

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

**[J] Monitoring and reviewing people with  
ME/CFS**

*NICE guideline NG201*

*Evidence reviews underpinning recommendations and research  
recommendations in the NICE guideline*

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*Final*

*These evidence reviews were developed  
by the National Guideline Centre*



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# 1 Monitoring and Review

## 1.1 Review question

What is the most clinically and cost-effective method of monitoring and reviewing people with ME/CFS?

### 1.1.1 Introduction

ME/CFS is a chronic complex, multisystem condition. Symptoms and clinical course can fluctuate with or without treatment interventions, making it difficult to have a fixed regime for the review of people with the illness. There is no established frequency, methodology or recording of monitoring or reviewing people with ME/CFS. Furthermore, the availability of ME/CFS specialist services in England and Wales means that review protocols are not consistent in the two countries. There is also a lack of consistency in recommendations for the diagnosis and management of the condition across European countries. Currently people are seen in ME/CFS specialist services for limited periods of time (usually 6 months to a year) and then discharged back to primary care. There is no clear guidance for primary care on follow up or monitoring. The current opportunistic approach for people with ME/CFS increases the risk that people will not be seen and in particular, that people most severely affected by ME/CFS will not be reviewed.

### 1.1.2 Summary of the protocol

For full details see the review protocol in Appendix A.

**Table 1: PICO characteristics of review question**

<b>Population</b>	Inclusion: Adults, children and young people who are diagnosed as having ME/CFS. Exclusion: Adults, children and young people with suspected ME/CFS
<b>Interventions and comparisons</b>	Any monitoring or reviewing strategies. These can be compared to each other or to a suitable comparator (i.e. no monitoring/review).
<b>Outcomes</b>	Longest follow up available:  CRITICAL OUTCOMES: <ul style="list-style-type: none"> <li>• Quality of life (any validated scales, for example, EQ-5D, SF-36)</li> <li>• Pain (VAS/NRS)</li> <li>• Fatigue/fatigability (any validated scales)</li> <li>• Physical functioning / exercise tolerance / ADL (any validated scales)</li> <li>• Cognitive functioning (any validated scales)</li> <li>• Sleep quality (any validated scales)</li> <li>• Adverse effects (any reported by the studies)</li> <li>• Psychological outcomes</li> <li>• Patient satisfaction</li> <li>• Benefit status/employment/school attendance/school absences</li> <li>• Update of diagnostic status</li> <li>• Comorbidities</li> <li>• Activity monitoring</li> <li>• Post exertional Malaise (PEM)/Post exertional symptom exacerbation (PESE)</li> </ul>
<b>Study design</b>	<ul style="list-style-type: none"> <li>• Systematic reviews</li> <li>• RCTs</li> </ul>

Non-randomised studies will be excluded unless no RCTs are found. If no RCTs are found non-randomised comparative trials will be considered (including prospective cohort studies) if they have attempted to detect, and if necessary adjust for, confounding.

### 1.1.3 Methods and process

This evidence review was developed using the methods and process described in [Developing NICE guidelines: the manual](#). Methods specific to this review question are described in the review protocol in appendix A and the methods document.

Declarations of interest were recorded according to [NICE's conflicts of interest policy](#).

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## **1.1.4 Effectiveness evidence**

### **1.1.4.1 Included studies**

A search was conducted for randomised trials and non-randomised comparative studies comparing the effectiveness of monitoring and review strategies versus each other or a suitable comparator (that is, no monitoring and review).

No relevant studies were identified.

### **1.1.4.2 Excluded studies**

See the excluded studies list in Appendix L.

## **1.1.5 Summary of studies included in the effectiveness evidence**

No relevant studies were identified.

## **1.1.6 Summary of the effectiveness evidence**

No evidence was identified.

## **1.1.7 Call for evidence**

See the methods document for detail on the process and methods for the call for evidence.

The committee identified monitoring and review as an area of the scope with a lack of published evidence and proposed a call for evidence to identify any relevant literature not identified in the searches. Submissions were received from 42 separate organisations or individuals, consisting of 508 reports or references to publications (after removal of duplicates). Of the submissions considered to be potentially relevant to this review question, all were excluded. For details why submitted evidence was not relevant see call for evidence excluded studies list in Appendix L.

## **1.1.8 Economic evidence**

### **1.1.8.1 Included studies**

No health economic studies were included.

### **1.1.8.2 Excluded studies**

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix I.

## **1.1.9 Economic model**

This area was highlighted as a potential priority for new cost-effectiveness analysis. However, no clinical evidence was found on which to base a model.

## **1.1.10 Evidence statements**

### **1.1.10.1 Effectiveness**

- No relevant published evidence was identified.

### **1.1.10.2 Economic**

- No relevant economic evaluations were identified.

## **1.2 The committee's discussion and interpretation of the evidence**

The committee discussed this evidence with the findings from the reviews on Information for people with ME/CFS and their families and carers (report A), Information and Support for health and social care professionals (report B), access to care (report C), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). Where relevant, this is noted.

### **1.2.1 The outcomes that matter most**

Quality of life, pain, fatigue/fatigability, physical functioning, cognitive functioning, sleep quality, adverse effects, psychological outcomes, patient satisfaction, benefit status, employment and educational attendance, diagnostic status, co-morbidities, activity monitoring and post exertional malaise were all agreed by the committee to be critical outcomes for decision making.

These outcomes reflect the direct impact ME/CFS symptoms have on a person (specifically levels of pain, fatigue, physical functioning cognitive functioning, sleep quality, psychological outcomes, post exertional malaise (PEM) , and in turn the impact on quality of life (specifically benefit status, employment and educational attendance).

The impact of the monitoring and review strategies can be measured by the outcomes listed above, if a strategy is successful symptoms would be managed appropriately and the impact on a person's life would be minimised compared to a strategy (including no review) that did not identify worsening symptoms.

The effectiveness of a strategy is also reflected in these outcomes: diagnostic status, co-morbidity identification, adverse effects and patient satisfaction. Diagnostic status and



comorbidity review and identification are key to ensuring that someone is receiving the correct intervention and management for their condition. If this is not picked up in a review this would have a detrimental impact on the person.

Any intervention for people with ME/CFS requiring contact with health and social care services is likely to affect their physical and emotional energy levels. It is key that any strategy should not make people with ME/CFS worse and strategies should ensure that they are able to access the service successfully. Measuring adverse effects and patient satisfaction address these concerns.

The committee acknowledged the lack of existing objective outcome measures of effectiveness of interventions for ME/CFS and the limitations of subjective measures (see Professor Edwards expert testimony – Appendix 3: Expert testimonies). Only validated outcome measurement scales were included in the evidence review.

### **1.2.2 The quality of the evidence**

No evidence was identified in the review or the call for evidence.

### **1.2.3 Benefits and harms**

The committee acknowledged there is a lack of evidence on monitoring and review strategies. However, the area is important to people with ME/CFS and providing guidance on monitoring and review is likely to improve the care delivered to people with ME/CFS. The committee made consensus recommendations informed by their own experience and evidence in other areas of the guideline.

Stakeholders in the scoping consultation highlighted that people with ME/CFS need to have regular monitoring and scheduled reviews of their health like all other people with a long term condition. This was described as an area of care that is inadequate and neglected in people with ME/CFS, people are lost to follow-up and do not receive appropriate support and care.

The committee noted that people with ME/CFS report little or no follow up care, monitoring or scheduled reviews. This is reflected in Evidence review C: Access to care and the reports on children and young people with ME/CFS (Appendix 1: Children and Young people), and people with severe ME/CFS (Appendix 2: People with severe ME/CFS). The majority of respondents with severe ME/CFS (41/60) reported not having any regular monitoring by any healthcare profession and 92% (55/60) have not had ongoing medical support for an illness (related or not related to ME/CFS). Poor experience of health and social care and lack of trust in health and social care services has resulted in people with ME/CFS not engaging with services and not receiving appropriate care or follow-up (see Evidence review C: Access to care).

The committee emphasised that inadequate or inappropriate follow up and review impacts not only on care related to ME/CFS but screening and assessment for other conditions and preventative care. This has the potential consequence of worsening of symptoms and overall deterioration in health.

### **Principles of monitoring and review**

The committee agreed that although all adults with ME/CFS should be seen by specialist services initially to confirm diagnosis and the development of a personalised care and support plan, most will be primarily monitored and reviewed in primary care and this was reflected in the recommendations (section 1.15 Review in primary care). The committee noted that healthcare professionals reported a lack of confidence and ability to manage people with ME/CFS (see Evidence review B: Information for health and social care professionals and Dr Muirhead's related expert testimony in appendix 3), to address this they recommended training in this area but also noted that within primary care settings where

people with ME/CFS are not commonly seen that care across a primary care network might be appropriate.

The committee agreed a copy of the care and support plan and clinical communications from the ME/CFS specialist team, including (if relevant) discharge letters should be sent to the person's GP. These should be comprehensive and have a detailed plan for monitoring and review in primary care. Specialist input may be needed for some people on an ongoing basis, or intermittently, but the committee are aware of the significant delays that people can experience in accessing specialist services after re-referral from primary services.

The committee noted that written assessments, and reassessments, are important for accessing disability support. A scheduled review with a healthcare professional is an opportunity to provide people with ME/CFS medical evidence of disability for the purpose of claiming benefits and accessing support. Access to written assessments by healthcare professionals is essential in supporting communication between educational providers and a child or young person's family. Evidence from assessments increases understanding of the child or young person's capabilities and provides information on adjustments to help them stay in education. It is also important in providing information to a local authority about why a child or young person may have reduced or no school attendance.

The committee noted as with any part of providing care for people with ME/CFS it is vital to consider and discuss with the person the most appropriate way for them to participate in a review of their care. The ME/CFS population is underserved by health and social care services and this is explored in Evidence review C: Access to care and information and Evidence review A: Information and support for people with ME/CFS. The committee have made recommendations on accessing services (see section 1.3 of the guideline) and providing information for people with ME/CFS (see section 1.4 of the guideline).

The committee noted that review of care may be required by more than one professional depending on the person's situation, for example someone with severe or very severe ME/CFS and who is immobile will need assessments for contractures, and pressure ulcers as well as other more general aspects of review.

The committee considered that a scheduled review alongside advice on self-management and advice on who to contact in periods of worsening health could help people with ME/CFS to feel more supported and able to better self-manage in between reviews.

### **Review process**

The committee considered that adults with ME/CFS would benefit from having a review of all aspects of their care at least annually. They acknowledged that not everyone might accept this and the need for an annual review will depend on the person's circumstances. Some people may not accept an annual review in primary care for various reasons, including involvement of secondary care services and attendance at other reviews or that the risk from the interaction is too great but the committee agreed it was important that people with ME/CFS were offered the opportunity to have care related to their ME/CFS reviewed at least once a year in line with other long term conditions.

The committee were clear that scheduled reviews (for both adults and children and young people) do not override the need for regular monitoring of symptoms and additional reviews in response to changing needs or episodes of acute illness. ME/CFS is a fluctuating medical condition that affects each person differently and can vary in symptom presentation and severity during the course of a day, week or longer. The impact of fluctuations can vary widely and can range from being severely debilitating to people being able to carry out most aspects of daily living. Additional monitoring and reviews may be needed for people with severe or very severe ME/CFS.

The committee added specific examples to the recommendations for children and young people. The committee discussed the needs of children and young people with ME/CFS

recognising that additional scheduled reviews may be necessary. They noted that when children and young people reach developmental milestones the understanding of their condition and management changes. During significant life changes (for example, school and college transitions, exam periods) more emotional and practical support may be required. After considering this the committee recommended that children and young people are offered a review of their care at least every six months.

The committee members working with children and young people with ME/CFS agreed that the process for monitoring and review is different from adults and needs to address the changing needs of children and young people as they develop. Supportive models of care, with primary care working alongside a specialist centre was described as one model of care that worked well. The committee members agreed that scheduled reviews for children and young people should be carried out by or overseen by a paediatrician with expertise in ME/CFS.

With particular reference to scheduled reviews, the committee observed that healthcare professionals should understand they are unlikely to see people at their worst because of the debilitating impact of their symptoms. These may prevent people from leaving their home, and if they have cognitive difficulties they may wait until they are able to speak and explain clearly before contacting services. Contacting services can cause symptoms to worsen, and people may not have the energy to expend on communication even when health or social care professionals are receptive. They may not contact professionals once they have improved because of the risk of making their symptoms worse. A comment in the report on People with severe ME/CFS (Appendix 2: People with severe ME/CFS) illustrates this: “any doctor visit makes me ill (even a home visit), so it is only worthwhile for a specific purpose.”

### **Content of a scheduled review**

The committee reflected on the evidence (see Evidence review B: Information for health and social care professionals and Dr Muirhead’s related expert testimony in appendix 3) that health care professionals lack the knowledge and training to confidently manage the care of people with ME/CFS and agreed to provide guidance on areas that should be considered during a scheduled review. The committee considered this could also be a useful resource for carers and families when monitoring a person’s symptoms and health between scheduled reviews (see evidence report A: information for people with ME/CFS).

The committee were hesitant to recommend specific tools or checklists, as evidence for their use in the monitoring and review of people with ME/CFS has not been reviewed. They noted there are scales being developed to use with people with ME/CFS to evaluate symptoms.

The committee agreed that as a minimum providing guidance of areas to assess would ensure that relevant topics are discussed with people with ME/CFS. The committee considered this guidance works best as a framework. A list could make a consultation constrained and rigid and not responsive to the person and their needs. A list that takes a long time to complete may be counterproductive, people with ME/CFS may find the time and energy to complete a long assessment prohibitive and even damaging to their health. In addition, the committee were aware that primary care consultation appointments are commonly limited to 10 minutes and any assessment has to be realistic within these time frames.

