amp; CFS Support</td>
<td>No</td>
<td>No comment</td>
</tr>
</tbody>
</table>

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
### 4a Stigma and discrimination

It should be taken into account that people with ME experience a type of stigma specifically associated with this chronic illness disability. Prejudice and misunderstanding has often been spread by the British media.

We believe that several sections of the current NICE guidelines (e.g. section 1.4.5) are not entirely without merit in content, if they existed in a socio-political vacuum and were read by entirely neutral professionals. However, our healthcare professionals, DWP assessors, insurers, employers, social workers and relatives do not live in this vacuum and their actions in relation to us are influenced by the sociopolitical context of ME. Colloquially the interpretation of the NICE guidelines can be that if people with ME, including people with Severe ME, ‘think positive and exercise’, this is enough to for us to get better. As the evidence we have presented above indicates, this is not the case and can lead to negative outcomes. We suggest that the wording of the guidelines needs to explicitly acknowledge and guard against these misconceptions.

Evidence of this issue can be found in a 2015 survey by Action for ME of 850 respondents (sample included representative proportions of mild, moderate and severe ME), 97% met the threshold of difficulties with daily living which may entitle them to a social care package according to criteria in the Care Act 2014. Only 6% actually had a social care package and only 16% had had a social care assessment in last 5 years. The study investigated barriers to accessing the social care system and found:

- 40% of respondents indicated a reluctance to ask for help due to the stigma attached to the ME.
- 84% agreed that they were worried the assessor would not believe that they were genuinely disabled
- 84% agreed that they were worried that they wouldn’t be considered deserving of help or support

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
Half of the respondents also offered further evidence indicating stigma was a significant factor in avoiding social care assessments. Responses included:

“The social worker said I should go swimming every week and do more exercise, even though she could see I couldn’t even stand up without falling onto the floor and my legs were going into visible spasms on that day.”

“I’m concerned that drawing too much attention to myself might end up with me being pressurized into having inappropriate treatment or wrongly being labelled as mentally ill when I’m not.”

“I’m fed up with being judged.”

“Because of the stigma with this illness, I have little confidence and the fact that it is a fluctuating illness and it is hard to make myself clear.”

“The community service worker mistook my cognitive symptoms for depression or anxiety. She told my consultant that I was afraid of activities of daily living. It was recommended I see a psychiatrist and I was questioned under guidelines of Mental Health Act and I thought I was about to lose my freedom.”

“The social worker told me that ‘everyone gets tired’”

4b Prejudice leading to pressure to comply

Although section 1.1.1.3 of the guidelines states that patients have the right to refuse or withdraw from any component of their health care plan without affecting care or future choices about care, we do not feel this statement goes far enough to protect ME patients given our context. Patients often feel compelled to undertake treatment such as graded exercise (which, as discussed above, is inappropriate for them). As a result, patients can experience serious consequences: child protection proceedings (see input from Tymes Trust); loss of benefits; difficulties with employers and insurance providers and withdrawal of family support. The BBC Radio 4 programme ‘File on 4’ recently highlighted the discrimination children and their parents face when children get diagnosed with ME. The programme discussed how the stigma surrounding the disease meant children were not treated appropriately and that parents were falsely accused of child abuse due to poor understanding of symptoms, care and treatment by healthcare professionals and schools (Radio 4, 2017). The result of knowing that at least 193
families have been through this ordeal is that other parents feel pressured to comply with GET, even though they fear it will make their child worse.

Given the context of this discrimination, we ask that the updated NICE guidelines be made clearer to account for the limitations of the evidence, patient reports of long term relapse following graded exercise, and the importance of genuine patient choice without reprisal (section 1.1.1.3).

We have divided references into key references, which is the main evidence we wish to draw your attention to, and additional references

Key evidence Q4


Additional References Q1-4


<table>
<thead>
<tr>
<th>Reference</th>
<th>Title</th>
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<tbody>
<tr>
<td>Fulcher, KY, and White, PD (1997), Randomised controlled trial of graded exercise in patients with the chronic fatigue syndrome, BMJ, 314(7095), 1647; doi:10.1136/bmj.314.7095.1647.</td>
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</tbody>
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Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53


Morris, G, Berk, M, Carvalho, AF, Caso, JR, Sanz, Y, and Maes, M (2016), The Role of Microbiota and Intestinal Permeability in the Pathophysiology of Autoimmune and Neuroimmune Processes with an Emphasis on Inflammatory Bowel Disease Type 1 Diabetes and Chronic Fatigue Syndrome, Curr Pharm Des, 22(40), 6058-6075.


