NIHR | National Institute for Health and Care Research

Health Technology Assessment

Check for updates

Research Article

Recent research in myalgic encephalomyelitis/chronic fatigue syndrome: an evidence map

Alex Todhunter-Brown,[1*] Pauline Campbell,[1] Cathryn Broderick,[2] Julie Cowie,[1] Bridget Davis,[1] Candida Fenton,[2] Sarah Markham,[3,4] Ceri Sellers[1] and Katie Thomson[1] on behalf of NIHR Evidence Synthesis Scotland Initiative (NESSIE)

[1]NESSIE, Glasgow Caledonian University, Glasgow, UK
[2]NESSIE, Usher Institute, University of Edinburgh, Edinburgh, UK
[3]NESSIE Patient and public involvement member, UK
[4]Department of Biostatistics and Health Informatics, King's College London, London, UK

[*]Corresponding author nessie@ed.ac.uk

Published March 2025
DOI: 10.3310/BTBD8846

Abstract

Background: Myalgic encephalomyelitis/chronic fatigue syndrome is a chronic condition, classified by the World Health Organization as a nervous system disease, impacting around 17 million people worldwide. Presentation involves persistent fatigue and postexertional malaise (a worsening of symptoms after minimal exertion) and a wide range of other symptoms. Case definitions have historically varied; postexertional malaise is a core diagnostic criterion in current definitions. In 2022, a James Lind Alliance Priority Setting Partnership established research priorities relating to myalgic encephalomyelitis/chronic fatigue syndrome.

Objective(s): We created a map of myalgic encephalomyelitis/chronic fatigue syndrome evidence (2018–23), showing the volume and key characteristics of recent research in this field. We considered diagnostic criteria and how current research maps against the James Lind Alliance Priority Setting Partnership research priorities.

Methods: Using a predefined protocol, we conducted a comprehensive search of Cochrane, MEDLINE, EMBASE and Cumulative Index to Nursing and Allied Health Literature. We included all English-language research studies published between January 2018 and May 2023. Two reviewers independently applied inclusion criteria with consensus involving additional reviewers.

Studies including people diagnosed with myalgic encephalomyelitis/chronic fatigue syndrome using any criteria (including self-report), of any age and in any setting were eligible. Studies with < 10 myalgic encephalomyelitis/chronic fatigue syndrome participants were excluded.

Data extraction, coding of topics (involving stakeholder consultation) and methodological quality assessment of systematic reviews (using A MeaSurement Tool to Assess systematic Reviews 2) was conducted independently by two reviewers, with disagreements resolved by a third reviewer. Studies were presented in an evidence map.

Results: Of the 11,278 identified studies, 742 met the selection criteria, but only 639 provided sufficient data for inclusion in the evidence map. These reported data from approximately 610,000 people with myalgic encephalomyelitis/chronic fatigue syndrome. There were 81 systematic reviews, 72 experimental studies, 423 observational studies and 63 studies with other designs. Most studies (94%) were from high-income countries. Reporting of participant details was poor; 16% did not report gender, 74% did not report ethnicity and 81% did not report the severity of myalgic encephalomyelitis/chronic fatigue syndrome. Forty-four per cent of studies used multiple diagnostic criteria, 16% did not specify criteria, 24% used a single criterion not requiring postexertional malaise and 10% used a single criterion requiring postexertional malaise. Most (89%) systematic reviews had a low methodological quality. Five main topics (37 subtopics) were included in the evidence map. Of the 639 studies; 53% addressed the topic 'what is the cause?'; 38% 'what is the problem?'; 26% 'what can we do about it?'; 15% 'diagnosis and assessment'; and 13% other topics, including 'living with myalgic encephalomyelitis/chronic fatigue syndrome'.

This article should be referenced as follows:
Todhunter-Brown A, Campbell P, Broderick C, Cowie J, Davis B, Fenton C, *et al.* Recent research in myalgic encephalomyelitis/chronic fatigue syndrome: an evidence map [published online ahead of print March 26 2025]. *Health Technol Assess* 2025. https://doi.org/10.3310/BTBD8846

Discussion: Studies have been presented in an interactive evidence map according to topic, study design, diagnostic criteria and age. This evidence map should inform decisions about future myalgic encephalomyelitis/chronic fatigue syndrome research.
Limitations: An evidence map does not summarise what the evidence says. Our evidence map only includes studies published in 2018 or later and in English language. Inconsistent reporting and use of diagnostic criteria limit the interpretation of evidence. We assessed the methodological quality of systematic reviews, but not of primary studies.
Conclusions: We have produced an interactive evidence map, summarising myalgic encephalomyelitis/chronic fatigue syndrome research from 2018 to 2023. This evidence map can inform strategic plans for future research. We found some, often limited, evidence addressing every James Lind Alliance Priority Setting Partnership priority; high-quality systematic reviews should inform future studies.
Funding: This article presents independent research funded by the National Institute for Health and Care Research (NIHR) Evidence Synthesis programme as award number NIHR159926.
A plain language summary of this research article is available on the NIHR Journals Library Website https://doi.org/10.3310/BTBD8846.

Background

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a chronic disease, classified by the World Health Organization as a disease of the nervous system,[1] with fluctuating symptoms affecting multiple body systems. ME/CFS is conservatively estimated to affect around 250,000 people in the UK and 17 million people worldwide, with an estimated *minimum* prevalence of 0.2% of the UK population.[2] ME/CFS is characterised by debilitating fatigue (physical and/or mental exhaustion) that is worsened by activity, postexertional malaise (PEM; a disproportionate worsening or triggering of symptoms following even minor cognitive, physical, emotional or social exertion) and several other common symptoms, including pain, unrefreshing sleep, cognitive impairment, gastrointestinal problems and orthostatic intolerance (OI).[2–6]

The ME/CFS has a substantial health burden, negatively impacting the ability to function and the quality of life.[7–9] While ME/CFS affects people of all ages and genders, it disproportionately affects women, and people who are older are more likely to be more severely affected.[5]

The ME/CFS remains a poorly understood condition.[6] In 2022, key stakeholders, including people living with ME/CFS, their families, carers and health professionals, worked in partnership in a James Lind Alliance Priority Setting Partnership (JLA PSP) to reach consensus on the research priorities for ME/CFS.[10,11] The resulting top 10+ research questions comprise a series of broad, overlapping questions primarily focused on the cause, diagnosis and treatment of ME/CFS.[10,11] To support and encourage future-informed, high-quality, useful collaborative research and research funding worldwide, a comprehensive map of existing research evidence (and evidence gaps) is essential.[12]

Synthesis of research evidence relating to ME/CFS is recognised to be challenging due to the use of a wide range of diverse case definitions and diagnostic criteria.[2] Historically, clinical labels have lacked consistency, including ME, CFS, CFS/ME, chronic fatigue, fatigue syndrome and other terms. Further, diagnostic criteria have varied, leading to inconsistencies in patient groups within studies. Diagnostic criteria in which PEM (sometimes referred to as postexertional symptom exacerbation) is a core component include: Canadian Consensus Criteria 2003 (CCC),[13] International Consensus Criteria 2011 (ICC) (this is an update of the CCC),[14] Institute of Medicine 2015 (IOM)[15] and National Institute for Health and Care Excellence (NICE) 2021.[6] Other diagnostic criteria in which PEM is not a core component include Oxford[16] and Fukuda [Centers for Disease Control (CDCs)][17] criteria. A comprehensive map of existing research evidence, including all research regardless of clinical terms and diagnostic criteria, will bring together studies that include varied populations of patients. Consequently, it is essential that the diagnostic criteria used in studies are central to mapping of this evidence.

