Evidence prioritisation feedback form

Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) (2007) NICE guideline CG53

Please complete this document and return to [NICE employee] by Wednesday 14 June.

10-year surveillance review

The NICE guideline surveillance team has examined new evidence to determine whether the guideline should be updated. This evidence has been gathered by:

A search for evidence (1 August 2010 to 3 January 2017) published since the 3-year surveillance decision in 2011 (no reviews took place since then as the guideline has been on the static list).

A questionnaire circulated to topic experts.

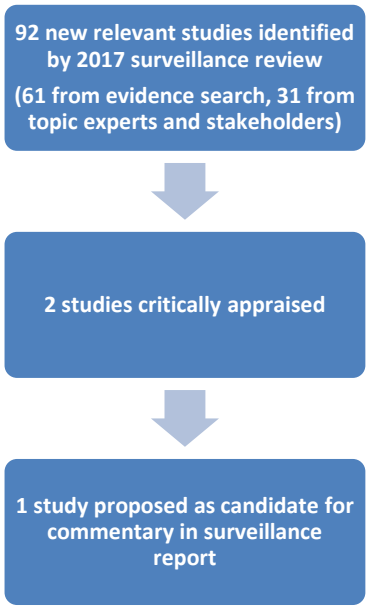
For full details of the methods and processes used in guideline surveillance see chapter 13 of 'Developing NICE guidelines: the manual'.

Previous surveillance reviews

3-year surveillance review (2011) – no update.

2014 static list review – place on static list.

Evidence selection flowchart



Including studies in the surveillance review

This is a 10-year surveillance review which would normally be limited to search for systematic reviews only. However, because many enquiries had been received about this guideline, particularly in relation to the PACE trial and diagnostic criteria for CFS/ME, the static list

review of NICE guideline CG53 was brought forward from its original schedule of 2019 for a full surveillance review. Therefore a 4/8 year surveillance process was used for the search strategy and so RCTs and systematic reviews were included. Other evidence types than RCTs and systematic reviews are also included if they were notified to us by topic experts – as long as the evidence falls within the scope of the original guideline.

Studies were not summarised if they relate to interventions or diagnostic strategies or prognostic tools that NICE has recently produced or is developing a publication on the same indication including:

- technology appraisal guidance,
- diagnostics guidance,
- medical technologies guidance or
- Medicines and Prescribing Programme evidence summary.

We inform the relevant NICE teams about any relevant new evidence identified in the surveillance review.

Selecting studies for commentary

2 studies were selected for consideration for individual commentary using the following criteria:

- Studies that reinforce or strengthen existing recommendations
- Studies that might impact on current guideline recommendations in the future although evidence is insufficient to impact on guidance at present
- Studies on a new intervention, diagnostic strategy, prognostic tool for which the evidence is insufficient to impact on guidance at present.
- Studies partly addressing a research recommendation although evidence is insufficient to impact on guidance at present?
- Studies highlighted through the topic expert questionnaire.
- Studies that were mentioned in the guideline as being of relevance but ongoing at the time of guideline development.

The surveillance report may contain detailed commentary on **up to 3 articles** felt to be of particular interest to this topic.

Your input will help us to finalise which studies we should write about in detail in the surveillance report.

Evidence prioritisation

The 2 studies that were critically appraised are presented in the table below.

We have matched the articles to the most applicable review question in the guideline. The numbers correspond to the order that they appear in the summary of new evidence document.

The NICE proposal for each study in the table below is either:

- 'Proposed for full commentary' – extended commentary will be written for the surveillance report.
- 'Not proposed for full commentary' – extended commentary will not be written for the surveillance report, but the article will still be included summary of new evidence and informs the overall surveillance decision.

Please bear in mind that only up to **3 studies** can be selected for commentary.

After critical appraisal, 1 study was proposed for full commentary in the surveillance report. Completed critical appraisal forms for each study are included at the end of the document.

Please add your comments on each study to the table based on the information in the table, the full text, the critical appraisal, and your expert opinion, knowledge and experience.

Please also consider:

- Should we write a detailed commentary on this article?
- Does the study have an impact on practice, implementation or current guideline recommendations?
- Have we overlooked any important pieces of evidence or key trials?
- Are there any equalities issues?[1]

Topic expert feedback table

Topic expert feedback on articles proposed for commentary

Article	NICE proposal	Topic expert comments
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?**	
Nijhof et al. (2012) Effectiveness of internet-based cognitive behavioural treatment for adolescents with chronic fatigue syndrome (FITNET): a randomised controlled	**Proposed for full commentary** CBT is already recommended by CG53 and this study shows it can be delivered via the internet, indicating an alternative mode of delivery for this treatment for this age group. Although the study was from the Netherlands, a UK trial is underway.	**AGREE** / ~~**DISAGREE**~~ (Delete as appropriate) **REASONS** My interpretation of the results of this trial is very different. The trial compared internet delivered psychoeducation plus cognitive behaviour therapy with an e-therapist plus a school mentor versus usual care