The committee were keen to reinforce that any review of care should be personalised and take into account the person’s own experience of ME/CFS. The committee observed it was important that any review or assessment should not be done in isolation and there should be access to the person’s care and support plan and any related clinical communications from their ME/CFS specialised team this should be reviewed with the person considering the assessment.

The committee used their experience of undertaking assessments and reviews to recommend areas for discussion under the following headings.

### **Current condition and self-management**

People should be asked about changes in their condition and the impact of any changes including what can and cannot be achieved. This is important to assess if someone has experienced any flare ups or relapses and if their condition is worsening impacting on their life. It is important to look at any self-management strategies, in particular those for energy management to see if the strategies are effective or need revising.

### **Symptoms**

As well as asking about someone's current condition the committee considered it was important to ask directly about current symptoms and if these had changed or if any new ones had developed. Then the current management of symptoms should be assessed to see if any changes are needed. The committee also considered that it is important to assess if any new symptoms or change in symptoms have been attributed to ME/CFS and evaluate if these need further investigation for other causes and conditions.

### **Current support**

The committee noted that when people are asked how they are managing, they may respond they are managing well, for example carrying out activities of daily living, but not explain that these are only possible with support from family members. The committee considered this was particularly relevant in children and young people that may require considerable support from their parents but need further questioning to assess accurately how they are managing. This is important in identifying how much support a family may need. The committee were aware that the level of care provided by family members is often unrecognised or are they seen as partners in the healthcare team.

### **Psychological, emotional and social wellbeing**

The committee considered that as part of any assessment someone should be asked about their psychological, emotional and social wellbeing and the impact of ME/CFS on their lives.

### **Any future plans**

People should be asked if they are considering any changes in their lives, or there are any expected challenges anticipated. This can support effective planning with the aim of preventing any flare ups and relapses.

The committee discussed how other areas of health can be forgotten when reviewing someone with ME/CS. Aspects of care such as bone health and skin care may be neglected if there is a focus on specific disease processes only. This is particularly pertinent to people with ME/CFS and reduced mobility who should be assessed for osteoporosis, pressure sores and relevant NICE guidelines are referenced in the recommendations.

In addition to this list the committee wanted to raise awareness that if the scheduled review identified any issues for concern related to a person's ME/CFS then a referral to their contact in their ME/CFS specialist team should be made. The committee noted that some of the symptoms of ME/CFS are similar to other those in other conditions and can be erroneously put down to ME/CFS (for example, dizziness). They were aware of conditions that had been undiagnosed or misdiagnosed and as a consequence treatment had been neglected causing harm. The committee made a recommendation in the suspecting ME/CFS section of the guideline raising the awareness of the possibility of other conditions. The committee made a similar recommendation here to remind health care professionals to refer any issues identified in the scheduled review to appropriate specialists for evaluation.

#### **1.2.4 Cost effectiveness and resource use**

No economic evidence on monitoring and reviewing people with ME/CFS was found.

There was no quantitative evidence for the frequency of review and so cost effectiveness is uncertain.

ME/CFS is often a fluctuating condition and the impact on quality of life is considerable.<sup>154</sup> In the committee's experience and in line with the qualitative evidence, a lack of monitoring can be a barrier to the effective management of ME/CFS. Therefore, the committee agreed that offering follow up yearly for adults and twice yearly for children would be important for assessing worsening or changing of symptoms and modifying the patients' care plan and would be commensurate with other long-term conditions.

An analysis of general practice records found that people with ME/CFS have an average of 7 GP consultations a year,<sup>97</sup> so these recommendations are unlikely to have a substantial resource impact. However, the qualitative evidence in this guideline suggests that some people with ME/CFS, including those with severe or very severe ME/CFS, do not get a clinical review routinely, so for some this will be a change in practice.

The committee decided that it would be helpful to provide guidance on topics that may need review for people with ME/CFS.

# Appendices

## Appendix A Review protocol

**Table 2: Review protocol for monitoring and review**

ID	Field	Content
	Scope	Monitoring and review
	Draft review questions	What is the most clinically and cost-effective method of reviewing people with ME/CFS? What is the most clinically and cost-effective method of monitoring people with ME/CFS?
0.	PROSPERO registration number	-
1.	Review title	What is the most clinically and cost-effective method of monitoring/reviewing people with ME/CFS?
2.	Review question	What is the most clinically and cost-effective method of monitoring/reviewing people with ME/CFS?
3.	Objective	To identify the most clinically and cost effective form of monitoring/reviewing to improve outcomes in adults and children with a diagnosis of ME/CFS.
4.	Searches	The following databases will be searched: <ul style="list-style-type: none"> <li>• Cochrane Central Register of Controlled Trials (CENTRAL)</li> <li>• Cochrane Database of Systematic Reviews (CDSR)</li> <li>• Embase</li> </ul>

		<ul style="list-style-type: none"> <li>• MEDLINE</li> <li>• Cinahl</li> </ul> <p>Searches will be restricted by:</p> <ul style="list-style-type: none"> <li>• English language studies</li> <li>• Human studies</li> <li>• Letters and comments are excluded.</li> </ul> <p>Other searches:</p> <ul style="list-style-type: none"> <li>• Inclusion lists of relevant systematic reviews will be checked by the reviewer.</li> </ul> <p>The searches may be re-run 6 weeks before final committee meeting and further studies retrieved for inclusion if relevant.</p> <p>The full search strategies will be published in the final review.</p>
5.	Condition or domain being studied	ME / CFS
6.	Population	<p>Inclusion: Adults, children and young people who are diagnosed as having ME/CFS.</p> <p>Exclusion: Adults, children and young people with suspected ME/CFS</p>
7.	Intervention/Exposure/Test	

8.	Comparator/Reference standard/Confounding factors	Any monitoring/reviewing strategies evaluated by the eligible literature. These can be compared to each other or to a suitable comparator (i.e. no monitoring/review).
9.	Types of study to be included	<ul style="list-style-type: none"> <li>• Systematic reviews</li> <li>• RCTs</li> </ul> <p>Non-randomised studies will be excluded unless no RCTs are found. If no RCTs are found non-randomised comparative trials will be considered (including prospective cohort studies) if they have attempted to detect, and if necessary adjust for, confounding.</p>
10.	Other exclusion criteria	<p>Non-English language studies.</p> <p>Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.</p>
11.	Context	N/A
12.	Primary outcomes (critical outcomes)	<p>Longest follow up available:</p> <p>CRITICAL OUTCOMES:</p> <ul style="list-style-type: none"> <li>• Quality of life (any validated scales, for example, EQ-5D, SF-36)</li> <li>• Pain (VAS/NRS)</li> <li>• Fatigue (any validated scales)</li> <li>• Physical functioning / exercise tolerance / ADL (any validated scales)</li> <li>• Cognitive functioning (any validated scales)</li> <li>• Sleep quality (any validated scales)</li> <li>• Adverse effects (any reported by the studies)</li> <li>• Psychological outcomes</li> <li>• Patient satisfaction</li> <li>• Benefit status/employment/school attendance/school absences</li> </ul>



		<ul style="list-style-type: none"> <li>• Update of diagnostic status</li> <li>• Comorbidities</li> <li>• Activity monitoring</li> <li>• post exertional symptom exacerbation</li> </ul>
13.	Secondary outcomes (important outcomes)	<ul style="list-style-type: none"> <li>• Care needs</li> <li>• Impact on the carer/family</li> </ul>
14.	Data extraction (selection and coding)	<p>EndNote will be used for reference management, sifting, citations and bibliographies. Titles and/or abstracts of studies retrieved using the search strategy and those from additional sources will be screened for inclusion.</p> <p>The full text of potentially eligible studies will be retrieved and will be assessed for eligibility in line with the criteria outlined above.</p> <p>10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer.</p> <p>An in-house developed database; EviBase, will be used for data extraction. A standardised form is followed to extract data from studies (see <a href="#">Developing NICE guidelines: the manual</a> section 6.4) and for undertaking assessment of study quality. Summary evidence tables will be produced including information on: study setting; study population and participant demographics and baseline characteristics; details of the intervention and control interventions; study methodology' recruitment and missing data rates; outcomes and times of measurement; critical appraisal ratings.</p>
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in <a href="#">Developing NICE guidelines: the manual</a> .

		<p><u>For Intervention reviews the following checklist will be used according to study design being assessed:</u></p> <ul style="list-style-type: none"> <li>• <u>Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS)</u></li> <li>• <u>Randomised Controlled Trial: Cochrane RoB (2.0)</u></li> </ul> <p>10% of all evidence reviews are quality assured by a senior research fellow. This includes checking:</p> <p>papers were included /excluded appropriately</p> <p>a sample of the data extractions</p> <p>correct methods are used to synthesise data</p> <p>a sample of the risk of bias assessments</p> <p>Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.</p>
16.	Strategy for data synthesis	<p>Where possible, data will be meta-analysed. Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5) to combine the data given in all studies for each of the outcomes stated above. A fixed effect meta-analysis, with weighted mean differences for continuous outcomes and risk ratios for binary outcomes will be used, and 95% confidence intervals will be calculated for each outcome.</p> <p>Heterogeneity between the studies in effect measures will be assessed using the I<sup>2</sup> statistic and visually inspected. We will consider an I<sup>2</sup> value greater than 50% indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented using random-effects.</p>

		<p>GRADE pro will be used to assess the quality of each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome.</p> <p>If the population included in an individual study includes children aged under 12, it will be included if the majority of the population is aged over 12, and downgraded for indirectness if the overlap into those aged less than 12 is greater than 20%.</p> <p>Publication bias is tested for when there are more than 5 studies for an outcome. Other bias will only be taken into consideration in the quality assessment if it is apparent.</p> <p>Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome.</p> <p>If sufficient data is available to make a network of treatments, WinBUGS will be used for network meta-analysis.</p>
17.	Analysis of sub-groups	<p>Stratification:</p> <ul style="list-style-type: none"> <li>• Age: children vs young people vs adults</li> <li>• Severity: severe vs not severe</li> </ul> <p>Subgroups to investigate if heterogeneity is present:</p> <ul style="list-style-type: none"> <li>• post infectious onset / no post infectious onset</li> <li>• Duration of illness (&lt;3 months symptoms/3-36 months/&gt;36 months)</li> <li>• Gender</li> <li>• When study was done (pre 2000/post 2000)</li> </ul>

18.	Type and method of review	<input checked="" type="checkbox"/> Intervention <input type="checkbox"/> Diagnostic <input type="checkbox"/> Prognostic <input type="checkbox"/> Qualitative <input type="checkbox"/> Epidemiologic <input type="checkbox"/> Service Delivery <input type="checkbox"/> Other (please specify)		
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	01/01/20		
22.	Anticipated completion date	01/01/21		
23.	Stage of review at time of this submission	<b>Review stage</b>	<b>Started</b>	<b>Completed</b>
		Preliminary searches	<input checked="" type="checkbox"/>	<input type="checkbox"/>
		Piloting of the study selection process	<input checked="" type="checkbox"/>	<input type="checkbox"/>
		Formal screening of search results	<input type="checkbox"/>	<input type="checkbox"/>

		against eligibility criteria		
		Data extraction	<input type="checkbox"/>	<input type="checkbox"/>
		Risk of bias (quality) assessment	<input type="checkbox"/>	<input type="checkbox"/>
		Data analysis	<input type="checkbox"/>	<input type="checkbox"/>
24.	Named contact	<p><b>5a. Named contact</b> National Guideline Centre</p> <p><b>5b Named contact e-mail</b></p> <p><b>5e Organisational affiliation of the review</b> National Institute for Health and Care Excellence (NICE) and the National Guideline Centre</p>		
25.	Review team members	<p>From the National Guideline Centre:</p> <ul style="list-style-type: none"> <li>• Dr Kate Kelley [Guideline lead]</li> <li>• Ms Maria Smyth [Senior systematic reviewer]</li> <li>• Ms Melina Vasileiou [Systematic reviewer]</li> <li>• Dr Richard Clubbe [Systematic reviewer]</li> <li>• Dr Karin van Bart [Systematic reviewer]</li> </ul>		

		<ul style="list-style-type: none"> <li>• Mr David Wonderling [Health economist]</li> <li>• Ms Agnes Cuyas [Information specialist]</li> <li>• Ms Kate Ashmore [Project manager]</li> </ul>
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of <u>Developing NICE guidelines: the manual</u> . Members of the guideline committee are available on the NICE website: <a href="https://www.nice.org.uk/guidance/indevelopment/gid-ng10091">https://www.nice.org.uk/guidance/indevelopment/gid-ng10091</a>
29.	Other registration details	
30.	Reference/URL for published protocol	
31.	Dissemination plans	<p>NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:</p> <ul style="list-style-type: none"> <li>• notifying registered stakeholders of publication</li> </ul>

		<ul style="list-style-type: none"> <li>publicising the guideline through NICE's newsletter and alerts</li> <li>issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.</li> </ul>
32.	Keywords	
33.	Details of existing review of same topic by same authors	N/A
34.	Current review status	<input checked="" type="checkbox"/> Ongoing <input type="checkbox"/> Completed but not published <input type="checkbox"/> Completed and published <input type="checkbox"/> Completed, published and being updated <input type="checkbox"/> Discontinued
35..	Additional information	N/A
36.	Details of final publication	<a href="http://www.nice.org.uk">www.nice.org.uk</a>

**Table 3: Health economic review protocol**

<b>Review question</b>	<b>All questions – health economic evidence</b>
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<b>Objectives</b>	To identify health economic studies relevant to any of the review questions.
<b>Search criteria</b>	<ul style="list-style-type: none"> <li>• Populations, interventions and comparators must be as specified in the clinical review protocol above.</li> <li>• Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis).</li> <li>• Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.)</li> <li>• Unpublished reports will not be considered unless submitted as part of a call for evidence.</li> <li>• Studies must be in English.</li> </ul>
<b>Search strategy</b>	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
<b>Review strategy</b>	<p>Studies not meeting any of the search criteria above will be excluded. Studies published before 2004, abstract-only studies and studies from non-OECD countries or the USA will also be excluded.</p> <p>Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).<sup>319</sup></p> <p><b>Inclusion and exclusion criteria</b></p> <ul style="list-style-type: none"> <li>• If a study is rated as both ‘Directly applicable’ and with ‘Minor limitations’ then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile.</li> <li>• If a study is rated as either ‘Not applicable’ or with ‘Very serious limitations’ then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile.</li> <li>• If a study is rated as ‘Partially applicable’, with ‘Potentially serious limitations’ or both then there is discretion over whether it should be included.</li> </ul> <p><b>Where there is discretion</b></p> <p>The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below.</p> <p>The health economist will be guided by the following hierarchies.</p>



*Setting:*

- UK NHS (most applicable).
- OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).
- OECD countries with predominantly private health insurance systems (for example, Switzerland).
- Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations.