Aim and objectives

We aimed to produce an evidence map. An evidence map summarises what evidence is available, but it does not summarise what the evidence says.[18]

Objective

Our objective was to produce an evidence map of national and international research in ME/CFS, considering diagnostic criteria and showing how current research maps against key topics covered by the JLA PSP research priorities.[10,11]

Review questions

1. What are the volume (number of studies and participants) and key characteristics (including study

design, population, and focus/topic) of research in this field?
2. Which key topics have research evidence that has (and has not) included participants with different diagnostic criteria?
3. Which of the JLA PSP research priority topics have/have not been addressed by research evidence? Where do evidence gaps remain?

Methods

Study design

Our study was designed to develop an interactive evidence map that brings together recently published literature relating to ME/CFS categorised using key topics identified from the JLA PSP top 10+ research questions.[10,11] A detailed study protocol was developed and published prior to the conduct of this work.[19] In below text, we summarise key aspects of our methods; further details, including justification for key elements, are available in the protocol.[19]

Inclusion criteria

We considered studies that included people of any age who were diagnosed with ME/CFS. Studies were included based on the study authors' definition of ME/CFS. This included studies in which any diagnostic criteria were used (e.g. CCC, ICC, IOM, NICE 2021, Oxford or Fukuda criteria) or there was a physician report or patient self-report of ME/CFS. We also included studies with a mixed population (i.e. people with a range of different health conditions) where this specifically included ME/CFS, and the number of people with ME/CFS were reported (≥ 10 people).

We included quantitative and qualitative research studies, systematic reviews (SRs) and economic evaluations. We included SRs regardless of the type of evidence synthesised (i.e. quantitative, qualitative and mixed-methods) and the type of question addressed (e.g. epidemiology, intervention effectiveness, diagnostic test accuracy and patient experiences), if they described a research process in which literature relevant to a stated question is identified and brought together (synthesised) using explicit methods.[20]

Exclusion criteria

We excluded studies which:

- included people with fatigue explicitly related to another health condition (e.g. cancer- or stroke-related fatigue) or pharmaceutical adverse reactions
- included people with work-/occupation-related fatigue
- included people with another condition [e.g. Gulf War syndrome, functional somatic disorders, fibromyalgia, postural orthostatic tachycardia syndrome (POTS), long coronavirus disease (COVID), Epstein–Barr virus (EBV) and broad groups of rheumatic disorders or autoimmune conditions] unless these studies included an identified subset of people with ME/CFS and met our inclusion criteria
- involved animals or animal tissue
- were audits, quality improvement projects, commentaries, opinion pieces and case studies/series with < 10 participants with ME/CFS
- were not published in the English language.

Identification of studies

Search strategy

The search strategy was developed by an information specialist. We searched four electronic databases:

- the Cochrane Central Register of Controlled Trials via Cochrane Register of Studies Online
- MEDLINE (Ovid MEDLINE Epub Ahead of Print, In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE)
- EMBASE via Ovid
- Cumulative Index to Nursing and Allied Health Literature via EBSCO.

Searches were restricted by date, starting from 1 January 2018 to 29 May 2023, and by language to English only. No filters were used for study type, so all publication types were retrieved. The MEDLINE search strategy is included in *Appendix 1*, which was adapted for other listed databases.

Management of searching and screening

Results of the search were de-duplicated in EndNote [Clarivate Analytics (formerly Thomson Reuters), Philadelphia, PA, USA] and were uploaded into Covidence (Covidence systematic review software. In: Veritas Health Innovation, Melbourne, VIC, Australia). Two reviewers independently applied selection criteria to titles and abstracts, deciding if each was an 'exclude' or 'potential include'. Disagreements between independent reviewers were discussed by two (different) reviewers who reached consensus on a decision.

Full texts were obtained for all studies considered as 'potential includes'. Two reviewers independently applied inclusion criteria, and consensus was reached through discussion between two (different) reviewers for any papers where there were disagreements. All full-text papers selected as 'include' at this stage were included in the review. We included at the study level (i.e. when there were multiple papers reporting the same study, we grouped these together and counted them as a single study). Reasons for exclusion were documented.

The results of the search are reported using a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart[21] that clearly details the decision processes at each stage of the review.

Data extraction and coding

Within Covidence, two reviewers independently extracted and coded the data from the included studies. Disagreements were resolved through discussion involving a third reviewer. Data items and codes are reported in our protocol.[19]

Piloting and development

We piloted our coding form with 30 included studies. We discussed the results of the pilot coding and refined categories accordingly. Clarification around operationalisation of the data codes was developed iteratively by discussing, at weekly meetings, coding queries, uncertainties and areas where there were commonly disagreements between independent reviewers. This led to clarifications around categorisation of the study design, introducing a flow diagram to aid decisions and limiting reviewers to only selecting one study design. Details of these changes/clarifications are provided in *Report Supplementary Material 1*.

Additional coding

Following the dual data extraction and coding within Covidence, we exported data into Microsoft Excel® (Microsoft Corporation, Redmond, WA, USA) and applied a series of pre-planned additional codes. These included:

- Country in which the study was conducted – one reviewer coded by geographical region and income using the World Bank Group (World Bank Group, Washington, DC, USA) database based on the extracted data relating to the country in which the study was conducted.
- Topics and subtopics – these were developed using a pre-planned iterative approach, initially building on the JLA PSP research priorities and involving rounds of consultation with stakeholders and development of codes suitable for all identified studies. Further details are provided in *Report Supplementary Material 2*, and final agreed topics and subtopics, with definitions, are provided in *Appendix 2*. Each study was discussed by two reviewers who agreed on the topics (and subtopics) it addressed.

Quality assessment of included studies

As planned, we assessed the risk of bias (ROB) of SRs. Our justification for this is that knowledge of the quality of SRs will be central to informing decisions about future research and to judgement of certainty in the findings of these SRs. We did not assess the ROB of primary research studies. Rationale for this is that evidence maps often do not involve conducting quality appraisals of studies due to the workload involved. Instead, as recommended, they are coded and filtered according to study design. Our justification for this was that, by capturing the study design, we were able to provide a sense of the type of work that is currently being conducted, informing decisions about future SRs and/or primary research.