<table>
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<tr>
<th>Year</th>
<th>Citation</th>
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<table>
<thead>
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<tbody>
<tr>
<td>Twisk, FN (2015), A critical analysis of the proposal of the Institute of Medicine to replace myalgic encephalomyelitis and chronic fatigue syndrome by a new diagnostic entity called systemic exertion intolerance disease, Current Medical Research and Opinion, 31(7), 1333-1347.</td>
</tr>
<tr>
<td>Royal College of Physicians</td>
</tr>
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<td>----------------------------</td>
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</table>


Thank you for considering our response.

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53.
<table>
<thead>
<tr>
<th>RCGP</th>
<th>Yes</th>
<th>• NHS England has acknowledged that recognition of PoTS and NHS service provision is inadequate. These patients should be entitled to the same level of diagnostics and care as those with other conditions. Inclusion of screening for PoTS as part of the CFS/ME Guidelines may assist in this matter (4).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regional Public Health Agency for Northern Ireland</td>
<td>Yes</td>
<td>CFS/ME as a medical condition currently does not have any professional college or faculty that 'owns' it. This weakens its lobby and reduces it to that of patients and a small number of professionals from various backgrounds that have made it their interest. NICE needs to take care to consider this when looking for evidence, which might be harder to find and come in ways not normally considered as 'good enough'.</td>
</tr>
<tr>
<td>False Allegations Support Organisation with Parents</td>
<td>Yes</td>
<td>I take equalities to include people with limited or different physical abilities (as well as gender &amp; race equality). I think this issue is very pertinent to the issue of physical disability because I think that in many cases the wrong questions are asked and that potentially very many people with hereditary collagen deficiency conditions such as Ehlers Danlos Syndrome and Marfan Syndrome with consequent cardiovascular and orthostatic problems (causing problems of fatigue) are being</td>
</tr>
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</table>

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
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<tr>
<th>Stakeholder</th>
<th>Comment</th>
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<tbody>
<tr>
<td>Protecting Children UK</td>
<td>missed and lumped together with people with viral myalgic encephalopathy - to the detriment of both groups. People with viral encephalopathy issues may therefore be prescribed exercise programmes which may exacerbate their conditions whilst people with disabling collagen deficiency conditions and consequent cardiovascular issues may be prescribed rest which will cause de-conditioning and consequent worsening of their symptoms. I believe that it is essential to train GPs and nurse practitioners to do basic orthostatic tolerance tests on anyone presenting with symptoms of extreme ongoing fatigue so that appropriate onward referrals can be made and correct treatments prescribed - I believe that this will enhance the health and independence of a significant number of people and is therefore relevant to equalities issues.</td>
</tr>
<tr>
<td>Local ME</td>
<td>No answer</td>
</tr>
<tr>
<td>ME-Letterforce</td>
<td>No answer</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Question 4 Comment 1</th>
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<tbody>
<tr>
<td>The Surveillance consultation period was too short for chronically ill and disabled people to give an adequate reply. Our group asked for an extension of 4 weeks but were only granted 1. This is not a time-critical process and it is important that as many patients as possible are consulted so we fail to understand why a longer consultation period was not given.</td>
</tr>
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<tr>
<th>Question 4 Comment 2</th>
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<tbody>
<tr>
<td>Patient surveys and experiences are not given a high enough weighting as evidenced in the original Guideline deliberations and in the Surveillance process.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 4 Comment 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>The views of Patient Representatives in the GDG were not given enough weighting or listened to as part of the original Guideline process. Patient Reps were unable to communicate this through the process due to confidentiality clauses.</td>
</tr>
</tbody>
</table>

decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
Tanya Harrison (patient Rep) said

"As you are all now aware, I have resigned from the NICE Guideline Development Group (GDG) on ME/CFS (August 2007). I originally requested that a statement went in the guidelines "Tanya felt unable to agree with the content of these guidelines", as I felt that I could not sign up to the guidelines, but did not want to resign, as I was, and still am, willing to be part of future re.writes/redrafts, which I feel are inevitable. However, this option was not available to me, and therefore I felt that I must resign, as I could not sign up to the guidelines. I hope that you will understand that I was not able to make my decision known until today, the date of publication for the guidelines, as I have always adhered to the confidentiality that was expected from being a member of the GDG."