*Health economic study type:*

- Cost–utility analysis (most applicable).
- Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis).
- Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations.

*Year of analysis:*

- The more recent the study, the more applicable it will be.
- Studies published in 2004 or later but that depend on unit costs and resource data entirely or predominantly from before 2004 will be rated as ‘Not applicable’.
- Studies published before 2004 will be excluded before being assessed for applicability and methodological limitations.

*Quality and relevance of effectiveness data used in the health economic analysis:*

- The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

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## Appendix B Literature search strategies

This literature search strategy was used for the following review question:

- What is the most clinically and cost-effective method of monitoring and reviewing people with ME/CFS?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.<sup>319</sup>

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

### B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve.

Searches for patient views were run in Medline (OVID), Embase (OVID), CINAHL, and PsycINFO (ProQuest).

**Table 4: Database date parameters and filters used**

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 23 June 2020	Exclusions
Embase (OVID)	1974 – 23 June 2020	Exclusions
The Cochrane Library (Wiley)	Cochrane Reviews to 2020 Issue 6 of 12 CENTRAL to 2020 Issue 6 of 12	None
CINAHL, Current Nursing and Allied Health Literature (EBSCO)	Inception – 23 June 2020	None
PsycINFO (ProQuest)	Inception – 23 June 2020	Exclusions
Epistemonikos (The Epistemonikos Foundation)	Inception - 23 June 2020	None

#### Medline (Ovid) search terms

1.	Fatigue Syndrome, Chronic/
2.	chronic* fatigue*.ti,ab.
3.	((fatigue* adj2 (disorder* or syndrome* or post viral or postviral or immune dysfunction* or post infection* or postinfection*)).ti,ab.
4.	((myalgic or post infection* or postinfection*) adj (encephalomyelitis or encephalopathy)).ti,ab.
5.	((ME adj CFS) or (CFS adj ME) or CFIDS or PVFS).ti,ab.
6.	(Systemic Exertion Intolerance Disease or SEID).ti,ab.
7.	((CFS adj SEID) or (SEID adj CFS) or (ME adj CFS adj SEID) or (ME adj SEID) or (SEID adj ME)).ti,ab.
8.	((Orthostatic intolerance or postural orthostatic tachycardia syndrome or postural tachycardia syndrome or POTS) adj6 (CFS or chronic* fatigue* or ME or myalgic or SEID or systemic exertion)).ti,ab.

9.	((Post-exertional or postexertional) adj2 malaise).ti,ab.
10.	(neurasthenic neuroses or epidemic neuromyasthenia or neurataxia or neuroasthenia or neurasthenia).ti,ab.
11.	((atypical or simulating or resembling) adj poliomyelitis).ti,ab.
12.	((chronic adj2 epstein Barr virus) or CEBV or CAEBV or chronic mononucleosis).ti,ab.
13.	xenotropic murine leukemia virus-related virus.ti,ab.
14.	effort syndrome*.ti,ab.
15.	((akureyri or iceland or tapanui or royal free or royal free hospital) adj disease*) or ((yuppie or yuppy or tapanui) adj flu)).ti,ab.
16.	or/1-15
17.	letter/
18.	editorial/
19.	news/
20.	exp historical article/
21.	Anecdotes as Topic/
22.	comment/
23.	case report/
24.	(letter or comment*).ti.
25.	or/17-24
26.	randomized controlled trial/ or random*.ti,ab.
27.	25 not 26
28.	animals/ not humans/
29.	exp Animals, Laboratory/
30.	exp Animal Experimentation/
31.	exp Models, Animal/
32.	exp Rodentia/
33.	(rat or rats or mouse or mice).ti.
34.	or/27-33
35.	16 not 34
36.	limit 35 to English language

#### Embase (Ovid) search terms

1.	chronic fatigue syndrome/
2.	chronic* fatigue*.ti,ab.
3.	(fatigue* adj2 (disorder* or syndrome* or post viral or postviral or immune dysfunction* or post infection* or postinfection*)).ti,ab.
4.	((myalgic or post infection* or postinfection*) adj (encephalomyelitis or encephalopathy)).ti,ab.
5.	((ME adj CFS) or (CFS adj ME) or CFIDS or PVFS).ti,ab.
6.	(Systemic Exertion Intolerance Disease or SEID).ti,ab.
7.	((CFS adj SEID) or (SEID adj CFS) or (ME adj CFS adj SEID) or (ME adj SEID) or (SEID adj ME)).ti,ab.
8.	((Orthostatic intolerance or postural orthostatic tachycardia syndrome or postural tachycardia syndrome or POTS) adj6 (CFS or chronic* fatigue* or ME or myalgic or SEID or systemic exertion)).ti,ab.
9.	((Post-exertional or postexertional) adj2 malaise).ti,ab.
10.	(neurasthenic neuroses or epidemic neuromyasthenia or neurataxia or neuroasthenia or neurasthenia).ti,ab.

11.	((atypical or simulating or resembling) adj poliomyelitis).ti,ab.
12.	((chronic adj2 epstein Barr virus) or CEBV or CAEBV or chronic mononucleosis).ti,ab.
13.	xenotropic murine leukemia virus-related virus.ti,ab.
14.	effort syndrome*.ti,ab.
15.	((akureyri or iceland or tapanui or royal free or royal free hospital) adj disease*) or ((yuppie or yuppy or tapanui) adj flu)).ti,ab.
16.	or/1-15
17.	letter.pt. or letter/
18.	note.pt.
19.	editorial.pt.
20.	case report/ or case study/
21.	(letter or comment*).ti.
22.	or/17-21
23.	randomized controlled trial/ or random*.ti,ab.
24.	22 not 23
25.	animal/ not human/
26.	nonhuman/
27.	exp Animal Experiment/
28.	exp Experimental Animal/
29.	animal model/
30.	exp Rodent/
31.	(rat or rats or mouse or mice).ti.
32.	or/24-31
33.	16 not 32
34.	limit 33 to English language

### Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Fatigue Syndrome, Chronic] this term only
#2.	chronic* fatigue*.ti,ab
#3.	(fatigue* near/2 (disorder* or syndrome* or post viral or postviral or immune dysfunction* or post infection* or postinfection*)):ti,ab
#4.	((myalgic or post infection* or postinfection*) near/1 (encephalomyelitis or encephalopathy)):ti,ab
#5.	((ME near/1 CFS) or (CFS near/1 ME) or CFIDS or PVFS):ti,ab
#6.	(Systemic Exertion Intolerance Disease or SEID):ti,ab
#7.	((CFS near/1 SEID) or (SEID near/1 CFS) or (ME near/1 CFS near/1 SEID) or (ME near/1 SEID) or (SEID near/1 ME)):ti,ab
#8.	(Orthostatic intolerance or postural orthostatic tachycardia syndrome or postural tachycardia syndrome or POTS)
#9.	((Post-exertional or postexertional) near/2 malaise):ti,ab
#10.	(neurasthenic neuroses or epidemic neuromyasthenia or neurataxia or neuroasthenia or neurasthenia):ti,ab
#11.	((atypical or simulating or resembling) near/1 poliomyelitis):ti,ab
#12.	((chronic epstein Barr virus) or CEBV or CAEBV or chronic mononucleosis):ti,ab
#13.	xenotropic murine leukemia virus-related virus:ti,ab
#14.	effort syndrome*:ti,ab
#15.	((akureyri or iceland or tapanui or "royal free" or "royal free hospital") near/1 disease*):ti,ab

#16.	((yuppie or yuppy or tapanui) near flu):ti,ab
#17.	(or #1-#16)

### CINAHL (EBSCO) search terms

S1.	(MH "Fatigue Syndrome, Chronic")
S2.	chronic* fatigue*
S3.	(fatigue* n2 (disorder* or syndrome* or post viral or postviral or immune dysfunction* or post infection* or postinfection*))
S4.	((myalgic or post infection* or postinfection*) and (encephalomyelitis or encephalopathy))
S5.	((ME and CFS) or (CFS and ME) or CFIDS or PVFS)
S6.	(Systemic Exertion Intolerance Disease or SEID)
S7.	((CFS and SEID) or (SEID and CFS) or (ME and CFS and SEID) or (CFS and ME and SEID) or (ME and SEID) or (SEID and ME))
S8.	((Orthostatic intolerance or postural orthostatic tachycardia syndrome or postural tachycardia syndrome) and (CFS or chronic* fatigue* or ME or myalgic or SEID or systemic exertion))
S9.	((Post-exertional or postexertional) n2 malaise)
S10.	(neurasthenic neuroses or epidemic neuromyasthenia or neurataxia or neuroasthenia)
S11.	((atypical or simulating or resembling) and poliomyelitis)
S12.	(chronic epstein Barr virus or chronic mononucleosis)
S13.	xenotropic murine leukemia virus-related virus
S14.	effort syndrome*
S15.	((akureyri or iceland or tapanui or royal free or royal free hospital) and disease*) or ((yuppie or yuppy or tapanui) and flu))
S16.	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15

### PsycINFO (ProQuest) search terms

1.	(((chronic* fatigue*) OR (fatigue* NEAR2 (disorder* OR syndrome* OR post viral OR postviral OR immune dysfunction* OR post infection* OR postinfection*)) OR ((myalgic OR post infection* OR postinfection*) NEAR1 (encephalomyelitis OR encephalopathy)) OR ((ME NEAR1 CFS) OR (CFS NEAR1 ME) OR CFIDS OR PVFS) OR (Systemic Exertion Intolerance Disease OR SEID) OR ((CFS NEAR1 SEID) OR (SEID NEAR1 CFS)) OR ((ME NEAR1 CFS NEAR1 SEID) OR (ME NEAR1 SEID) OR (SEID NEAR1 ME)) OR ((Orthostatic intolerance OR postural orthostatic tachycardia syndrome OR postural tachycardia syndrome OR POTS) NEAR6 (CFS OR chronic* fatigue* OR ME OR myalgic OR SEID OR systemic exertion)) OR (neurasthenic neuroses OR epidemic neuromyasthenia OR neurataxia OR neuroasthenia OR neurasthenia) OR ((atypical OR simulating OR resembling) NEAR1 poliomyelitis)) OR (((chronic NEAR2 epstein Barr virus) OR CEBV OR CAEBV OR chronic mononucleosis) OR (xenotropic murine leukemia virus-related virus) OR (effort syndrome*)) OR ((akureyri OR iceland OR tapanui OR royal free OR royal free hospital) NEAR1 disease*) OR ((yuppie OR yuppy OR tapanui) NEAR1 flu) OR MAINSUBJECT.EXACT.EXPLODE("Chronic Fatigue Syndrome")) AND (stpe.exact("Scholarly Journals") AND la.exact("ENG") AND po.exact("Human") NOT (me.exact("Empirical Study" OR "Quantitative Study" OR "Longitudinal Study" OR "Clinical Trial" OR "Qualitative Study" OR "Prospective Study" OR "Followup Study" OR "Literature Review" OR "Retrospective Study" OR "Systematic Review" OR "Meta Analysis") AND po.exact("Human"))
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### Epistemonikos search terms