Risk of bias of included SRs was assessed using A MeaSurement Tool to Assess systematic Reviews 2 (AMSTAR2) (a critical appraisal tool for SRs).[22] Two independent reviewers made AMSTAR2 judgements, with disagreements resolved through discussion. We documented areas of disagreement and iteratively developed notes to support consistent responses. We planned, if necessary, to consult with stakeholders to inform our decisions, but this was not required. Following completion of all agreed A MeaSurement Tool to Assess systematic Reviews (AMSTAR) judgements, we rated our confidence in the results of each review as high, moderate, low or critically low confidence, using the approach recommended by Shea (2017).[22] We summarised the AMSTAR2 judgements using the Robvis tool [URL: https://mcguinlu.shinyapps.io/robvis/ (accessed 20 February 2025)].[23] This was not pre-stated in our protocol; details are provided in *Appendix 3*.

These ROB assessments were judgements relating to the methodological quality of the conduct (and reporting) of the SRs. We did *not* assess the quality of evidence within the review or consider the diagnostic criteria applied by SR authors when selecting studies for inclusion.

Evidence map

Following discussion with stakeholders about what items they felt were most important to include, we produced an interactive evidence map using EPPI-Mapper (EPPI Centre, London, UK).[24] The primary constructs of interest reflected within the map included:

- topics/subtopics (as columns)
- study designs (as rows)

- ME/CFS diagnostic criteria used within study (as filter 1)
- the age of the population included in the study (as filter 2).

A draft map was initially generated and modified following written and verbal feedback from stakeholders. This feedback primarily focused on the topics/subtopics (see *Additional coding*) and informed agreed terms and definitions for study designs (see *Appendix 4*). Stakeholders also provided input to the title, background information and layout of the map.

Synthesis

A brief narrative synthesis summarising the volume (number and size of studies) and key characteristics (e.g. study design, country and population) of the research evidence relating to key areas of ME/CFS (according to the topics and subtopics) was produced. As planned, this commentary does not bring together the results of the identified studies. The narrative also discusses the volume of evidence in relation to the JLA PSP top 10+ questions, identifying where there is study evidence and where there are gaps.

Dissemination/knowledge mobilisation

We developed a knowledge mobilisation plan, which we discussed with our stakeholders and planned to refine iteratively throughout the course of the project. However, following consultation with the National Institute for Health and Care Research (NIHR) and the Department of Health and Social Care (DHSC) on appropriate communication strategies, and given the sensitive and conflicting nature of the topic of this review, it was agreed that the DHSC would manage all communications of findings. This would ensure a comprehensive process to communicate with researchers and research funders.

Patient and public involvement

A NIHR Evidence Synthesis Scotland InitiativE (NESSIE) patient and public involvement (PPI) co-investigator has overseen the stakeholder involvement in this review.

Stakeholder Involvement

We included a range of stakeholders in this work, including people with lived experience of ME/CFS and people with clinical and research expertise. We followed national standards and principles,[25–27] and we considered the lessons related to accessibility, which were produced by the ME/CFS JLA PSP. We formed two Review Advisory Groups. One group comprised three patient members of a third-sector ME/CFS Patient Advisory Group; two representatives from the DHSC ME/CFS Research Working Group; two scientific/academic members involved in ME/CFS research; a third-sector representative; a NIHR representative research manager; and our NESSIE PPI co-applicant. The second group comprised three people with lived experience of ME/CFS. We sought input that influenced decisions during the planning stages and during the final synthesis and writing-up stages of our work. Details of our stakeholder involvement are provided in *Report Supplementary Material 3*; this includes reporting the involvement of stakeholders using the Authors and Consumers Together Impacting on eVidencE framework and Guidance for Reporting Involvement of Patients and the Public 2 reporting checklist (short form).[28,29]

Equality, diversity and inclusion

We aimed to integrate equality, diversity and inclusion with our overall PPI and dissemination strategy, while ensuring we did not overburden minoritised groups. For this ME/CFS review, we ensured engagement with relevant third-sector and representative organisations in the scoping of the review by using established networks where appropriate. Our Evidence Synthesis Group also benefited from the inclusion of co-applicants who are experienced advocates for LGBT+ and disability issues, all of whom had input in this review.

Results

Results of the search

We screened the titles and abstracts of 11,278 studies and then considered the full text of 1410 studies. Of these, 668 studies were excluded. The main reasons for excluding studies were publication prior to 2018 (n = 249) and wrong study design (n = 137) (see *Report Supplementary Material 4*).

We included 742 studies (reported across 851 records; see *Report Supplementary Material 5* for details of studies with multiple publications). Of these 742 studies, 639 met our criteria for inclusion in the evidence map.[7,10,30–666]

The PRISMA flow chart given in *Figure 1* shows the flow of studies across the review.

Of the 742 studies, 103 (14%) studies were primarily focused on another health condition and contained limited data relating to participants with ME/CFS. Consequently, we did not complete any further data extraction relating to these studies. These studies are listed in *Report Supplementary Material 6*, with reasons, and these are not included within the synthesis given below or in the evidence map. The following section