**Question 4 Comment 4**

Our group recommends that NICE consider the discrimination experienced by ME patients who have little or no medical care, as the current clinics are using Guidelines designed on a psycho-social model, using evidence based on papers that did not consider the Cardinal symptoms of their own disease.

See our earlier Comment 1 to question 3 of other issues of discrimination patients with ME face. The publication of the original NICE Guideline has resulted in NHS clinics that proport to treat and diagnose "CFS/ME" but in reality, discriminate against ME patients and concentrate resources on those with chronic fatigue.


| Suffolk Youth & Parent Support Group1 & Norfolk & Suffolk Service Design and Service Implementation Group2. | Yes | There is some irony in this question, given that one of the points of information that the Institute declined to provide to practitioners and patients in CG53 is that ‘ME/CFS’ is a disease that can be covered by the then Disability Discrimination Act - provisions since subsumed under the Equality Act 2010. This review appears inconsistent with other NICE consultations I have recently contributed to. And I ask NICE to conform whether it’s approach is equitable with other NICE reviews and processes?

To summarise
A review of CG53 needs to be done, to achieve compliance with and be reflective of the 2012 Health & Social Care Act, the 2003 Standards for Better Health which underpin the working practices of the CQC and their core requirements.

NICE Guidance currently fails to separate the “sheep fro the goats”; ie, true presentations of ME and CFS as opposed to patients with vague non specific fatigue. This is it’s greatest failing.

Because the current guideline and emphasis directs patient care down a vague fatigue and mental health approach, the result is that it effectively obstructs patients’ access to appropriate biological testing, treatment and support. Misdiagnosis is rife with peer 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 |

Thank you for your response.

Following further consideration of new evidence and information from stakeholders, alongside the evidence identified through the surveillance review, we have decided to fully update NICE’s guideline on Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) with a modified scope. Information obtained through the surveillance review, including feedback from stakeholders through this consultation, will be passed onto developers for consideration during the update of the guideline.
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reflective of the current debate, emerging exciting new international research findings, and state of play about the nature and optimal management of ME/CFS.

A reminder as Sir Mark suggests you use “Standards:
The Nice review needs to reflect services capacity to deliver the following;
STANDARDS FOR BETTER HEALTH
Aims (my emphasis)
7. The final but key aim of these standards is to underpin the delivery of high quality services which are fair, personal and responsive to patients’ needs and wishes, which are provided equitably and which deliver improvements in the health and well-being of the population. This aim can only be achieved if these benefits are delivered to all groups within our society. The standards must therefore be interpreted and implemented in ways which:
• Challenge discrimination
• Promote equality of access and quality of services
• Support the provision of services appropriate to individual needs, preferences and choices
• Respect and protect human rights
• Further the NHS’s reputation as a model employer
• Enable NHS organisations to contribute to economic success and community cohesion.
This spells matters out clearly.
STANDARDS FOR BETTER HEALTH require following;
How the standards framework is structured
16. The standards set out in this document are organised within seven “domains”, which are designed to cover the full spectrum of health care as defined in the Health and Social Care (Community Health and Standards) Act 2003. The domains encompass all facets of health care, including prevention, and are described in terms of outcomes. The seven domains are:
• Safety
• Clinical and Cost Effectiveness
• Governance
• Patient Focus
• Accessible and Responsive Care • Care Environment and Amenities • Public Health
It is my understanding that the guidelines will be based on, and only on, the findings of RCT and studies that tick the boxes for what the Institute considers to be ‘evidence’, according to set parameters. Is the same true of the Guideline reviews?

When the ‘CFS/ME’ guideline was being developed (2007) those of us who are aware of the immense damage that exercise (GET) causes to PwME could cite real life examples, however, ‘NICE’ were not interested in “informal” feedback from patients, support organisations and charities.

However, NHS STANDARDS FOR BETTER HEALTH require a new approach.

- Since the original CFS and ME Guideline was developed, the law regarding both Health & Social Care (2012) and government guidance on consultation has radically changed.
- The climate has changed with Expert Patient initiatives and other requirements relating to patients which must be taken into account.
- The NICE guidance and Reviews therefore must be compliant with the new legislation Health and Social Care Act domains and the CQC three important domains which are assessed by CQC.
- Patient experiences can be found in NHS local services annual change audits and in local provider patient surveys. Has NICE collated this publicly available information?
- Findings of CURRENT biomedical research studies which clearly contraindicate exercise (GET) must be evaluated.
Accountability

Care Quality Commission The Core Standards- these need to be re examined in relation to the current 2007 guidance.