1.	(advanced_title_en:((advanced_title_en:((chronic* fatigue* syndrome*) OR (fatigue* syndrome* OR fatigue* disorder* OR postviral fatigue* OR post viral fatigue* OR fatigue* immune dysfunction OR post infection fatigue* OR postinfection fatigue*)) OR (encephalomyelitis OR encephalopathy) OR ("ME/CFS" OR "CFS/ME" OR "CFIDS"
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OR "PVFS") OR (Systemic Exertion Intolerance Disease OR SEID) OR ((CFS AND SEID) OR (SEID AND CFS) OR (ME AND CFS AND SEID) OR (ME AND SEID) OR (SEID AND ME)) OR (Orthostatic intolerance OR postural orthostatic tachycardia syndrome OR postural tachycardia syndrome OR POTS) OR ((Post-exertional OR postexertional) AND malaise) OR (neurasthenic neuroses OR epidemic neuromyasthenia OR neurataxia OR neuroasthenia OR neurasthenia) OR (atypical poliomyelitis OR simulating poliomyelitis OR resembling poliomyelitis) OR (chronic epstein Barr virus OR CEBV OR CAEBV OR chronic mononucleosis) OR (xenotropic murine leukemia virus-related virus) OR (effort syndrome\*) OR (akureyri OR iceland disease OR tapanui OR royal free disease) OR (yuppie flu OR yuppy flu OR tapanui flu)) OR advanced\_abstract\_en:((chronic\* fatigue\* syndrome\*) OR (fatigue\* syndrome\* OR fatigue\* disorder\* OR postviral fatigue\* OR post viral fatigue\* OR fatigue\* immune dysfunction OR post infection fatigue\* OR postinfection fatigue\*) OR (encephalomyelitis OR encephalopathy) OR ("ME/CFS" OR "CFS/ME" OR "CFIDS" OR "PVFS") OR (Systemic Exertion Intolerance Disease OR SEID) OR ((CFS AND SEID) OR (SEID AND CFS) OR (ME AND CFS AND SEID) OR (ME AND SEID) OR (SEID AND ME)) OR (Orthostatic intolerance OR postural orthostatic tachycardia syndrome OR postural tachycardia syndrome OR POTS) OR ((Post-exertional OR postexertional) AND malaise) OR (neurasthenic neuroses OR epidemic neuromyasthenia OR neurataxia OR neuroasthenia OR neurasthenia) OR (atypical poliomyelitis OR simulating poliomyelitis OR resembling poliomyelitis) OR (chronic epstein Barr virus OR CEBV OR CAEBV OR chronic mononucleosis) OR (xenotropic murine leukemia virus-related virus) OR (effort syndrome\*) OR (akureyri OR iceland disease OR tapanui OR royal free disease) OR (yuppie flu OR yuppy flu OR tapanui flu)))) OR advanced\_abstract\_en:((advanced\_title\_en:((chronic\* fatigue\* syndrome\*) OR (fatigue\* syndrome\* OR fatigue\* disorder\* OR postviral fatigue\* OR post viral fatigue\* OR fatigue\* immune dysfunction OR post infection fatigue\* OR postinfection fatigue\*) OR (encephalomyelitis OR encephalopathy) OR ("ME/CFS" OR "CFS/ME" OR "CFIDS" OR "PVFS") OR (Systemic Exertion Intolerance Disease OR SEID) OR ((CFS AND SEID) OR (SEID AND CFS) OR (ME AND CFS AND SEID) OR (ME AND SEID) OR (SEID AND ME)) OR (Orthostatic intolerance OR postural orthostatic tachycardia syndrome OR postural tachycardia syndrome OR POTS) OR ((Post-exertional OR postexertional) AND malaise) OR (neurasthenic neuroses OR epidemic neuromyasthenia OR neurataxia OR neuroasthenia OR neurasthenia) OR (atypical poliomyelitis OR simulating poliomyelitis OR resembling poliomyelitis) OR (chronic epstein Barr virus OR CEBV OR CAEBV OR chronic mononucleosis) OR (xenotropic murine leukemia virus-related virus) OR (effort syndrome\*) OR (akureyri OR iceland disease OR tapanui OR royal free disease) OR (yuppie flu OR yuppy flu OR tapanui flu)) OR advanced\_abstract\_en:((chronic\* fatigue\* syndrome\*) OR (fatigue\* syndrome\* OR fatigue\* disorder\* OR postviral fatigue\* OR post viral fatigue\* OR fatigue\* immune dysfunction OR post infection fatigue\* OR postinfection fatigue\*) OR (encephalomyelitis OR encephalopathy) OR ("ME/CFS" OR "CFS/ME" OR "CFIDS" OR "PVFS") OR (Systemic Exertion Intolerance Disease OR SEID) OR ((CFS AND SEID) OR (SEID AND CFS) OR (ME AND CFS AND SEID) OR (ME AND SEID) OR (SEID AND ME)) OR (Orthostatic intolerance OR postural orthostatic tachycardia syndrome OR postural tachycardia syndrome OR POTS) OR ((Post-exertional OR postexertional) AND malaise) OR (neurasthenic neuroses OR epidemic neuromyasthenia OR neurataxia OR neuroasthenia OR neurasthenia) OR (atypical poliomyelitis OR simulating poliomyelitis OR resembling poliomyelitis) OR (chronic epstein Barr virus OR CEBV OR CAEBV OR chronic mononucleosis) OR (xenotropic murine leukemia virus-related virus) OR (effort syndrome\*) OR (akureyri OR iceland disease OR tapanui OR royal free disease) OR (yuppie flu OR yuppy flu OR tapanui flu))))))

## B.2 Health economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to ME/CFS population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA – this ceased to be updated after March 2018), with no date restrictions. NHS EED and HTA databases are

hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics.

**Table 5: Database date parameters and filters used**

Database	Dates searched	Search filter used
Medline	2014 – 30 June 2020	Exclusions Health economics studies
Embase	2014 –30 June 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - 2003 – 31 March 2018 NHSEED - 2003 to 31 March 2015	None

**Medline (Ovid) search terms**

1.	Fatigue Syndrome, Chronic/
2.	chronic* fatigue*.ti,ab.
3.	(fatigue* adj2 (disorder* or syndrome* or post viral or postviral or immune dysfunction* or post infection* or postinfection*)).ti,ab.
4.	((myalgic or post infection* or postinfection*) adj (encephalomyelitis or encephalopathy)).ti,ab.
5.	((ME adj CFS) or (CFS adj ME) or CFIDS or PVFS).ti,ab.
6.	(Systemic Exertion Intolerance Disease or SEID).ti,ab.
7.	((CFS adj SEID) or (SEID adj CFS) or (ME adj CFS adj SEID) or (ME adj SEID) or (SEID adj ME)).ti,ab.
8.	((Orthostatic intolerance or postural orthostatic tachycardia syndrome or postural tachycardia syndrome or POTS) adj6 (CFS or chronic* fatigue* or ME or myalgic or SEID or systemic exertion)).ti,ab.
9.	((Post-exertional or postexertional) adj2 malaise).ti,ab.
10.	(neurasthenic neuroses or epidemic neuromyasthenia or neurataxia or neuroasthenia or neurasthenia).ti,ab.
11.	((atypical or simulating or resembling) adj poliomyelitis).ti,ab.
12.	((chronic adj2 epstein Barr virus) or CEBV or CAEBV or chronic mononucleosis).ti,ab.
13.	xenotropic murine leukemia virus-related virus.ti,ab.
14.	effort syndrome*.ti,ab.
15.	((akureyri or iceland or tapanui or royal free or royal free hospital) adj disease*) or ((yuppie or yuppy or tapanui) adj flu)).ti,ab.
16.	or/1-15
17.	letter/
18.	editorial/
19.	news/
20.	exp historical article/
21.	Anecdotes as Topic/
22.	comment/
23.	case report/
24.	(letter or comment*).ti.
25.	or/17-24
26.	randomized controlled trial/ or random*.ti,ab.

27.	25 not 26
28.	animals/ not humans/
29.	exp Animals, Laboratory/
30.	exp Animal Experimentation/
31.	exp Models, Animal/
32.	exp Rodentia/
33.	(rat or rats or mouse or mice).ti.
34.	or/27-33
35.	16 not 34
36.	limit 35 to English language
37.	Economics/
38.	Value of life/
39.	exp "Costs and Cost Analysis"/
40.	exp Economics, Hospital/
41.	exp Economics, Medical/
42.	Economics, Nursing/
43.	Economics, Pharmaceutical/
44.	exp "Fees and Charges"/
45.	exp Budgets/
46.	budget*.ti,ab.
47.	cost*.ti.
48.	(economic* or pharmaco?economic*).ti.
49.	(price* or pricing*).ti,ab.
50.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
51.	(financ* or fee or fees).ti,ab.
52.	(value adj2 (money or monetary)).ti,ab.
53.	or/37-52
54.	36 and 53

#### Embase (Ovid) search terms

1.	chronic fatigue syndrome/
2.	chronic* fatigue*.ti,ab.
3.	(fatigue* adj2 (disorder* or syndrome* or post viral or postviral or immune dysfunction* or post infection* or postinfection*)).ti,ab.
4.	((myalgic or post infection* or postinfection*) adj (encephalomyelitis or encephalopathy)).ti,ab.
5.	((ME adj CFS) or (CFS adj ME) or CFIDS or PVFS).ti,ab.
6.	(Systemic Exertion Intolerance Disease or SEID).ti,ab.
7.	((CFS adj SEID) or (SEID adj CFS) or (ME adj CFS adj SEID) or (ME adj SEID) or (SEID adj ME)).ti,ab.
8.	((Orthostatic intolerance or postural orthostatic tachycardia syndrome or postural tachycardia syndrome or POTS) adj6 (CFS or chronic* fatigue* or ME or myalgic or SEID or systemic exertion)).ti,ab.
9.	((Post-exertional or postexertional) adj2 malaise).ti,ab.
10.	(neurasthenic neuroses or epidemic neuromyasthenia or neurataxia or neuroasthenia or neurasthenia).ti,ab.



11.	((atypical or simulating or resembling) adj poliomyelitis).ti,ab.
12.	((chronic adj2 epstein Barr virus) or CEBV or CAEBV or chronic mononucleosis).ti,ab.
13.	xenotropic murine leukemia virus-related virus.ti,ab.
14.	effort syndrome*.ti,ab.
15.	((akureyri or iceland or tapanui or royal free or royal free hospital) adj disease*) or ((yuppie or yuppy or tapanui) adj flu)).ti,ab.
16.	or/1-15
17.	letter.pt. or letter/
18.	note.pt.
19.	editorial.pt.
20.	case report/ or case study/
21.	(letter or comment*).ti.
22.	or/17-21
23.	randomized controlled trial/ or random*.ti,ab.
24.	22 not 23
25.	animal/ not human/
26.	nonhuman/
27.	exp Animal Experiment/
28.	exp Experimental Animal/
29.	animal model/
30.	exp Rodent/
31.	(rat or rats or mouse or mice).ti.
32.	or/24-31
33.	16 not 32
34.	limit 33 to English language
35.	health economics/
36.	exp economic evaluation/
37.	exp health care cost/
38.	exp fee/
39.	budget/
40.	funding/
41.	budget*.ti,ab.
42.	cost*.ti.
43.	(economic* or pharmaco?economic*).ti.
44.	(price* or pricing*).ti,ab.
45.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
46.	(financ* or fee or fees).ti,ab.
47.	(value adj2 (money or monetary)).ti,ab.
48.	or/35-47
49.	34 and 48

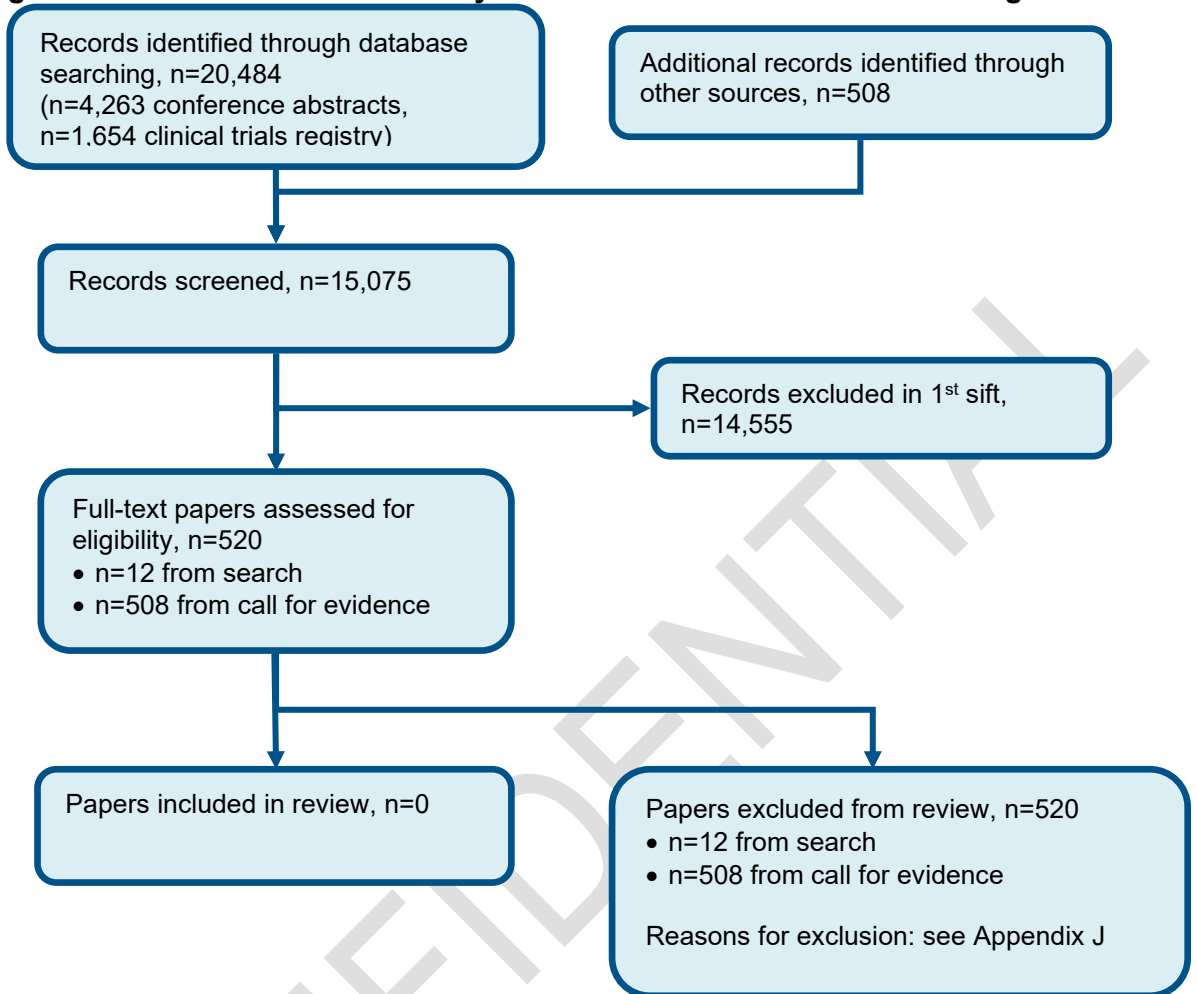
#### NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Fatigue Syndrome, Chronic
#2.	(chronic fatigue or fatigue syndrome*)