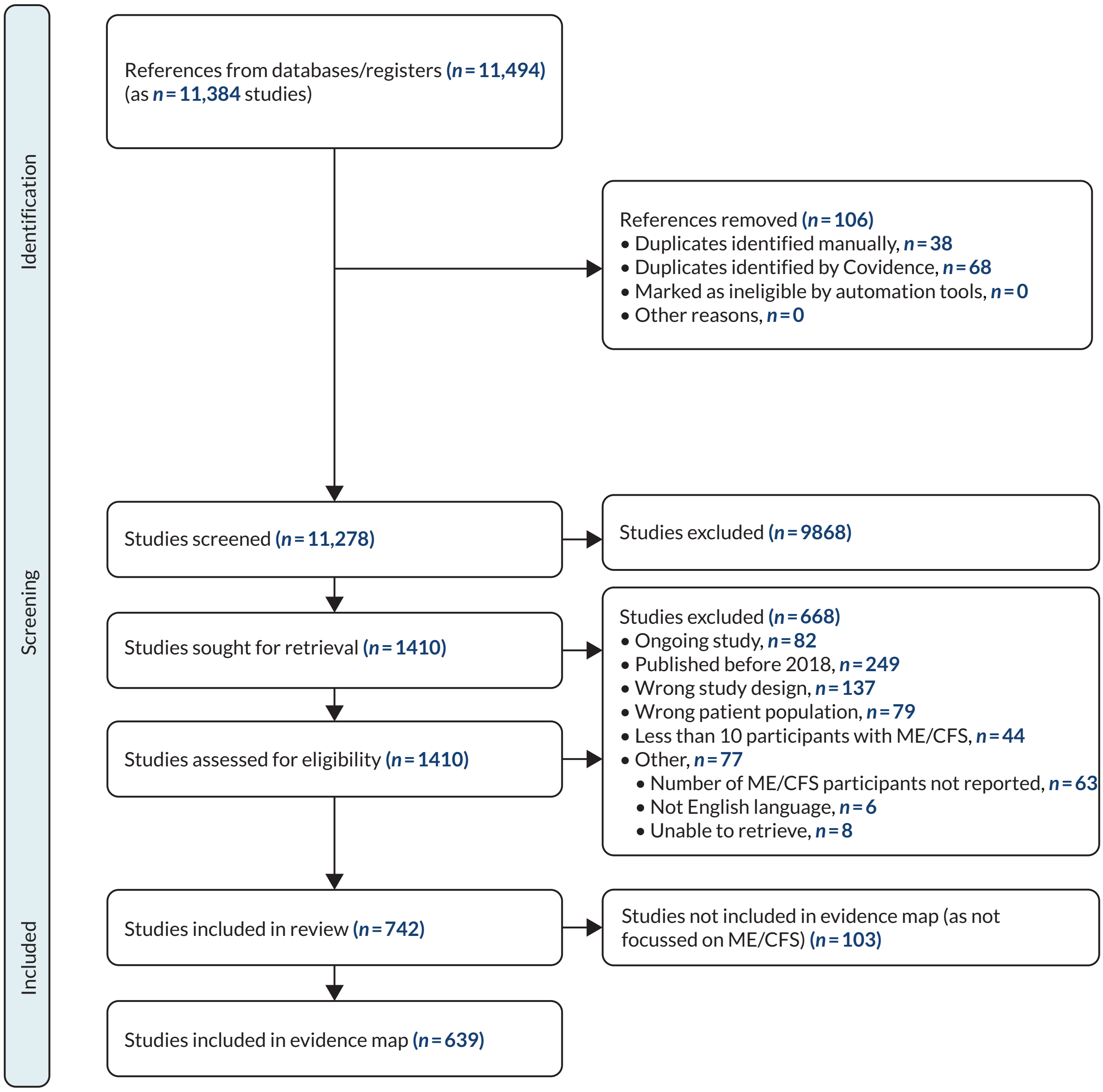

FIGURE 1 The PRISMA flow chart.

therefore contains data relating to the remaining included 639 studies.

Key characteristics of included studies

The 639 included studies contain data relating to approximately 610,000 people with ME/CFS. Most of these studies used an observational study design (423/639). The remaining studies included 81 SRs, 72 experimental studies of which 29 were randomised controlled trials (RCTs), and 63 other designs (of which 25 were qualitative studies). The interactive evidence map (available in *Report Supplementary Material 7*) provides greater detail in relation to the number of studies addressing different research subtopics. *Table 1* summarises numbers of included studies and participants, with characteristics of included studies provided in *Report Supplementary Material 8*.

Countries in which studies were conducted

Seventy-nine per cent (508/639) of studies were conducted in a single country. These countries were: USA (*n* = 120), UK (*n* = 106), Australia (*n* = 37), Netherlands (*n* = 34), Norway (*n* = 30), Sweden (*n* = 24), China (*n* = 23), Spain (*n* = 22), Germany (*n* = 17), Belgium (*n* = 13), Japan (*n* = 13), France (*n* = 9), Latvia (*n* = 8), Taiwan (*n* = 8), New Zealand (*n* = 7), Italy (*n* = 6), Republic of Korea (*n* = 6), Poland (*n* = 6), Canada (*n* = 2), Denmark (*n* = 2), Finland (*n* = 2), Russian Federation (*n* = 2), and 1 study from Austria, Bulgaria, India, Islamic Republic of Iran, Ireland, Israel, Saudi Arabia, South Africa, Switzerland, Turkey and Ukraine (*Figure 2*). Nineteen per cent (110/639) were conducted in more than one country, and 2% (12/639) did not report the country. For studies conducted in a single country: 94% (477/508) were from high-income countries,

DOI: 10.3310/BTBD8846

TABLE 1 Summary of numbers of studies and number of participants

Type of design	Study design	Total number of studies	Studies reporting participant numbers	Total number of participants with ME/CFS	Mean number of participants with ME/CFS per study	Minimum number of participants with ME/CFS in a study	Maximum number of participants with ME/CFS in a study
Evidence studies	SR	81	71	139,881	1970.2	63	23,906
Experimental studies	RCT	29	29	2713	93.6	11	290
	Non-randomised study	43	43	5300	123.3	10	1226
Observational studies	Biospecimen study	137	136	18,436	135.6	10	2992
	Case-control study	116	115	34,248	297.8	10	9896
	Cohort study (prospective/retrospective)	51	51	280,937	5508.6	10	266,444
	Survey/cross-sectional study	118	118	27,283	231.2	11	1534
	Case series (> 10 participants)	1	1	42	42.0	42	42
Other	Economic evaluation	2	1	85	85.0	85	85
	Mixed-methods	8	8	21,348	2668.5	39	20,140
	Qualitative	25	25	1004	40.2	10	541
	Other: analyses of data sets	25	25	77,763	3110.5	10	31,578
	Other: combined – two study phases with different designs	2	2	281	140.5	99	182
	Other: prioritisation	1	1	1332	1332.0	1332	1332
Total (primary studies)		639	626	610,653[a]	975.5	10	266,444

a This number is likely to be an overestimation of the individual people involved in studies, as some participants will be included in multiple publications, which we have not identified as being the same study. Further, some studies are focused on analyses of large data sets, and there is likely to be duplication between these. Numbers included in SRs are not included here, as this will duplicate numbers presented in primary studies.

This article should be referenced as follows:
Todhunter-Brown A, Campbell P, Broderick C, Cowie J, Davis B, Fenton C, *et al.* Recent research in myalgic encephalomyelitis/chronic fatigue syndrome: an evidence map [published online ahead of print March 26 2025]. *Health Technol Assess* 2025. https://doi.org/10.3310/BTBD8846

5% (28/508) from upper middle-income countries and 1% (3/508) from lower middle-income countries.

Demographics of participants in studies

Age

Most of the studies only included adults (71%; 453/639), and 10% (63/639) only included children and young people. Seven per cent (46/639) included both children and adults. None of the studies only included older adults. Age was not reported in 12% of studies (77/639).

Gender/sex

Most studies (74.5%; 476/639) included both men and women, with nine (1.4%) of these studies also reporting people identifying as genders other than men or women. Nine per cent (56/639) included women only, and 0.5% (3/639) included men only. Gender was not clearly reported in 16% (104/639) of studies.

Race/ethnicity

Most studies did not report any data relating to race or ethnicity (77%; 493/639). In 12% (74/639), a large majority (generally, 95–99%) of the participants were described as white. Eleven per cent of studies (69/639) provided a more detailed breakdown of the race or ethnicity of participants.

Diagnosis of myalgic encephalomyelitis/chronic fatigue syndrome

Sixteen per cent (101/639) of the studies did not state how ME/CFS was diagnosed for the included participants or were unclear. Thus, we only have data relating to the diagnostic criteria for 84% (538/639) of studies. Of these studies, 56% (300/538) used a single diagnostic criterion, while 44% (238/538) reported use of more than one diagnostic criterion (see data given in *Table 2*). *Figure 3* illustrates the combinations of diagnostic criteria reported, showing that there were 22 different combinations of multiple diagnostic criteria reported by three or more studies.

In 3.5% (23/639) of included studies, there was clear diagnosis information only for some participants. Thirty-one per cent (199/639) of studies used an 'other' diagnostic criteria (either a single diagnostic criterion, or a combination of 'other' criteria). 'Other' criteria used by studies included self-report, health record data and other published case definitions.