[1] The 2010 Equality Act prohibits discrimination, harassment, and victimisation in relation to people who share the protected characteristics of age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex, and sexual orientation. NICE needs to have due regard to the need to eliminate discrimination, advance equality of opportunity, and foster good relations in relation to people who share the protected characteristics, apart from that of marriage and civil partnership.
Consideration of equalities includes interventions unsuitable for a population who share a protected characteristic. For example, an alarm for bed-wetting in children may not be useful for children with hearing impairment. Another possible consideration is whether a study excludes people who share a protected characteristic.

trial. Lancet 379: 1412–8 Link to critical appraisal	There were some issues with the study (blinding was not possible due to nature of interventions, and usual care varied because the quality and quantity of CBT differed according to local availability and was often combined with other treatments such as GET). These issues would be discussed in full in the commentary.	following NICE Guidelines in CG53 offering cognitive behaviour therapy of graded exercise therapy without school involvement. In this small RCT, the performance of routinely delivered CBT or graded exercise was poor with only 5/63 (8%) recovered at 6 months and only 50% attending school. We know very little about the quality of care of this CBT or GET or even if there was any contact with the school in the usual care arm but presumably not. In the FITNET group, we know that the CBT was quite good quality but we know very little about the actual use or role of the school mentor. Without additional information, which is promised in the article in a subsequent publication that would be important to get hold of, it is difficult to be sure about the final conclusions of the study. However, on the face of it and given the results of other RCTs, it suggests that young people should receive a school mentor together with CBT and GET, which can be successfully delivered by the internet, not just CBT or GET alone. That means the current recommendations in CG53 for young people will need to be revised.
Beasant et al. (2014) Adolescents and mothers value referral to a specialist service for chronic fatigue syndrome or myalgic encephalopathy (CFS/ME). Prim Health Care Res Dev. 15: 134-42 Link to critical appraisal	**Not proposed for full commentary** Referral to specialist care is recommended by CG53, and this study shows that adolescents and their mothers value referral to a specialist service. However there were several issues with the study (small sample n=25, did not include severe CFS, study was nested within a feasibility study, sampling was based on judgement, variability in the timepoints when interviews were conducted, interview protocols evolved over time). These issues may limit the strength of the study findings and therefore a commentary may not be warranted on this evidence.	**AGREE** / ~~**DISAGREE**~~ (Delete as appropriate) **REASONS** I don't think the study adds much to the already recognised issues that it is difficult to get help with CFS with barriers at a number of different levels. Many of these have been described before e.g. Chew-Graham et al (2010) which is a better paper. The problem here is the selection of people in a RCT. If they had a good experience of the RCT they are bound to have a favourable view of the clinic that is conducting the RCT in contrast to what happened before. However, any RCT that is well-conducted is very different from what may happen in usual care. Trial teams go out of their way to accommodate people participating in it; usual care often has a much more take it or leave it approach to care. Such accommodation from enthusiastic health professional is likely to contrast

		well with other types of care. In my experience care from specialist services is not always great particularly if they tell people they have an incurable condition that is unlikely to improve as some do. This sometimes removes hope from the patient who I then have to see to treat their depression precipitated by the specialist CFS/ME clinic. Some of what you identify as methodological weaknesses would be in my eyes methodological strengths for this type of thematic analysis. A thematic approach is by definition highly inductive as opposed to a framework approach and so it would be a matter of concern if the interview schedule did not evolve and adapt as interviews were conducted. Adding two extra questions to the interview schedule is exactly what I would expect to see and is not a methodological weakness whereas it might well be in a framework analysis (unless the data showed that the framework from previous research was not applicable in this situation). Rightly the authors took a thematic approach because there was insufficient knowledge from previous studies to apply a framework analysis. The other major weakness in my eyes, like a lot of acceptability studies being currently published, is the absence of data from those who refused to take part in the study and if these could not be obtained, from their referrers. Studying acceptability without interviewing people who were the most dissatisfied or disinterested seems to me to be fundamentally flawed. In this instance though the problem is confounded by participation in a RCT. The paper is about the acceptability among those who gave consent of taking part in a randomised controlled trial run through a specialist clinic, not the acceptability of the clinic itself. In this sense the study is quite misleading. [Please provide your reasons]
Additional articles for NICE's attention		

[Please add details of any other articles that you strongly feel should have a full commentary in the surveillance report]

[Please provide reasons for your suggestions.]