#3.	((myalgic adj (encephalomyelitis or encephalopathy)))
#4.	((((ME adj CFS) or (CFS adj ME)))
#5.	(post viral fatigue or post viral syndrome* or viral fatigue syndrome* or PVFS )
#6.	#1 OR #2 OR #3 OR #4 OR #5
#7.	(neurasthenic neuroses or epidemic neuromyasthenia or post infectious encephalomyelitis or neurataxia or neuroasthenia )
#8.	((((atypical or simulating or resembling) adj poliomyelitis))
#9.	(chronic epstein Barr virus or chronic mononucleosis)
#10.	(xenotropic murine leukemia virus-related virus)
#11.	((((chronic fatigue and immune dysfunction syndrome*) or cfids or chronic fatigue-fibromyalgia syndrome* or chronic fatigue disorder* or Systemic Exertion Intolerance Disease or SEID or effort syndrome or post infectious fatigue))
#12.	(((((akureyri or iceland or tapanui or royal free or royal free hospital) adj disease*) or ((yuppie or yuppy or tapanui) adj flu)))
#13.	#7 OR #8 OR #9 OR #10 OR #11 OR #12
#14.	#6 or #13

## Appendix C Effectiveness evidence study selection

Figure 1: Flow chart of clinical study selection for the review of monitoring and review



## **Appendix D Effectiveness evidence**

None.

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## Appendix E Forest plots

None.

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## Appendix F Effectiveness evidence

None.

CONFIDENTIAL

## Appendix G Forest plots

None.

CONFIDENTIAL

## Appendix H GRADE and/or GRADE-CERQual tables

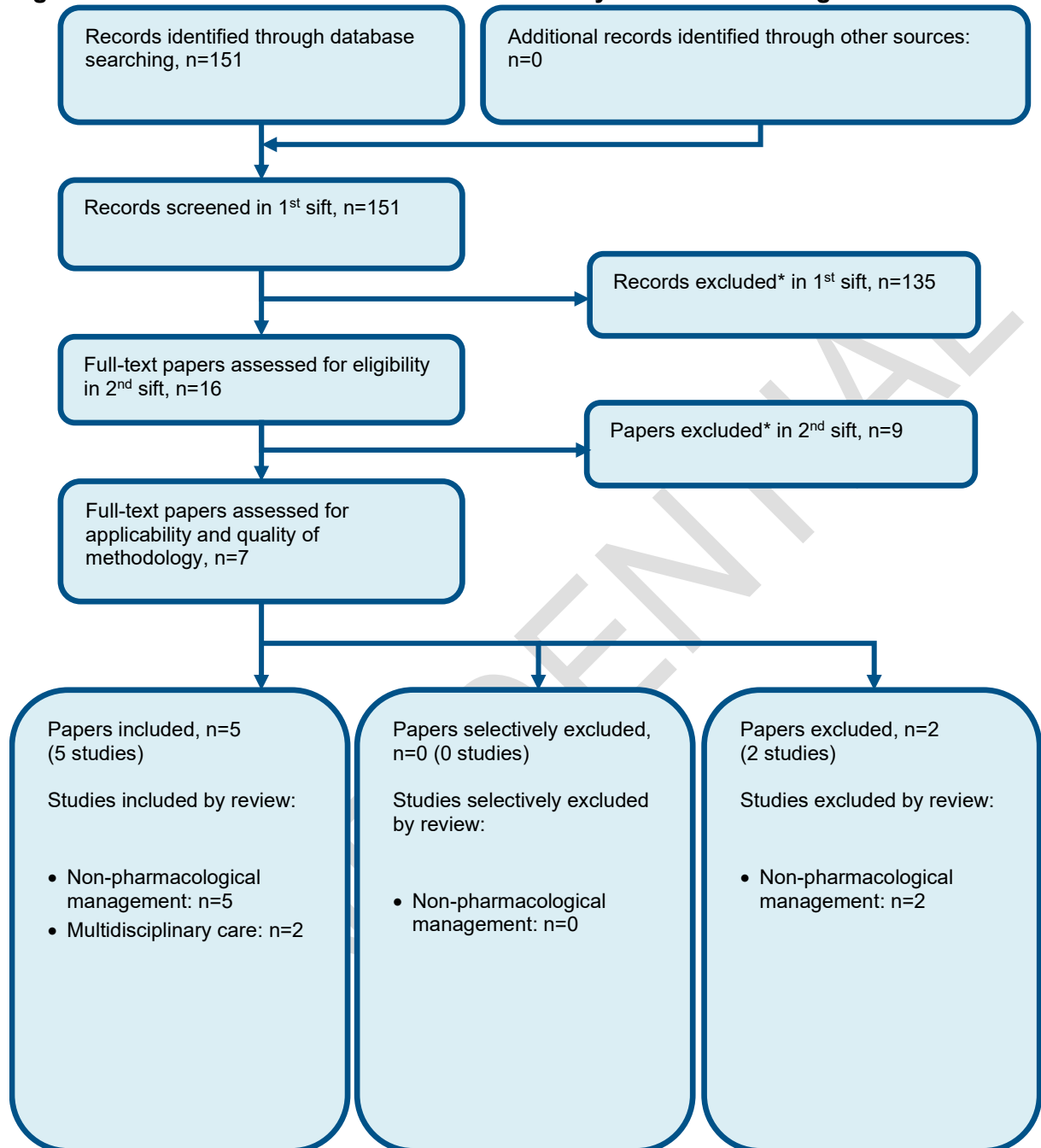
None.

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## Appendix I Economic evidence study selection

Figure 2: Flow chart of health economic study selection for the guideline



\* Non-relevant population, intervention, comparison, design or setting; non-English language

NB. Two papers were included in both the non-pharma and the multidisciplinary care reviews, in parallel with the review of clinical effectiveness.

## Appendix J Economic evidence tables

None.

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## **Appendix K Health economic model**

No original economic modelling was undertaken.

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## Appendix L Excluded studies

### L.1 Clinical studies

**Table 6: Studies excluded from the clinical review**

Study	Exclusion reason
Allen 2008 <sup>10</sup>	Incorrect study design - not an intervention study (literature review and expert opinion on the treatment/care of women with ME/CFS during pregnancy/postpartum period)
Brown 1999 <sup>57</sup>	Incorrect study design - not an intervention study (describes a treatment programme used at a hospital)
Bryan 1992 <sup>58</sup>	Incorrect study design - not an intervention study (describes an approach to treatment/management and monitoring/review in people with ME/CFS)
Christley 2012 <sup>90</sup>	Incorrect study design - not an intervention study (literature review on reproductive and pregnancy related issues and management in people with ME/CFS)
Jason 1994 <sup>215</sup>	Incorrect study design - not an intervention study (case study describing the use of a symptom rating scale to monitor fluctuation in symptoms over time)
Jason 2000 <sup>212</sup>	Incorrect study design - not an intervention study (describes a model which aims to measure illness stage/progression in people with ME/CFS)
Jason 2009 <sup>216</sup>	Incorrect study design - non-comparative study with no relevant outcomes (study used activity log to examine patterns, intensity and qualitative nature of activity in people with ME/CFS)
Kuehn 2018 <sup>254</sup>	Incorrect study design - not a research article (news article describing ME/CFS)
Roor 2020 <sup>385</sup>	Incorrect study design (assesses efficacy of intervention on the validity of cognitive performance measure results)
Ross 2004 <sup>386</sup>	Incorrect study design/intervention - no relevant monitoring/reviewing interventions (systematic review on interventions, patient characteristics, neuropsychological test reliability and comorbid psychiatric conditions in people with ME/CFS)
Tillett 2000 <sup>456</sup>	Incorrect study design - not an intervention study (study examines school attendance, management, and nature of follow-up in a cohort of school children diagnosed with ME/CFS)
Weatherburn 2007 <sup>499</sup>	Incorrect study design - non-comparative study and no relevant outcomes (study examining the feasibility of teleconference distance review in a group of patients with ME/CFS)

A call for evidence was sent out for three review questions for which the committee anticipated that there would be limited published evidence. Some articles were submitted with a clear indication of which of the three review questions they related to, but for many there was no clear indication. Regardless, all articles were assessed for eligibility for inclusion in all three reviews and one main table was created for all studies/articles submitted that were subsequently excluded. For some articles, there were multiple reasons for exclusion across the three review questions. The exclusion reason listed is the main reason for exclusion from the review that the article was judged to be most relevant to. For example, a quantitative study on the effectiveness of an intervention in people diagnosed with ME/CFS was considered to be most relevant to the experiences of interventions question, but the review protocol specified only qualitative studies to be included, so the main reason for

exclusion would be incorrect study design. Some articles were relevant to the guideline in general but did not specifically attempt to answer any of the three review questions.

**Table 7: Studies excluded from call for evidence**

Study	Exclusion reason
Action for ME 2001 <sup>2</sup>	Incorrect study design (quantitative survey)
Action for ME 2014 <sup>345</sup>	No relevant themes
Action for ME 2019 Results from our big survey <sup>1</sup> (unpublished)	Incorrect study design (quantitative survey)
Action for ME and Association of Young People with ME (UK) 2008 <sup>3</sup>	Incorrect study design (qualitative survey)
Adamowicz 2014 <sup>4</sup>	Systematic review with different PICO
Adamson <sup>5</sup> (unpublished)	Incorrect study design (cohort)
Adedeji 2012 <sup>6</sup>	Study/article does not address any of the call for evidence review questions
Adelakun <sup>7</sup>	No useable data - qualitative data reported as most frequently occurring words
Ahmed 2020 <sup>8</sup>	Incorrect study design (systematic review; no qualitative data)
All-Party Parliamentary Group on ME 2010 <sup>9</sup>	Not a qualitative study
Allwright 2019 <sup>11</sup>	No relevant themes
Anderson 1997 <sup>13</sup>	Mixed method study design with no extractable themes
Anderson <sup>12</sup> (unpublished)	Incorrect study design (qualitative)
Anon <sup>429</sup>	Incorrect study design (quantitative survey)
Anon <sup>398</sup>	Incorrect study design (non-comparative intervention study)
Anon <sup>14</sup>	Incorrect study design (non-comparative intervention study with quantitative outcomes)
Anon 2013 <sup>346</sup> (unpublished)	Incorrect study design (quantitative survey)
Anon 2015 <sup>95</sup>	Trial registry record; no results posted
Anon 2015 <sup>399</sup>	Incorrect study design (quantitative)
Anon 2015 <sup>15</sup>	Unable to obtain
Anon 2016 <sup>28</sup> (unpublished)	Letter/commentary/expert opinion
Anon 2016 <sup>372</sup>	Study/article does not address any of the call for evidence review questions
Anon 2017 <sup>152</sup>	Study/article does not address any of the call for evidence review questions
Anon 2018 <sup>363</sup>	Not research article
Antcliff 2019 <sup>16</sup>	Incorrect population (HCPs)
Antiel 2011 <sup>17</sup>	Incorrect interventions (no intervention)
Armstrong 2012 <sup>18</sup>	Study/article does not address any of the call for evidence review questions
Arnold 2015 <sup>19</sup>	Incorrect study design (RCT)
Ates 2016 <sup>20</sup>	Study/article does not address any of the call for evidence review questions
Augusto 2018 <sup>21</sup>	Study/article does not address any of the call for evidence review questions
BACME 2019 <sup>22</sup>	Incorrect population (survey of CFS/ME services)