Thirty-seven per cent (234/639) of studies used diagnostic criteria that included a requirement for PEM. However, of these, 69% (161/234) *also* cited diagnosis criteria that did not have a specific requirement for PEM, meaning that we can only be confident that PEM was a criterion for all participants in 11% (73/639) of studies. For further clarification of the diagnostic criteria used across studies, detailed appraisal of each individual study is required, exploring whether studies reporting multiple criteria are using these in an additive (e.g. all participants fulfil Fukuda AND IOM criteria) or alternative (e.g. all participants fulfil Fukuda OR IOM criteria) approach.

FIGURE 2 Countries in which studies were conducted.

TABLE 2 Numbers of studies reporting use of one, or multiple, diagnostic criteria

	Studies where this is used as:	
Diagnosis criteria	**One of criteria**	**Only criterion**
CCC (Carruthers 2003)[13]	170	38
ICC (Carruthers 2011)[14]	95	13
IOM (IOM 2015)[15]	47	10
NICE (2021)[6]	2	2
Oxford criteria (Sharpe 1991)[16]	51	8
Fukuda (CDC)[17]	334	148

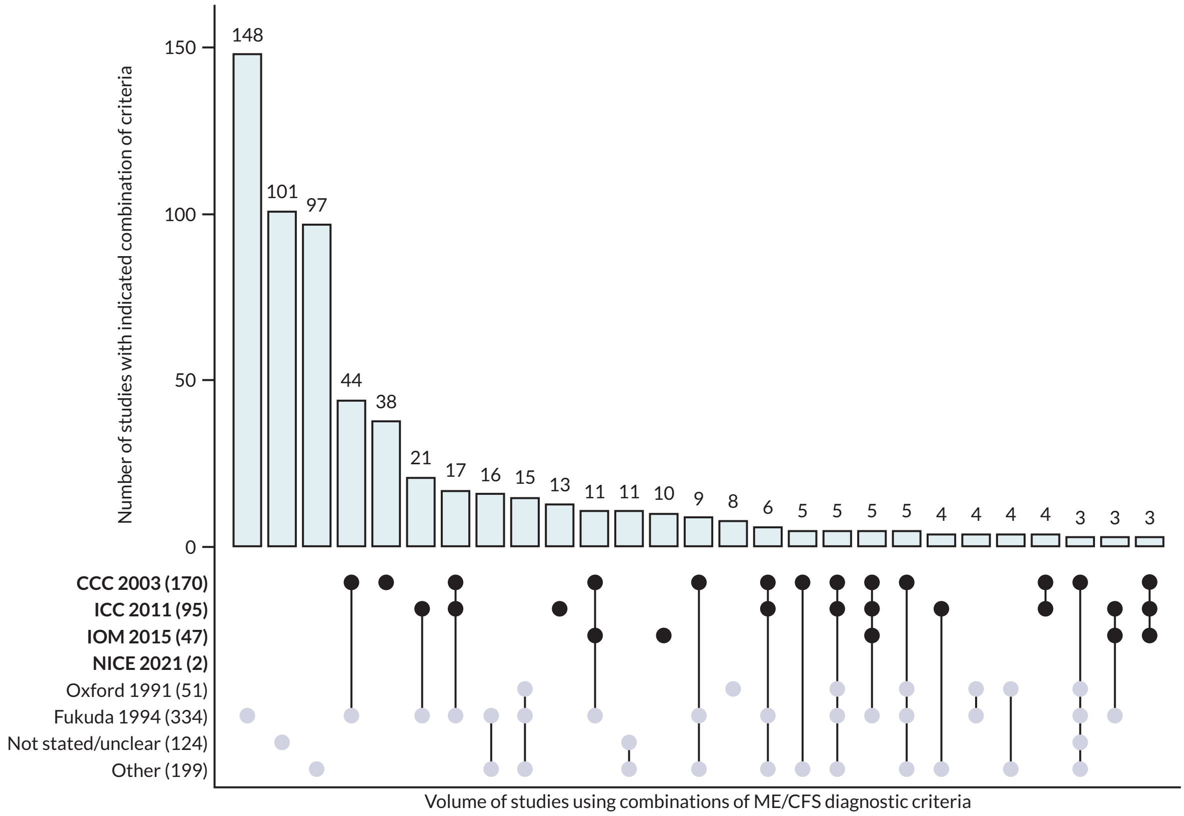

FIGURE 3 Combinations of diagnostic criteria reported by studies. Note: Included diagnostic criteria listed on bottom left of graph; criteria in bold require PEM; total number of studies using each criteria is in brackets. Dots represent criteria, or combination of criteria; bar graph illustrates number of studies with each criteria/combination of criteria. Combinations of diagnostic criteria used by < 3 studies are excluded from this figure (e.g. 170 studies used CCC 2003 criteria; 44 used CCC 2003 in combination with Fukuda 1994).

Severity of myalgic encephalomyelitis/chronic fatigue syndrome

Most studies (81%; 515/639) did not report the level of severity of ME/CFS, although often there were outcome assessments that provided information on the severity of some symptoms. The remaining 19% (124/639) explicitly reported the level of severity of ME/CFS. These studies reported including participants with:

- mild ME/CFS – in 59/124 (48%) studies
- moderate ME/CFS – in 75/124 (60%) studies
- severe ME/CFS – in 87/124 (70%) studies
- very severe ME/CFS – in 17/124 (14%) studies.

Risk of bias

As planned, we only assessed ROB of the SRs (n = 81) and did not assess ROB of primary studies. The AMSTAR2 judgements for ROB for each SR are provided in *Report Supplementary Material 9*, and a summary of these judgements are provided in *Report Supplementary Material 10*. *Appendix 5* provides a brief overview of the included SRs, including a statement of the overall confidence in each review, based on the AMSTAR2 ROB judgements. Our overall confidence in the methodological quality of the SRs was moderate for 9, low for 20 and critically low for 52. These judgements do not reflect the quality or the diagnostic criteria used by studies included in these SRs.

Evidence map

The evidence map is available at *Report Supplementary Material 7*, with a supporting video to describe how to use the map at *Report Supplementary Material 11* and transcript of the video at *Report Supplementary Material 12*.

Topics and subtopics addressed

The interactive evidence map (see *Report Supplementary Material 7*) details the topics and subtopics addressed using studies of different designs and enables the data to be viewed according to the diagnostic criteria for ME/CFS and by population age (adult/children and young people). *Appendix 6*, *Tables 3–8* summarise the total volume of data for each topic/subtopic, and there is a brief narrative synthesis for each subtopic in the section below. References to studies are provided in the evidence map. Aims of the SRs, and number of studies identified, are shown in *Appendix 5*.

Diagnosis and assessment

A total of 99 studies addressed this topic, of which around 48% of studies described using diagnostic criteria in which PEM was an essential component.

Diagnosis of myalgic encephalomyelitis/chronic fatigue syndrome

Thirty-eight studies (including 275,432 participants) addressed this subtopic. These include 4 SRs (confidence in results: low for two; critically low for two), 27 observational studies and 7 studies using other designs (all of which involved analysis of data sets); most participants (266,444) came from a single study.[589]

Biomarkers for diagnosis

Fifteen studies (including 1022 participants) addressed this subtopic; all of these were observational studies.