What happens if it all goes wrong i.e. the guidance approach is suggested or proven to result in harm- who, (if anyone) will be deemed at fault & accountable?

A service Provider will follow NICE or interpret the guidance. If that guidance is fundamentally flawed and not fit for purpose- harm can be done. Who is responsible? The provider or NICE?

“There is ample evidence of the guidance being used and resulting in harm. If NICE had collated patient experience feedback from Local Providers Annual Change Audits, which are a contractual Key Performance Indicators and Contractual obligation, they would have a clearer idea of where the Guidelines are failing and would, via review, be able to start to put matters right. Whilst this may not form part of the “formal” evidence base outlined in the Parameter used by NICE, however, under the requirements of the 2012 Health & Social Care Act,

STANDARDS FOR BETTER HEALTH the following - • Safety • Clinical and Cost Effectiveness • Governance • Patient Focus • Accessible and Responsive Care • Care Environment and Amenities • Public Health, cannot be ignored or swept under the carpet.

Comment from Dr Charles Shepherd, ME Association: Written question submitted to Professor Baker prior to the 2014 Forward ME meeting:

“Given the fact that ME/CFS covers a wide variety of clinical presentations and disease pathways, and that patient evidence consistently indicates that the majority of people find that CBT is ineffective; around 50% report that GET makes their condition worse; and over 90% find that pacing is the safest and most effective form of management, why does NICE continue to recommend the use of CBT and GET for everyone with mild to moderate ME/CFS?

“And why does the NICE guideline fail to provide any information or guidance on the management of a number of very disabling symptoms and problems associated with autonomic nervous system dysfunction – neurally mediated hypotension and POTS (postural orthostatic tachycardia syndrome) in particular?

“This evidence, along with other evidence submitted during the recent consultation process on the proposal to place the NICE guideline on ME/CFS in the new static list, indicate that there is a need to review and revise a NICE guideline that was signed off nearly seven years ago.”

Dr Charles Shepherd
Hon Medical Adviser, ME Association

This was an extremely informative meeting with Professor Mark Baker from the National Institute for Health and Clinical Excellence (NICE) – he is their Director of the Centre for Clinical Practice.

As can be seen from the Minutes, Professor Baker accepts that the NICE guideline on ME/CFS is no longer meeting the needs of people with ME/CFS and it fails to take proper account of the wide variety of clinical presentations and disease pathways that come under the ME/CFS umbrella.

Professor Mark Baker, NICE

2.1 The Chairman introduced Prof Baker who explained he had been in post for about two years. The Professor said he would start with an explanation of the process by which subjects come before NICE. Originally they had just responded to whoever wanted guidance. Then around 2005-6 a formal process of topic selection, with specialist panels, was set up. That process was changed around the end of 2010 when the man political parties preferred “standards” to guidelines in the NHS. In March 2012 a Library of Quality Standards Topics was established; it included a number of NICE guidelines but ME/CFS was not among them and he did not know why. It was not feasible to update or change guidelines not in the Library until at least 2017. The Library was now the responsibility of NHS England, not of the Department of Health.
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Woefully inadequate and sometimes a travesty of Justice - FII cases locally.

30% of patients are regarded as Severely Affected and effectively have no care - being lost to the system.
Unfortunately, it was stated above that NICE no longer decides which guidelines they are going to tackle afresh. This decision is now made by NHS England.

1. Who do I need to copy this into at NHS England?
2. Will the urgent need for a review of this outdated clinical guideline be raised once again with NHS England?
3. What was the response to the following letter - Communication with NICE about the revision of the Clinical Guideline 53 Margaret Williams 12th March 2017 to Sir Mark Baker? [Link](http://www.margaretwilliams.me/2017/open-memo-to-nice.pdf)
4. Please note, NHS Suffolk Commissioning, with whom we have been working with for 10 years must be commended for their robust adherence to the NHS standards of;
   - Promoting attempts to provide equality of access and quality of services
   - Supporting the provision of services appropriate to individual needs, preferences and choices
   - Respecting and protect human rights of their ME and CFS patients.
   - Most of all they must be commended for having regard to NICE Guidance but rejecting aspects of it in favour of the International Consensus Criterial. This has led to a new service specification and service development which is supported by patients and may better meet their specific needs in the future.

| Appendix C: stakeholder consultation comments table for 10-year surveillance of – Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53 | 209 of 209 |