Study	Exclusion reason
Balaguru 2012 <sup>23</sup>	Study/article does not address any of the call for evidence review questions
Baos 2019 <sup>24</sup>	RCT protocol
Baraniuk 2017 <sup>26</sup>	Study/article does not address any of the call for evidence review questions
Baraniuk 2018 <sup>25</sup>	Study/article does not address any of the call for evidence review questions (BMJ best practice)
Barnden 2016 <sup>27</sup>	Study/article does not address any of the call for evidence review questions
Bazelmans 2004 <sup>29</sup>	Incorrect population (therapists)
Bazelmans 2005 <sup>30</sup>	Incorrect study design (quantitative)
Bazilevskaya 2006 <sup>31</sup>	Study/article does not address any of the call for evidence review questions
Beasant <sup>32</sup> (unpublished)	Incorrect study design (qualitative)
Belgian Ministry of Social Affairs, Public Health and Environment 2000 <sup>33</sup>	Guidelines including systematic review of the evidence (unclear source of data on patient experience of CBT)
Bell 2016 <sup>34</sup>	Letter/commentary/expert opinion
Berkovitz 2009 <sup>35</sup>	Incorrect interventions (no intervention)
Blease 2017 <sup>36</sup>	Incorrect study design (review article)
Blout 2015 <sup>37</sup>	Incorrect study design (quantitative)
Blue Ribbon for the Awareness of Myalgic Encephalomyelitis 2010 <sup>38</sup> (unpublished)	Incorrect study design (quantitative survey; no qualitative data)
Boneva 2019 <sup>39</sup>	Incorrect interventions (no intervention)
Bould 2011 <sup>41</sup>	Review
Bould 2013 <sup>40</sup>	Not relevant to any call for evidence questions
Bowers 2019 <sup>42</sup>	Study/article does not address any of the call for evidence review questions
Brigden <sup>46</sup> (unpublished)	Incorrect study design (qualitative)
Brigden 2018 <sup>45</sup>	No intervention
Brigden 2018 <sup>43</sup>	No relevant themes
Brigden 2016 <sup>44</sup>	RCT protocol
Bringsli 2014 <sup>47</sup>	Incorrect study design (quantitative survey)
Bristol CFS/ME Service <sup>49</sup>	Incorrect study design (survey)
Bristol CFS/ME Service <sup>48</sup> (unpublished)	Incorrect study design (qualitative)
Britain 2019 <sup>50</sup>	Conference abstract
Brooks 2011 <sup>51</sup>	Incorrect study design (quantitative)
Broughton 2017 <sup>52</sup>	Incorrect interventions (specialist services rather than specific interventions)
Brouwers 2002 <sup>53</sup>	Incorrect study design (RCT)
Brown 2012 <sup>55</sup>	Study/article does not address any of the call for evidence review questions
Brown 2005 <sup>56</sup>	Study/article does not address any of the call for evidence review questions
Brown 2015 <sup>54</sup>	Study/article does not address any of the call for evidence review questions

Study	Exclusion reason
Buchachenko 2013 <sup>63</sup>	Study/article does not address any of the call for evidence review questions
Buchachenko 2005 <sup>61</sup>	Study/article does not address any of the call for evidence review questions
Buchachenko 2006 <sup>62</sup>	Study/article does not address any of the call for evidence review questions
Buchachenko 2017 <sup>60</sup>	Study/article does not address any of the call for evidence review questions
Buchachenko 2019 <sup>59</sup>	Study/article does not address any of the call for evidence review questions
Burgess 2012 <sup>64</sup>	Incorrect study design (RCT)
Burke 1986 <sup>65</sup>	Study/article does not address any of the call for evidence review questions
Butland 1982 <sup>66</sup>	Study/article does not address any of the call for evidence review questions
Calello 2018 <sup>67</sup>	Study/article does not address any of the call for evidence review questions
Carpenter 2013 <sup>68</sup>	Study/article does not address any of the call for evidence review questions
Carruthers 2011 <sup>71</sup>	Study/article does not address any of the call for evidence review questions
Carruthers 2012 <sup>70</sup>	Study/article does not address any of the call for evidence review questions
Carruthers 2003 <sup>69</sup>	Guidelines
Casanova 2011 <sup>72</sup>	Study/article does not address any of the call for evidence review questions
Castro-Marrero 2016 <sup>74</sup>	Incorrect study design (RCT)
Castro-Marrero 2017 <sup>73</sup>	Study/article does not address any of the call for evidence review questions
Cella 2011 <sup>76</sup>	Incorrect study design (quantitative)
Cella 2011 <sup>75</sup>	Incorrect study design (quantitative)
Centers for Disease Control and Prevention 2019 <sup>77</sup>	Study/article does not address any of the call for evidence review questions
CFS/ME National Outcomes Database Team 2016 <sup>78</sup>	Incorrect study design (non-comparative observational study)
CFS/ME Service for South Yorkshire and North Derbyshire 2019 <sup>79</sup>	Incorrect study design (quantitative survey)
CFS/ME Service for South Yorkshire and North Derbyshire <sup>80</sup>	Incorrect study design (quantitative survey)
CFS/ME Working Group 2002 <sup>81</sup> (unpublished)	No relevant themes
Chaudhuri 2003 <sup>88</sup>	Study/article does not address any of the call for evidence review questions
Chalder 1993 <sup>83</sup>	Study/article does not address any of the call for evidence review questions
Chalder 2010 <sup>84</sup>	Incorrect study design (RCT)
Chalder 2010 <sup>82</sup>	Incorrect study design (review, not qualitative)
Chalder 2015 <sup>85</sup>	Incorrect study design (quantitative)
Chan 2019 <sup>86</sup>	Not a qualitative study

Study	Exclusion reason
Chang 2012 <sup>87</sup>	Incorrect interventions (no intervention)
Childs 2019 <sup>89</sup>	Incorrect study design (quantitative survey); no qualitative data
Chu 2018 <sup>91</sup>	Study/article does not address any of the call for evidence review questions
Claypoole 2007 <sup>92</sup>	Incorrect interventions (no intervention)
Cleare 2004 <sup>93</sup>	Incorrect study design (quantitative)
Cliff 2019 <sup>94</sup>	Study/article does not address any of the call for evidence review questions
Cockshell 2010 <sup>96</sup>	Incorrect interventions (no intervention)
Collin 2018 <sup>101</sup>	Study/article does not address any of the call for evidence review questions
Collin 2017 <sup>99</sup>	Incorrect study design (non-comparative cohort study)
Collin 2017 <sup>97</sup>	Incorrect study design (case-control)
Collin 2017 <sup>98</sup>	Study/article does not address any of the call for evidence review questions
Collin 2016 <sup>102</sup>	Study/article does not address any of the call for evidence review questions
Collin 2015 <sup>103</sup>	Study/article does not address any of the call for evidence review questions
Collin 2012 <sup>104</sup>	Incorrect study design (quantitative survey)
Collin 2011 <sup>100</sup>	Study/article does not address any of the call for evidence review questions
Comhaire 2018 <sup>105</sup>	Incorrect study design (quantitative)
Cook 2017 <sup>106</sup>	Incorrect interventions (no intervention)
Cooper 2019 <sup>107</sup>	No relevant themes (qualitative data on an ME/CFS service, not specific interventions)
Corsius 2019 <sup>108</sup>	Report summary; full report in Dutch
Costa 1995 <sup>109</sup>	Study/article does not address any of the call for evidence review questions
Crawford 2010 <sup>111</sup>	Study/article does not address any of the call for evidence review questions
Crawford 2012 <sup>110</sup>	Letter/commentary/expert opinion
Crawford 2012 <sup>112</sup>	Study advertisement
Crawley 2018 <sup>118</sup>	Not relevant to monitoring/review question
Crawley 2013 <sup>115</sup>	Incorrect interventions
Crawley 2013 <sup>113</sup>	No relevant outcomes
Crawley 2011 <sup>117</sup>	No intervention
Crawley 2009 <sup>114</sup>	Study/article does not address any of the call for evidence review questions
Crawley 2009 <sup>116</sup>	Study/article does not address any of the call for evidence review questions
Crowhurst 2005 <sup>119</sup>	Letter/commentary/expert opinion
Crowhurst 2007 <sup>120</sup>	No relevant themes
Currell <sup>121</sup>	No relevant themes (qualitative data on a specialist service, not specific interventions)
DARPA 2017 <sup>122</sup>	Study/article does not address any of the call for evidence review questions
Davenport 2010 <sup>127</sup>	Incorrect study design (conceptual model; not qualitative)



Study	Exclusion reason
Davenport 2019 <sup>123</sup>	Study/article does not address any of the call for evidence review questions
Davenport 2011 <sup>125</sup>	Study/article does not address any of the call for evidence review questions
Davenport 2011 <sup>124</sup>	Incorrect study design (quantitative)
Davenport 2019 <sup>126</sup>	Letter/commentary/expert opinion
Davies 2008 <sup>128</sup>	Study/article does not address any of the call for evidence review questions
Dawes 2019 <sup>153</sup>	Executive summary of an excluded survey
Deale 2001 <sup>136</sup>	Incorrect study design (RCT)
Deale 1998 <sup>135</sup>	Incorrect study design (quantitative)
Deale 1997 <sup>134</sup>	Incorrect study design (RCT)
De Becker 2000 <sup>130</sup>	Study/article does not address any of the call for evidence review questions
De Becker 2001 <sup>129</sup>	Study/article does not address any of the call for evidence review questions
de Carvalho 2011 <sup>131</sup>	Study/article does not address any of the call for evidence review questions
Deftereos 2016 <sup>137</sup>	Incorrect population (expert clinicians)
de Lange 2008 <sup>132</sup>	Incorrect study design (quantitative)
DeLuca 2004 <sup>138</sup>	Incorrect interventions (no intervention)
de Vega 2017 <sup>133</sup>	Study/article does not address any of the call for evidence review questions
Devasahayam 2012 <sup>139</sup>	Study/article does not address any of the call for evidence review questions
Diao 2017 <sup>140</sup>	Study/article does not address any of the call for evidence review questions
Dobson 2007 <sup>141</sup>	Study/article does not address any of the call for evidence review questions
Dougall 2014 <sup>142</sup>	Incorrect study design (RCT)
Doukrou 2019 <sup>143</sup>	Incorrect study design (no qualitative data)
Dowsett 1997 <sup>144</sup>	Study/article does not address any of the call for evidence review questions
Duyn 2017 <sup>145</sup>	Study/article does not address any of the call for evidence review questions
Dyda 2018 <sup>146</sup>	Study/article does not address any of the call for evidence review questions
Effective Health Care Program: Agency for Healthcare Research and Quality <sup>147</sup>	Systematic review protocol
Emerge Australia 2018 <sup>148</sup>	Incorrect study design (quantitative survey)
Emerge Australia 2019 <sup>149</sup>	Incorrect study design (quantitative survey)
Encephalitis Society 2017 <sup>150</sup>	Study/article does not address any of the call for evidence review questions (website information)
Eroshenko 2004 <sup>151</sup>	Study/article does not address any of the call for evidence review questions
Falk Hvidberg 2015 <sup>154</sup>	Incorrect interventions (no intervention)
Faulkner 2016 <sup>155</sup>	Letter/commentary/expert opinion
Fisher 2013 <sup>156</sup>	No relevant themes

Study	Exclusion reason
Fisk 1994 <sup>157</sup>	Not relevant to any call for evidence questions
Flo 2014 <sup>158</sup>	Incorrect study design (quantitative)
Fluge 2019 <sup>160</sup>	Incorrect study design (RCT)
Fluge 2015 <sup>161</sup>	Incorrect study design (quantitative)
Fluge 2016 <sup>159</sup>	Study/article does not address any of the call for evidence review questions
Forward ME Survey 2019 <sup>336</sup>	Incorrect study design (survey)
Franklin 2018 <sup>162</sup>	Incorrect study design (quantitative)
Fukuda 2016 <sup>163</sup>	Incorrect study design (RCT)
Garner 2019 <sup>164</sup>	Study/article does not address any of the call for evidence review questions
Geraghty 2018 <sup>168</sup>	Incorrect study design (narrative review)
Geraghty 2016 <sup>170</sup>	Incorrect study design (debate article)
Geraghty 2019 <sup>169</sup>	Incorrect study design (literature review)
Geraghty 2019 <sup>166</sup>	Letter/commentary/expert opinion
Geraghty 2017 <sup>165</sup>	Incorrect study design (analysis of quantitative survey data)
Geraghty 2019 <sup>167</sup>	Study/article does not address any of the call for evidence review questions
Ghatineh 2017 <sup>171</sup>	Review of an RCT
Gielissen 2007 <sup>172</sup>	Study/article does not address any of the call for evidence review questions
Gieré 2016 <sup>173</sup>	Study/article does not address any of the call for evidence review questions
Gilder 2018 <sup>174</sup>	Study/article does not address any of the call for evidence review questions
Gladwell 2013 <sup>175</sup>	Incorrect study design (survey)
Goedendorp 2009 <sup>176</sup>	Study/article does not address any of the call for evidence review questions
Haig-Ferguson 2019 <sup>177</sup>	No relevant themes
Haig-Ferguson 2009 <sup>178</sup>	No relevant themes
Halapy 2017 <sup>179</sup>	Letter/commentary/expert opinion
Harada 1999 <sup>180</sup>	Study/article does not address any of the call for evidence review questions
Haywood 2012 <sup>182</sup>	Study/article does not address any of the call for evidence review questions
Haywood 2014 <sup>181</sup>	Systematic review with different PICO
Heald 2019 <sup>183</sup>	Study/article does not address any of the call for evidence review questions
Healthwatch Trafford 2017 <sup>185</sup>	No relevant themes
Healthwatch Lancashire 2017 <sup>184</sup>	Different focus to review question
Heins 2013 <sup>187</sup>	Incorrect study design (quantitative)
Heins 2013 <sup>186</sup>	Incorrect study design (quantitative)
Heins 2011 <sup>188</sup>	Incorrect study design (quantitative)
Heins 2010 <sup>189</sup>	Incorrect study design (quantitative)
Hives 2017 <sup>190</sup>	Incorrect study design (diagnostic accuracy study)
Hodges 2018 <sup>191</sup>	Incorrect interventions (no intervention)