Critical appraisal of selected studies

Beasant et al. (2014) Adolescents and mothers value referral to a specialist service for chronic fatigue syndrome or myalgic encephalopathy (CFS/ME). Prim Health Care Res Dev. 15: 134-42

	Yes	Unclear	Partially reported	No
Was there a clear statement of aims of the research?	✓			
Is a qualitative methodology appropriate? Consider if the research seeks to interpret actions or subjective experiences of the participants	✓			
Was the research design appropriate to address the aims of the research?	✓			
Was the recruitment appropriate to the aims of the research?		✓1		
Was the data collected in a way that addressed the research issue? Consider if the researcher has discussed saturation of data, if the methods for data collection were clear and justified.		✓2		
Has the relationship between researcher and participants been adequately considered? Consider if the researcher looked at their own potential biases in the developments of the questions and data collection, and their role and adaptability during the study.		✓3		
Have ethical issues been considered?	✓			
Was the analysis sufficiently rigorous? For example, if the data was sufficient to support the findings, if it was explained why the specific examples were used from the original data, how much contradictory data was considered, if the researcher looked at their own potential biases during analysis and data selection, if there were clear themes if a thematic analysis was used.		✓4		
Is there a clear statement of findings?	✓			

Footnotes: 1. This study was nested within another study and so was not specifically designed to address this research question, and also recruitment to the primary study will have influenced inclusion into this sub-study. Sampling was 'purposive' (i.e. researcher relies on their own judgment to choose participants) – it was stated that this was to ensure an appropriate cross-section, though this technique can introduce bias. People with severe CFS were excluded from the study. Also only mothers (not fathers) were interviewed. 2. Interviews were done at 3 possible timepoints: after initial assessment, after randomisation, and after intervention. For adolescents, the interviews were not evenly spread across these timepoints and none happened at initial assessment – no explanation was provided for this. 3. The study used a constant comparative method (simultaneously coding and analysing as the data is gathered) and stated that this led to 2 additional prompts being added to the interview schedule. It was also stated that data analysis was an ongoing and iterative process informing further sampling and data collection. This may have introduced some bias as the interviews went on. 4. Interviews were done at 3 possible timepoints: after initial assessment, after randomisation, and after intervention. No sub-analysis of these timepoints took place, but receiving the intervention may have affected responses (e.g. the study notes that some adolescents did not like the fact that the treatment approach limited activity). Five mothers were interviewed at all 3 timepoints to form case studies, but the progression of these women was not further discussed.

Applicability to guideline	
Were all important outcomes considered? Consider whether there is other information you would like to have seen.	The effectiveness of the interventions analysed by the primary study (of which this was a substudy) may have affected how participants value specialist referral, but this was not discussed.
How do the results fit with evidence reviewed for the guideline? For example: exact population or outcomes, or suggests a need to change the question.	The study is relevant to CG53 which recommends referral to specialist care. The study only included people with mild to moderate CFS whereas the scope of CG53 also includes severe CFS.

Nijhof et al. (2012) Effectiveness of internet-based cognitive behavioural treatment for adolescents with chronic fatigue syndrome (FITNET): a randomised controlled trial. Lancet 379: 1412–8

(Note: The study protocol is described in detail in Nijhof et al. [2011] Fatigue In Teenagers on the interNET – The FITNET Trial. A randomized clinical trial of web-based cognitive behavioural therapy for adolescents with chronic fatigue syndrome: study protocol)

	Low	Unclear	High
Study methodology			
Random sequence generation Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.	✓		

Allocation concealment Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.	✓		
Blinding of participants and personnel Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.			✓
Blinding of outcome assessment Detection bias due to knowledge of the allocated interventions by outcome assessors.	✓		
Incomplete outcome data Attrition bias due to amount, nature or handling of incomplete outcome data.	✓		
Selective reporting Reporting bias due to selective outcome reporting.	✓		
Other bias Bias due to problems not covered elsewhere in the table.			✓

Overall concerns	Support for judgement
Mainly low (though some concerns over blinding, and variability of usual care)	High risk aspects: Blinding of participants and personnel: Blinding of participants and personnel not possible due to nature of interventions in active and control groups. Other bias: Detailed data about the specific interventions in the usual care group could not be provided because the quality and quantity of CBT differed according to local availability and was often combined with other treatments such as GET. Physicians referring patients to the study seemed to find the diagnosis of CFS difficult (the study authors noted high numbers of other primary diagnoses and patients who did not meet CDC criteria). Low risk aspects: Random sequence generation/Allocation concealment: The concealed random allocation sequence was computer-generated with a block size of six by a data management centre. Blinding of outcome assessment: Primary outcomes were assessed with computerised questionnaires, and the main outcome (school attendance) was checked and double checked by the investigators, parents, teachers, and therapists. Incomplete outcome data: Loss to follow up was relatively low (8/135), fully described, and similar (4 patients each) between groups. The baseline characteristics of these patients did not differ from those who adhered to the study schedule. Analysis was intention-to-treat. Selective reporting: Study protocol was clearly defined and all outcomes reported.

Applicability to guideline	
Were all important outcomes considered? Consider whether there is other information you would like to have seen.	Fatigue, physical functioning and school attendance are key outcomes and were considered by the NICE guideline. FITNET has not been trialled in the UK (this study was in the Netherlands) and there is currently no evidence on cost effectiveness. A UK trial (FITNET-NHS) is recruiting but results will not be available for 5 years.
How do the results fit with evidence reviewed for the guideline? For example: exact population or outcomes, or suggests a need to change the question.	CDC criteria for CFS were used to recruit participants, which has some overlap with but is not identical to the NICE diagnostic criteria. CBT is already recommended by CG53 and this study shows it can be delivered via the internet, indicating an alternative mode of delivery for this treatment for this age group.