Distinguishing different kinds of myalgic encephalomyelitis/chronic fatigue syndrome

Thirty-six studies (including 7981 participants) addressed this subtopic. These include 34 observational studies and 2 studies using other designs (both of which involved an analysis of the data sets).

Diagnosis of postexertional malaise

Fourteen studies (including 3699 participants) addressed this subtopic. This includes 3 SRs (confidence in results: low for 1; critically low for 2), 10 observational studies and 1 qualitative study.

Assessment of myalgic encephalomyelitis/chronic fatigue syndrome symptoms

Forty-one studies (including 7098 participants) addressed this subtopic. This includes 34 observational studies and 7 studies using other designs (3 qualitative, 1 mixed-method and 3 involving analyses of data sets).

Other (diagnosis)

Six studies (including 20,711 participants) addressed this subtopic. This includes four observational studies and two studies using other designs (one qualitative, one mixed-methods). One large mixed-method study contributed most participants.[440]

What is the problem?

A total of 246 studies addressed this topic, of which around 36% of studies described using diagnostic criteria in which PEM was an essential component.

Signs and symptoms

Eight SRs and 127 studies (including 31,628 participants) addressed this subtopic. Primary studies were mainly observational studies (n = 109). Five of the studies using other designs were analyses of data sets, while two were studies that integrated more than one study design. Confidence in results of SRs was moderate for one, low for three and critically low for four. The moderate-confidence review synthesised the results of 63 papers that reported results of neuroimaging to investigate brain abnormalities in ME/CFS.[512] Study findings were brought together within a narrative synthesis, with a number of consistent findings across studies identified. Most of the included studies (54/63) used the Fukuda diagnostic criteria.

Course of myalgic encephalomyelitis/chronic fatigue syndrome over time

One review (critically low confidence) and 24 primary studies (including 3300 participants) addressed this subtopic. We only identified 13 cohort studies (with 2447 participants), demonstrating that there is limited research evidence that explores the course of ME/CFS over time.

Comparison with symptoms (and diagnosis) of other conditions

Five reviews (all critically low confidence) and 93 primary studies (including 311,379 participants) addressed this subtopic. Most studies (85 studies, 277,175 participants) were observational; most participants (266,444) came from a single study,[589] which compared data from people with a diagnosis of ME or CFS with people diagnosed with lupus and multiple sclerosis. Other conditions compared with ME/CFS within two or more studies included fibromyalgia, long COVID, asthma, Q-fever syndrome, major depressive disorders, Gulf War illness, cancer-related fatigue, herpes viruses and irritable bowel syndrome.

Prevalence

Three SRs and 16 primary studies (including 338,015 participants) addressed this subtopic. Most participants (266,444) came from the same single study as cited above.[589] Confidence in results of SRs was moderate for one and critically low for two. The moderate-confidence review examined the prevalence of ME/CFS across Europe; only three relevant studies were identified, two of which used the Fukuda diagnostic criteria and one which used both Fukuda and CCC 2003 criteria.[199]

What is the cause?

A total of 339 studies addressed this topic, of which around 44% of studies described using diagnostic criteria in which PEM was an essential component.

General/multiple risk factors

Four SRs and 30 studies (including 17,922 participants) addressed this subtopic. The majority (26/30) of studies had an observational design. Confidence in results of SRs was low for one and critically low for three. One of these reviews was a scoping review that aimed to identify studies which explored potential causal factors of ME/CFS; 1161 primary studies, published between January 1979 and June 2019, were identified.

Biological mechanisms of postexertional malaise

Two SRs and 6 studies (including 591 participants) addressed this subtopic. This included a very small trial (11 people with ME/CFS) that investigated different protocols relating to vascular changes after maximum-intensity aerobic exercise and five small observational studies. Confidence in results of SRs was critically low. One of these reviews identified 36 studies (2270 participants) that assessed heart rate responses during cardiopulmonary testing, indicating that there is a body of earlier research addressing this topic.

Behavioural/lifestyle risk factors

Four SRs and 15 observational studies (including 5302 participants) addressed this subtopic. Confidence in results of SRs was moderate for one and low or critically low for three. The moderate-confidence review was primarily focused on 'medically unexplained symptoms' and included 12 studies with people with 'chronic fatigue syndrome', but it did not specify how this was diagnosed.[497]

Physiological risk factors (general/other)

Seven SRs (all critically low confidence) and 56 studies (including 6526 participants) addressed this subtopic. Studies were mainly observational (54/56), and more than half focused on the investigation of biospecimens.

Physiological risk factors: immune system

Twelve SRs (2 low and 10 critically low confidence) and 105 studies (including 15,285 participants) addressed this subtopic. Over three-quarters (81/105) of the studies focused on the investigation of features relating to biospecimens collected from people with ME/CFS.

Physiological risk factors: mitochondrial dysfunction/oxygen

Six SRs (1 low and 5 critically low confidence) and 25 studies (including 1402 participants) addressed this subtopic. The majority of the studies (21/25) focused on the investigation of biospecimens.

Physiological risk factors: nervous system function

Six SRs and 44 studies (including 1889 participants) addressed this subtopic. Most studies (30/44) were case-control studies. Confidence in the results of SRs was moderate for one, low for two and critically low for three. The moderate-confidence review addressed the need for a better-informed hypothesis around ME/CFS aetiology, including 63 studies with neuroimaging[512] (see also *Signs and symptoms*).

Demographic risk factors

One SR (low-confidence) and 14 studies (including 4618 participants) addressed this subtopic. A wide range of risk factors were investigated within the observational studies.

Environmental risk factors

One SR (low-confidence) and nine studies (including 1273 participants) addressed this subtopic. Risk factors investigated by observational studies included exposure to disinfectants, dampness and mould, social support, workplace and history of physical trauma.

Genetic risk factors

Three SRs (all critically low-confidence) and 44 studies (including 43,176 participants) addressed this subtopic. Almost all studies were observational, with most (39/44) focusing on the investigation of biospecimens. One study contributed 31,578 of the participants; this was a data linkage study, exploring family genetic risk scores in a Swedish population.[305]

Comorbidities

Five SRs and 49 studies (including 35,872 participants) addressed this subtopic. Most studies (47/49) were observational and included some large case-control studies. Examples of comorbidities investigated included arthritis, burns injuries, cancer, depression, dry eye syndrome, fibromyalgia, hypermobility, inflammatory bowel disease, long COVID, Lyme disease, multiple sclerosis, peptic ulcer disease, POTS, psoriasis, psychiatric disorders, sleep disorders, Tarlov cysts and tuberculosis. Confidence in the results of SRs was moderate for one, low for one and critically low for three. The moderate-confidence review, which has also been categorised and described under *Behavioural/lifestyle risk factors*, focused on medically unexplained symptoms and did not report the diagnostic criteria used by the 12 studies focused on 'chronic fatigue syndrome'.[497]

What can we do about it?