Study	Exclusion reason
Holtzman 2019 <sup>192</sup>	Study/article does not address any of the call for evidence review questions
Hughes 2002 <sup>194</sup>	Review article
Hughes 2018 <sup>193</sup>	Study/article does not address any of the call for evidence review questions
Huibers 2004 <sup>195</sup>	Incorrect population (some met criteria for CFS, some did not and results not reported separately)
Ickmans 2014 <sup>196</sup>	Incorrect interventions (no intervention)
ICNIRP Project Group 2017 <sup>197</sup>	Study/article does not address any of the call for evidence review questions
Ingman 2016 <sup>200</sup>	Incorrect study design (quantitative)
Ingman <sup>199</sup>	Unable to obtain
Ingman <sup>198</sup>	Unable to obtain
Institute of Medicine 2015 <sup>201</sup>	Study/article does not address any of the call for evidence review questions
ISRCTN Registry 2015 <sup>202</sup>	Study/article does not address any of the call for evidence review questions
Jackson 2012 <sup>203</sup>	Study/article does not address any of the call for evidence review questions
Janse 2019 <sup>204</sup>	Prognostic study looking at predictors of outcome of CBT - none relevant to CFE questions
Janse 2019 <sup>206</sup>	Incorrect study design (non-randomised quantitative study)
Janse 2018 <sup>208</sup>	Incorrect study design (RCT)
Janse 2017 <sup>205</sup>	Incorrect study design (RCT)
Janse 2016 <sup>207</sup>	Incorrect population (idiopathic chronic fatigue); incorrect study design (RCT)
Janse 2015 <sup>209</sup>	RCT protocol
Jason 2006 <sup>211</sup>	Study/article does not address any of the call for evidence review questions
Jason 2008 <sup>217</sup>	Study/article does not address any of the call for evidence review questions
Jason 2009 <sup>210</sup>	Incorrect study design (quantitative)
Jason 2009 <sup>213</sup>	Study/article does not address any of the call for evidence review questions
Jason 2015 <sup>218</sup>	Review article
Jason 2018 <sup>214</sup>	Not relevant to any call for evidence question
Jelinek 2001 <sup>219</sup>	Study/article does not address any of the call for evidence review questions
Jenkins 2005 <sup>220</sup>	Study/article does not address any of the call for evidence review questions
Jones 2012 <sup>221</sup>	Incorrect study design (quantitative)
Josev 2019 <sup>222</sup>	Incorrect interventions (no intervention)
Juutilainen 2018 <sup>223</sup>	Study/article does not address any of the call for evidence review questions
Kapitein 2015 <sup>224</sup>	Study/article does not address any of the call for evidence review questions
Kasevich 2002 <sup>225</sup>	Study/article does not address any of the call for evidence review questions
Keller 2014 <sup>226</sup>	Incorrect interventions (no intervention)

Study	Exclusion reason
Kempke 2013 <sup>227</sup>	Study/article does not address any of the call for evidence review questions
Kenyon 2019 <sup>228</sup>	Incorrect study design (quantitative)
Kim 2019 <sup>229</sup>	Study/article does not address any of the call for evidence review questions
Kindlon 2011 <sup>237</sup>	Letter/commentary/expert opinion
Kindlon 2017 <sup>231</sup>	Letter/commentary/expert opinion
Kindlon 2009 <sup>230</sup>	Letter/commentary/expert opinion
Kindlon 2010 <sup>239</sup>	Letter/commentary/expert opinion
Kindlon 2010 <sup>241</sup>	Letter/commentary/expert opinion
Kindlon 2011 <sup>233</sup>	Letter/commentary/expert opinion
Kindlon 2012 <sup>234</sup>	Letter/commentary/expert opinion
Kindlon 2012 <sup>235</sup>	Letter/commentary/expert opinion
Kindlon 2015 <sup>232</sup>	Letter/commentary/expert opinion
Kindlon 2015 <sup>240</sup>	Letter/commentary/expert opinion
Kindlon 2015 <sup>242</sup>	Letter/commentary/expert opinion
Kindlon 2011 <sup>236</sup>	Letter/commentary/expert opinion
Kindlon 2009 <sup>238</sup>	Letter/commentary/expert opinion
Kingdon 2018 <sup>243</sup>	Study/article does not address any of the call for evidence review questions
Knoester 2019 <sup>244</sup>	Study/article does not address any of the call for evidence review questions
Knoop 2008 <sup>249</sup>	Incorrect study design (RCT)
Knoop 2007 <sup>248</sup>	Incorrect study design (quantitative)
Knoop 2007 <sup>246</sup>	Incorrect study design (quantitative)
Knoop 2007 <sup>245</sup>	Incorrect study design (quantitative)
Knoop 2008 <sup>247</sup>	Incorrect study design (RCT)
Knudsen 2011 <sup>250</sup>	Study/article does not address any of the call for evidence review questions
Kodama 2013 <sup>251</sup>	Study/article does not address any of the call for evidence review questions
Kreyberg 2007 <sup>252</sup>	Guidelines
Kreyberg 2007 <sup>253</sup>	Incorrect population (nursing staff)
Lacerda 2018 <sup>255</sup>	Study/article does not address any of the call for evidence review questions
Lacerda 2019 <sup>256</sup>	No relevant themes
LaManca 1998 <sup>257</sup>	Incorrect interventions (no intervention)
Lapp 2019 <sup>258</sup>	Letter/commentary/expert opinion
Larun 2014 <sup>259</sup>	Incorrect study design (systematic review of RCTs)
Leaman 1997 <sup>260</sup>	Study/article does not address any of the call for evidence review questions
Leone 2006 <sup>262</sup>	Not relevant to any call for evidence question
Lewis 2013 <sup>263</sup>	Incorrect interventions (no intervention)
Lien 2019 <sup>264</sup>	Study/article does not address any of the call for evidence review questions
Light 2009 <sup>265</sup>	Incorrect study design (quantitative)
Lincolnshire Partnership 2019 <sup>266</sup>	Qualitative data in the form of quotes - no thematic analysis

Study	Exclusion reason
Liu 2018 <sup>267</sup>	Study/article does not address any of the call for evidence review questions
Lloyd 2012 <sup>269</sup>	Incorrect study design (quantitative)
Lloyd 2012 <sup>268</sup>	Incorrect study design (RCT)
Loades 2016 <sup>273</sup>	Systematic review with different PICO
Loades 2019 <sup>270</sup> (unpublished)	Incorrect population (already diagnosed with ME/CFS); incorrect study design (cross-sectional epidemiological study with no interventions)
Loades 2019 <sup>274</sup>	Incorrect study design (qualitative); also excluded from experiences of interventions review due incorrect population (healthcare professionals)
Loades 2019 <sup>271</sup>	Incorrect study design (quantitative)
Loades 2018 <sup>272</sup>	Study/article does not address any of the call for evidence review questions
Loy 2016 <sup>275</sup>	Incorrect study design (quantitative)
Lyshevski 2001 <sup>276</sup>	Study/article does not address any of the call for evidence review questions
Maes 2006 <sup>279</sup>	Study/article does not address any of the call for evidence review questions
Maes 2009 <sup>280</sup>	Study/article does not address any of the call for evidence review questions
Maes 2012 <sup>281</sup>	Study/article does not address any of the call for evidence review questions
Marshall 1997 <sup>282</sup>	Not relevant to any call for evidence question
Marshall 1996 <sup>283</sup>	Incorrect study design (quantitative)
Mathew 2009 <sup>284</sup>	Study/article does not address any of the call for evidence review questions
May 2010 <sup>285</sup>	Study/article does not address any of the call for evidence review questions
McCourt 2019 <sup>286</sup>	Study/article does not address any of the call for evidence review questions
McDermott 2006 <sup>287</sup>	Study/article does not address any of the call for evidence review questions
McGregor 2016 <sup>288</sup>	Study/article does not address any of the call for evidence review questions
McGregor 2019 <sup>289</sup>	Study/article does not address any of the call for evidence review questions
McManimen 2016 <sup>291</sup>	Study/article does not address any of the call for evidence review questions
McManimen 2019 <sup>290</sup>	Incorrect study design (qualitative)
McPhee 2019 <sup>292</sup>	Qualitative section was related to information given to patients about possible harms, data about harm was quantitative
ME Action 2019 <sup>261</sup>	Incorrect study design (survey)
ME/cvs Vereniging 2016 <sup>293</sup>	Report summary; full report in Dutch
Meeus 2015 <sup>294</sup>	Incorrect study design (RCT)
ME Group 2019 <sup>278</sup>	No qualitative findings/data analysis reported
ME Group 2014 <sup>277</sup>	No qualitative findings/data analysis reported
Melamed 2019 <sup>295</sup>	Study/article does not address any of the call for evidence review questions

Study	Exclusion reason
Mihelicova 2016 <sup>296</sup>	Study/article does not address any of the call for evidence review questions
Miller 2015 <sup>297</sup>	Study/article does not address any of the call for evidence review questions
Millions Missing Canada 2017 <sup>298</sup>	Incorrect study design (quantitative survey)
Missen 2012 <sup>299</sup>	No relevant outcomes
Moneghetti 2018 <sup>300</sup>	Incorrect interventions (no intervention)
Montoya 2018 <sup>301</sup>	Incorrect study design (RCT)
Montoya 2013 <sup>302</sup>	Incorrect study design (RCT)
Moore 2000 <sup>303</sup>	Study/article does not address any of the call for evidence review questions
Moore 2015 <sup>304</sup>	Study/article does not address any of the call for evidence review questions
Morens 2019 <sup>305</sup>	Study/article does not address any of the call for evidence review questions
Morris 2014 <sup>306</sup>	Study/article does not address any of the call for evidence review questions
Murdock 2017 <sup>307</sup>	Study/article does not address any of the call for evidence review questions
Myalgic Encephalomyelitis / Chronic Fatigue Syndrome Advisory Committee 2019 <sup>308</sup>	Study/article does not address any of the call for evidence review questions
Nacul 2011 <sup>311</sup>	Study/article does not address any of the call for evidence review questions
Nacul 2011 <sup>312</sup>	Study/article does not address any of the call for evidence review questions
Nacul 2018 <sup>313</sup>	Study/article does not address any of the call for evidence review questions
Nacul 2019 <sup>310</sup>	Study/article does not address any of the call for evidence review questions
Nacul 2019 <sup>309</sup>	Study/article does not address any of the call for evidence review questions
Nagy-Szakal 2018 <sup>314</sup>	Study/article does not address any of the call for evidence review questions
Natelson 2017 <sup>316</sup>	Study/article does not address any of the call for evidence review questions
Natelson 2017 <sup>315</sup>	Study/article does not address any of the call for evidence review questions
National Centers for Environmental Information <sup>317</sup>	Study/article does not address any of the call for evidence review questions
National Collaborating Centre for Primary Care 2007 <sup>318</sup>	Study/article does not address any of the call for evidence review questions
Naviaux 2016 <sup>321</sup>	Study/article does not address any of the call for evidence review questions
Naviaux 2017 <sup>320</sup>	Study/article does not address any of the call for evidence review questions
Newberry 2018 <sup>322</sup>	Study/article does not address any of the call for evidence review questions
Newton 2010 <sup>323</sup>	Study/article does not address any of the call for evidence review questions

Study	Exclusion reason
NHS North Bristol 2019 <sup>324</sup>	No relevant themes (qualitative data on specialist services, not specific interventions)
Nijhof 2014 <sup>328</sup>	Incorrect study design (quantitative)
Nijhof 2013 <sup>327</sup>	Incorrect study design (quantitative)
Nijhof 2012 <sup>325</sup>	Incorrect study design (RCT)
Nijhof 2011 <sup>326</sup>	RCT protocol
Norfolk and Suffolk Service 2009 <sup>329</sup>	Unable to obtain (web link unavailable)
Norris 2017 <sup>330</sup>	Incorrect study design (cross-sectional analysis of quantitative data)
Ocon 2012 <sup>331</sup>	Study/article does not address any of the call for evidence review questions
Odoom 2018 <sup>332</sup>	Study/article does not address any of the call for evidence review questions
Office for National Statistics 2018 <sup>333</sup>	Not relevant to any call for evidence questions
Ojo-Amaize 1994 <sup>334</sup>	Study/article does not address any of the call for evidence review questions
Oliver 2018 <sup>335</sup>	Incorrect study design (quantitative survey)
PACE Trial participant dataset <sup>337</sup>	Study/article does not address any of the call for evidence review questions
Packer 1997 <sup>338</sup>	Study/article does not address any of the call for evidence review questions
Pakpoor 2017 <sup>339</sup>	Study/article does not address any of the call for evidence review questions
Parslow 2018 <sup>341</sup>	No relevant themes
Parslow 2017 <sup>343</sup>	Incorrect study design (qualitative)
Parslow 2017 <sup>342</sup>	Systematic review with different PICO
Parslow 2015 <sup>340</sup>	Incorrect study design (qualitative; assessed for monitoring and review question)
Pastula 2014 <sup>344</sup>	Study/article does not address any of the call for evidence review questions
Patrick Neary 2008 <sup>347</sup>	Incorrect interventions (no intervention)
Peci 2015 <sup>348</sup>	Study/article does not address any of the call for evidence review questions
Peckerman 2003 <sup>349</sup>	Study/article does not address any of the call for evidence review questions
Pemberton 2014 <sup>351</sup>	No relevant themes
Pemberton 2014 <sup>350</sup>	No relevant themes
Peterson 1991 <sup>356</sup>	Not relevant to any call for evidence question
Peterson 1994 <sup>357</sup>	Incorrect interventions (no intervention)
Perrin 1993 <sup>353</sup>	Review; study/article does not address any of the call for evidence review questions
Perrin 1998 <sup>354</sup>	Incorrect study design (non-randomised quantitative study)
Perrin 2011 <sup>355</sup>	Incorrect study design (non-randomised quantitative study)
Pheby 2009 <sup>358</sup>	Incorrect study design (survey) and no useable data
Physios for M.E <sup>359</sup> (unpublished)	Incorrect study design (qualitative)