A total of 164 studies addressed this topic, of which around 24% of studies described using diagnostic criteria in which PEM was an essential component.

Treatment/management (general/mixed)

Six SRs and 11 studies (including 14,536 participants) addressed this subtopic. We found no experimental studies (but, given the broad nature of this subtopic, we were unlikely to categorise experimental studies). Confidence in the results of SRs was low for four and critically low for two.

Energy management

Three SRs and 11 studies (included 2340 participants) addressed this subtopic. This included two small, pilot/feasibility RCTs, which both investigated cognitive behaviour therapy and/or graded exercise therapy (GET) for young people with ME/CFS. Confidence in the results of SRs was low for 2 and critically low for 1 review; SRs contained between 8 and 18 studies, demonstrating a body of earlier research.

Physical function management

Four SRs and 11 studies (including 640 participants) addressed this subtopic. This included three very small RCTs, investigating exercise interventions. Confidence in the results of SRs was low for 2 and critically low for 2; SRs comprised between 4 and 18 studies, demonstrating some earlier research.

Orthostatic intolerance management

One RCT (including 16 participants) investigated the use of compression stockings to improve cardiac outcomes in people with ME/CFS to manage OI.

Pain management

We found no studies addressing this subtopic.

Diet and supplements

Four SRs and 16 studies (including 899 participants) addressed this subtopic. This included four small RCTs, investigating (1) oral coenzyme Q10 and a reduced form of nicotinamide adenine dinucleotide, (2) ginseng, (3) hydrogen-enriched water and (4) probiotics. Confidence in results of SRs was low for one and critically low for three. There were nine studies included in a SR that focused on mitochondrial-targeting nutraceuticals, while SRs investigating probiotics and ginseng each only found two relevant studies.

Psychological management

Seven SRs and 22 studies (including 7640 participants) addressed this subtopic. This includes seven RCTs, investigating cognitive–behavioural therapy (CBT), stress-management, alternative and psycho-spiritual interventions. There was moderate confidence in the results of three SRs (and low in two and critically low in two other reviews). One moderate-confidence SR synthesised 15 studies that investigated either CBT or GET.[273] None of the 15 included studies used diagnostic criteria in which PEM was an essential criterion. Another moderate-confidence SR also investigated CBT, but it included a broader group of participants (12 studies which included people with 'chronic fatigue syndrome', but with no diagnostic criteria specified).[497] The third moderate-confidence SR included 12 studies that investigated the use of mind–body interventions (MBIs);[309] and only 4 of the 12 included studies used diagnostic criteria requiring PEM.

Pharmacological treatments (general/other)

Six SRs and 24 studies (including 1866 participants) addressed this subtopic. There was moderate confidence in the results of one SR (and low in two and critically low in three other reviews). The moderate-confidence SR included 84 RCTs, which explored 69 kinds of Chinese herbal medicine (CHM).[662] The review authors included studies that used a range of different diagnostic criteria and did not present information relating to this for individual studies.

Non-pharmacological treatments (general/other)

Three SRs and five studies (including 1335 participants) addressed this subtopic. There was moderate confidence in the results of one SR (and low in two reviews). The moderate-confidence SR included 21 studies that investigated a range of medicinal herbs (including Angelicae Gigantis Radix, Ginseng Radix, Glycyrrhizae Radix, Atractylodis Rhizoma Alba, Bupleuri Radix and

Astragali Radix) for patients with idiopathic chronic fatigue; 19 of the studies included participants diagnosed with CFS using the Fukuda criteria, 1 included participants with fatigue of no identifiable cause for at least 6 months and 1 included participants diagnosed with neurasthenia.[312]

Complementary/alternative therapies

Eight SRs and eight RCTs (including 809 participants) addressed this subtopic. There was moderate confidence in the results of three SRs (and low in four and critically low in one other review). The moderate-confidence SRs addressed the use of MBIs (12 studies; of which 4 used diagnostic criteria requiring PEM),[309] CHMs (84 studies with a range of diagnostic criteria, not presented for individual studies in the review)[662] and acupuncture (an overview of 10 SRs, which include a total of 30 studies, with no specified diagnosis criteria for inclusion within the overview).[654]

Organisation of care and support

Five SRs (1 judged as low confidence; 4 as critically low confidence) and 32 studies (including 28,123 participants) addressed this subtopic. One of the two RCTs investigated the Lightening Process in addition to specialist medical care for young people, while the other investigated an internet-based specialist treatment, also for young people. Most of the participants (20,140) were accounted for by a single mixed-methods study, which collected and explored primary care data in Australia.

Specific treatments

The evidence map aimed to bring studies together according to the broad topics they addressed. However, stakeholders requested that evidence relating to two s*pecific treatments* was brought together within the evidence map. These were GETs, for which four SRs and four studies (including 4084 participants) were identified, and the Lightening process, for which one RCT (including 100 participants) was identified. It was noted in the definitions of these subtopics that NICE (2021) recommends that these treatments are not offered (see *Appendix 2*).[6]

Other

A total of 83 studies addressed this topic, of which around 19% of studies described using diagnostic criteria in which PEM was an essential component.

Living with myalgic encephalomyelitis/chronic fatigue syndrome

Six SRs (one low confidence, five critically low) and 63 studies (including 34,201 participants) addressed this subtopic. Primary studies were mainly surveys (cross-sectional studies) (n = 25) and qualitative studies (n = 22), focusing on experiences of people with ME/CFS.

Economics/cost

Two SRs and 8 studies (including 267,182 participants) addressed the economic and cost implications of living with ME/CFS. Most of the data come from a single large cohort study (266,444 participants); this US study, which has been described under subtopics relating to diagnosis, comparison with other conditions and prevalence, also explored the costs of ME/CFS using large-scale medical claims data.[589] Confidence in results of SRs was moderate for one and low for one. The moderate-confidence review explored the cost-effectiveness of interventions for a range of conditions; eight of the included studies focused on ME/CFS, but the diagnostic criteria used in these studies are not reported.[640]

Other

Three studies (including 2945 participants) were classified as 'other' as their topics did not fit well into our topics and subtopics. One of these papers was the report of the JLA priority setting project, one was related to antibody responses in both ME/CFS and coronavirus disease discovered in 2019 (COVID-19) and one explored biases relating to the use of patient-reported outcome measures within research studies.

Discussion

Summary of findings

We found 742 studies published from 2018 onwards which relate to ME/CFS; 103 were focused on other topics and were judged not to contain data specific to people with ME/CFS. Therefore, 639 studies have been published in the last 5 years, which provide research data about ME/CFS. These studies are referenced within an interactive evidence map (see *Report Supplementary Material 7*) that reflects the volume of studies, study design and the focus/topic of each study. This evidence map can be explored with reference to the reported diagnostic criteria and age of participants included in the study.