Study	Exclusion reason
Plascencia-Villa 2016 <sup>360</sup>	Study/article does not address any of the call for evidence review questions
Polli 2019 <sup>361</sup>	Incorrect study design (quantitative)
Polo 2019 <sup>362</sup>	Incorrect study design (no qualitative data)
Prins 2005 <sup>364</sup>	Incorrect study design (quantitative)
Prins 2001 <sup>365</sup>	Incorrect study design (RCT)
Prokhorov 2016 <sup>366</sup>	Study/article does not address any of the call for evidence review questions
Puri 2011 <sup>367</sup>	Incorrect study design (diagnostic accuracy study)
Quarmby 2007 <sup>368</sup>	Incorrect study design (quantitative)
Raine 2004 <sup>369</sup>	Incorrect population (GPs)
Rand Corporation <sup>370</sup>	Study/article does not address any of the call for evidence review questions
Rawlins 2008 <sup>371</sup>	Study/article does not address any of the call for evidence review questions
Regland 2015 <sup>373</sup>	Incorrect study design (quantitative)
Reynolds 2014 <sup>374</sup>	Incorrect interventions (no intervention)
Richardson 2002 <sup>375</sup>	Review article
Rimes 2014 <sup>376</sup>	Incorrect study design (quantitative)
Roberts 2016 <sup>379</sup>	Study/article does not address any of the call for evidence review questions
Roberts 2009 <sup>377</sup>	Incorrect study design (quantitative)
Roberts 2018 <sup>378</sup>	Study/article does not address any of the call for evidence review questions
Roe <sup>380</sup>	No relevant themes (qualitative data on a specialist service, not specific interventions)
Roerink 2017 <sup>383</sup>	Study/article does not address any of the call for evidence review questions
Roerink 2017 <sup>381</sup>	Incorrect study design (RCT)
Roerink 2015 <sup>382</sup>	RCT protocol
Roma 2019 <sup>384</sup>	Incorrect interventions (no intervention)
Rowe 2019 <sup>387</sup>	No relevant themes
Rowe 2017 <sup>388</sup>	Review article
Ruggieri 2017 <sup>389</sup>	Study/article does not address any of the call for evidence review questions
Santini 2018 <sup>390</sup>	Study/article does not address any of the call for evidence review questions
Šarić 2016 <sup>391</sup>	Study/article does not address any of the call for evidence review questions
Scheeres 2009 <sup>392</sup>	Study/article does not address any of the call for evidence review questions
Scheeres 2008 <sup>394</sup>	Incorrect study design (quantitative)
Scheeres 2008 <sup>393</sup>	Incorrect study design (quantitative)
Scheeres 2007 <sup>395</sup>	Study/article does not address any of the call for evidence review questions
Schmaling 2019 <sup>396</sup>	Study/article does not address any of the call for evidence review questions
Schweitzer 1995 <sup>397</sup>	Not relevant to any call for evidence question
Severens 2004 <sup>400</sup>	Letter/commentary/expert opinion



Study	Exclusion reason
Shakespeare 2017 <sup>401</sup>	Study/article does not address any of the call for evidence review questions
Shan 2018 <sup>402</sup>	Study/article does not address any of the call for evidence review questions
Sharpe 1991 <sup>404</sup>	Study/article does not address any of the call for evidence review questions
Sharpe 2015 <sup>403</sup>	Incorrect study design (RCT)
Shukla 2015 <sup>405</sup>	Incorrect study design (quantitative)
Shungu 2012 <sup>406</sup>	Study/article does not address any of the call for evidence review questions
Smith 2014 <sup>408</sup>	Incorrect study design (systematic review of RCTs)
Smith 2013 <sup>409</sup>	Systematic review with different PICO
Smith 2015 <sup>407</sup>	Incorrect study design (systematic review of RCTs)
Snell 2013 <sup>410</sup>	Study/article does not address any of the call for evidence review questions
Snounou 2019 <sup>411</sup>	Incorrect study design (qualitative)
Solomon-Moore 2019 <sup>412</sup>	Incorrect study design (baseline cross-sectional data from an RCT)
Stahl 2014 <sup>413</sup>	Incorrect study design (quantitative)
Staud 2017 <sup>415</sup>	Incorrect study design (RCT)
Staud 2018 <sup>414</sup>	Incorrect study design (quantitative)
Steffen 2002 <sup>416</sup>	Study/article does not address any of the call for evidence review questions
Stevellink 2019 <sup>417</sup>	Study/article does not address any of the call for evidence review questions
Stevens 2018 <sup>418</sup>	Study/article does not address any of the call for evidence review questions
Stevens 2010 <sup>419</sup>	Incorrect study design (case study)
Stoll 2017 <sup>420</sup>	Systematic review with different PICO
Stordeur 2008 <sup>421</sup>	Study/article does not address any of the call for evidence review questions
Strassheim 2018 <sup>422</sup>	Study/article does not address any of the call for evidence review questions
Strawbridge 2019 <sup>423</sup>	Not relevant to any call for evidence question
Strayer 2012 <sup>424</sup>	Incorrect study design (RCT)
Strbak 2011 <sup>425</sup>	Study/article does not address any of the call for evidence review questions
Stulemeijer 2005 <sup>426</sup>	Incorrect study design (RCT)
Sumathipala 2008 <sup>427</sup>	Incorrect population (medically unexplained symptoms)
Sunnquist 2018 <sup>428</sup>	Incorrect study design (quantitative)
Suvorov 1998 <sup>430</sup>	Study/article does not address any of the call for evidence review questions
Swinscow 1997 <sup>431</sup>	Study/article does not address any of the call for evidence review questions
Taylor 2004 <sup>434</sup>	Incorrect study design (RCT)
Taylor 2019 Leeds and York CFS/ME Service <sup>433</sup> (unpublished)	No qualitative data
Taylor 2016 <sup>432</sup>	Study/article does not address any of the call for evidence review questions

Study	Exclusion reason
Teitelbaum 2001 <sup>435</sup>	Incorrect study design (RCT)
Terzi 2016 <sup>436</sup>	Study/article does not address any of the call for evidence review questions
The 2010 <sup>449</sup>	Incorrect study design (RCT)
The 2007 <sup>450</sup>	Incorrect study design (RCT)
The Consortium of Multiple Sclerosis Centers Health Services Research Subcommittee 1997 <sup>448</sup>	Not relevant to any call for evidence questions
The 25% ME Group 2010 <sup>437</sup>	Different focus to review question
The 25% ME Group 2014 <sup>438</sup> (unpublished)	Report on a research presentation; no qualitative data from people with ME/CFS
The 25% ME Group 2004 <sup>447</sup>	Incorrect study design (quantitative survey)
The 25% ME Group 2000 <sup>444</sup>	Incorrect study design (quantitative survey)
The 25% ME Group 2001 <sup>439</sup>	Incorrect study design (quantitative survey)
The 25% ME Group <sup>446</sup>	Article; no qualitative data from people with ME/CFS
The 25% ME Group 2002 <sup>443</sup> (unpublished)	Incorrect study design (quantitative survey)
The 25% ME Group 2017 <sup>441</sup>	Not relevant to any call for evidence questions
The 25% ME Group 2018 <sup>440</sup>	Not relevant to any call for evidence questions
The 25% ME Group 2001 <sup>442</sup>	Incorrect study design (quantitative survey)
The 25% ME Group 2016 <sup>445</sup>	Study/article does not address any of the call for evidence review questions (newsletter)
The ME Association 2010 <sup>451</sup>	Incorrect study design (quantitative survey)
The ME Association 2015 <sup>452</sup>	Survey including quantitative and qualitative data, but no analysis on the qualitative data
The Neurological Alliance 2019 <sup>453</sup>	Incorrect study design (quantitative survey)
Thomas 2009 <sup>454</sup>	Incorrect interventions (no intervention)
Tiersky 2001 <sup>455</sup>	Incorrect study design (quantitative)
Timbol 2019 <sup>457</sup>	No relevant themes
Togo 2015 <sup>458</sup>	Incorrect interventions (no intervention)
Trabal 2012 <sup>459</sup>	Study/article does not address any of the call for evidence review questions
Tummers 2013 <sup>462</sup>	Incorrect study design (quantitative)
Tummers 2012 <sup>461</sup>	Incorrect study design (RCT)
Tummers 2010 <sup>460</sup>	Incorrect study design (quantitative)
Twisk 2014 <sup>467</sup>	Letter/commentary/expert opinion
Twisk 2017 <sup>464</sup>	Letter/commentary/expert opinion
Twisk 2018 <sup>463</sup>	Report summary; full report in Dutch
Twisk 2015 <sup>466</sup>	Study/article does not address any of the call for evidence review questions
Twisk 2015 <sup>465</sup>	Incorrect study design (review article)
Van Campen 2018 <sup>468</sup>	Incorrect interventions (no intervention)
Van Campen 2018 <sup>470</sup>	Study/article does not address any of the call for evidence review questions
Van Campen 2019 <sup>469</sup>	Incorrect study design (quantitative)

Study	Exclusion reason
Van Den Eede 2011 <sup>471</sup>	Study/article does not address any of the call for evidence review questions
Van Der Schaaf 2015 <sup>473</sup>	RCT protocol
Van Der Schaaf 2017 <sup>472</sup>	Study/article does not address any of the call for evidence review questions
Van Der Werf 2002 <sup>474</sup>	Study/article does not address any of the call for evidence review questions
Van Konynenburg 2010 <sup>475</sup>	Conference abstract
Van Kuppeveld 2010 <sup>476</sup>	Study/article does not address any of the call for evidence review questions
VanNess 2007 <sup>477</sup>	Incorrect interventions (no intervention)
VanNess 2010 <sup>478</sup>	Incorrect intervention (exercise test)
Velleman 2016 <sup>479</sup>	Incorrect population (siblings) and no relevant themes
Vercoulen 1996 <sup>481</sup>	Incorrect study design (RCT)
Vercoulen 1996 <sup>480</sup>	Study/article does not address any of the call for evidence review questions
Vermeulen 2010 <sup>482</sup>	Study/article does not address any of the call for evidence review questions
Vermeulen 2014 <sup>483</sup>	Study/article does not address any of the call for evidence review questions
Vernon 2004 <sup>484</sup>	Unable to obtain
Verspaandonk 2015 <sup>485</sup>	Incorrect study design (quantitative)
Vink 2017 <sup>486</sup>	Incorrect study design (quantitative)
Vink 2018 <sup>489</sup>	Review of an RCT
Vink 2018 <sup>488</sup>	Incorrect study design (reanalysis of a Cochrane review); no qualitative data
Vink 2019 <sup>490</sup>	Review article
Vink 2019 <sup>487</sup>	Incorrect study design (reanalysis of a Cochrane review); no qualitative data
Wallis 2016 <sup>492</sup>	Study/article does not address any of the call for evidence review questions
Wallis 2018 <sup>491</sup>	Incorrect study design (quantitative)
Wang 2017 <sup>494</sup>	Study/article does not address any of the call for evidence review questions
Watt 2012 <sup>495</sup>	Incorrect study design (quantitative)
Wearden 2006 <sup>498</sup>	Study/article does not address any of the call for evidence review questions
Wearden 2010 <sup>496</sup>	Incorrect study design (RCT)
Wearden 2013 <sup>497</sup>	Incorrect study design (prognostic)
Webb 2011 <sup>500</sup>	No relevant themes
Werbach 2000 <sup>501</sup>	Incorrect study design (literature review)
White 2007 <sup>504</sup>	RCT protocol
White 2011 <sup>503</sup>	Incorrect study design (RCT)
White 2013 <sup>502</sup>	Study/article does not address any of the call for evidence review questions
Whitehead 2009 <sup>505</sup>	Study/article does not address any of the call for evidence review questions
Whitehead 2002 <sup>506</sup>	Study/article does not address any of the call for evidence review questions

Study	Exclusion reason
Wiborg 2010 <sup>508</sup>	Incorrect study design (reanalysis of RCTs)
Wiborg 2014 <sup>510</sup>	Incorrect study design (quantitative)
Wiborg 2015 <sup>509</sup>	Incorrect study design (RCT)
Wiborg 2011 <sup>507</sup>	Incorrect study design (quantitative)
Wieczorek 2017 <sup>493</sup>	Study/article does not address any of the call for evidence review questions
Wilshire 2018 <sup>514</sup>	Incorrect study design (reanalysis of an RCT)
Wilshire 2019 <sup>513</sup>	Letter/commentary/expert opinion
Wilshire 2017 <sup>511</sup>	Incorrect study design (critical commentary and reanalysis of an RCT)
Wilshire 2017 <sup>512</sup>	Letter/commentary/expert opinion
Worm-Smeitink 2019 <sup>516</sup>	Incorrect study design (RCT)
Worm-Smeitink 2017 <sup>515</sup>	Study/article does not address any of the call for evidence review questions
Worm-Smeitink 2016 <sup>517</sup>	Incorrect study design (quantitative)
Yorkshire Fatigue Clinic 2019 <sup>352</sup>	Incorrect study design (survey)
Zablotskii 2016 <sup>518</sup>	Study/article does not address any of the call for evidence review questions
Zablotskii 2018 <sup>519</sup>	Study/article does not address any of the call for evidence review questions
Zhi 2017 <sup>520</sup>	Study/article does not address any of the call for evidence review questions
Zielinski 2019 <sup>521</sup>	Study/article does not address any of the call for evidence review questions

## L.2 Health economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2004 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

None.

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