Two-thirds of these studies have an observational research design; given the prioritisation of research questions relating to the mechanism of ME/CFS, the large proportion of observational study designs seems appropriate to addressing known priorities. We found 81 SRs, but our confidence in the results were low or critically low for 72 of these, leaving only 9 reviews in which we had moderate confidence in the results. The lack of high-quality SRs in this field, given the large numbers of primary studies, is a key limitation. Common methodological limitations of SRs, contributing to the downgrading of judgements, included the lack of an a priori protocol, insufficient details relating to search strategy, lack of dual data extraction, failure to detail excluded studies and insufficient consideration of bias and heterogeneity when interpreting findings.

The use of, and reporting of, diagnostic criteria for ME/CFS within these studies varied enormously, and the lack of consistency provides challenges to the synthesis and interpretation of evidence in this field. Nineteen per cent of studies did not state how ME/CFS was diagnosed, and many studies reported use of multiple diagnostic criteria, leaving few studies (11%) in which it was clear that PEM was an essential component of diagnosis. The lack of clarity and complexities around the use of multiple criteria limit the generalisability of study data. Many studies failed to report basic participant details such as age, gender, ethnicity and severity of ME/CFS.

Future research: are the James Lind Alliance Priority Setting Partnership research priority topics addressed by research studies?

Our evidence map demonstrates that there are studies which are relevant to all of the JLA top 10+ research questions.[10,11] *Report Supplementary Material 13* contains a narrative summary of the volume and nature of evidence addressing each of the top 10+ questions, and this is further summarised here:

- Priority 1 (biological mechanisms and management of PEM): Compared to other priorities, there are relatively few studies addressing this priority. We found no robust SR. The studies addressing PEM appear to be small and varied in study design, and it is unlikely that these will support definitive conclusions relating to the cause or optimal management of PEM. A future comprehensive and methodologically robust SR of the existing studies may identify mechanisms and interventions which merit further investigation within primary research studies.
- Priority 2 (potential drug treatments): While we identified 164 studies which focused on treatment and management of ME/CFS, only 24 investigated pharmacological interventions; there may be evidence within these which can inform future developments and studies relating to drug treatments.
- Priority 3 (diagnosis): The evidence base is currently substantially limited by inconsistencies and variations in diagnostic criteria and terminology. Gaining international consensus over diagnostic criteria is arguably a fundamental and urgent step prior to further research relating to diagnostic testing.
- Priorities 4, 6, 7, 8, 10 (physiological and genetic risk factors): There are hundreds of studies which, if brought together in a systematic and robust manner to address specific questions, could provide important insight into these priorities.
- Priority 5 (different kinds of ME/CFS): We identified 36 studies, but no SR which synthesised studies, relating to different kinds of ME/CFS; the absence of a comprehensive, robust SR of these studies is a key gap. Our data suggest that two SRs may be beneficial, one synthesising studies focused on distinguishing different kinds of ME/CFS and another exploring recovery over time. However, we did find that there is limited research evidence (only 13 cohort studies) exploring the course of ME/CFS over time.
- Priority 9 (severity): This priority asks a very broad question and may be better addressed through more focused questions which investigate specific potential risk factors for severity. To ensure that the evidence base can answer questions relating to severity, it is important that future primary studies and SRs consider the severity of ME/CFS and record and report this in a standardised and transparent manner.

Lessons learned

The volume and nature of research studies relating to ME/CFS have been summarised within an interactive evidence map (see *Report Supplementary Material 7*). This can be used to inform decisions relating to further research to address priority questions relating to ME/CFS. During the synthesis of this evidence, we made the following key observations relating to research in this field.

Use and reporting of diagnostic criteria are inconsistent

At the protocol stage, the importance of identifying the diagnostic criteria used was identified. Rather than study authors selecting and using one single set of criteria, we found it was common for studies to refer to the use of multiple different diagnostic criteria; these might be presented as 'alternatives' (i.e. participants included in the study must meet one of two or more published criteria); or 'additives' (i.e. participants included in the study must meet all of two or more published criteria); or may be used in combination (e.g. one diagnostic criterion is used to screen potential participants, and another for confirming inclusion). This is problematic in terms of being able to synthesise, sensibly combine and interpret evidence from different studies.

The nature and design of many studies mean that often participants either self-report that they have ME/CFS or have had a clinical diagnosis of ME/CFS. While this is often a pragmatic and arguably appropriate approach, the known variations in use of diagnostic criteria have the potential to substantially reduce confidence in the findings of these studies.

International agreement and use of shared terminology and clarity around the best practice for use and reporting of diagnostic criteria within clinical practice and research would be beneficial. This would require international consensus among people with ME/CFS, clinicians and researchers and active knowledge mobilisation to ensure widespread implementation.

Many studies address questions which are not top priorities for research

We identified 246 studies that explored the aspects of 'what is the problem'; most of these studies focused on reporting signs and symptoms and comparing symptoms of people with ME/CFS with other health conditions. Only 24 of these studies potentially addressed an aspect of the JLA priority question relating to whether different types of ME/CFS have different chances of recovery, and we think it is unlikely that many (or any) provide sufficient data that are directly relevant to this question. Within the 164 studies focused on treatment and management of ME/CFS, a considerable proportion explore the effectiveness of psychological therapies; the JLA top research priorities do not identify this as a research priority. Further, 63 studies have been published since 2018, which were focused primarily on the experience and impact of living with ME/CFS; a topic which is not directly reflected in the JLA top priorities, although the identified studies could potentially contain relevant data (e.g. could inform acceptability of treatment or indicate potential risk factors). Thus, considerable time and resource were spent by researchers for conducting and reporting studies that do not address what matters most to people living with ME/CFS. Researchers and funders should ensure that future research addresses topics that are of greatest priority to people living with ME/CFS.

Poor reporting of basic demographic information is common

Sixteen per cent (103/639) of studies did not report the gender of participants, 12% (77/639) did not report age, 77% (493/639) did not report race/ethnicity and 81% (515/639) did not explicitly report the severity of ME/CFS. This lack of reporting of basic participant demographic information poses a key barrier to the interpretation of evidence. International consensus agreement on a minimum set of variables for reporting characteristics of participants with ME/CFS would be beneficial.

High-quality systematic reviews addressing specific questions are required

Over 10% of the studies (81/639) were SRs; however, we only had moderate confidence in the results of 9 of these. The lack of high-quality SRs in this field, given the large numbers of primary studies, is a key limitation. While we judged 72 SRs to have low or critically low quality, it is important to note that we applied a very broad definition of SR and then assessed all reviews with the same tool. Some of the included reviews did not aim to provide a comprehensive or methodologically robust summary of evidence that addressed specific and focused questions but rather were designed as narrative discussions or had broad objectives.

Comparison with other published myalgic encephalomyelitis/chronic fatigue syndrome research priorities

In May 2024 (after the date of our work),

> *National Institutes of Health (NIH), led by the National Institute of Neurological Disorders and Stroke (NINDS), developed the Research Roadmap for ME/CFS to identify the highest priorities for research with emphasis on research that will lead to clinical treatment trials.*[667]

Through a series of meetings, involving people with lived experience of ME/CFS, a long list of 'critical priorities for research' were agreed on eight pre-determined topics relevant to ME/CFS (with a total of 254 individual priorities). This list is, arguably, of a similar nature to the original long list of questions generated for the JLA PSP. Our evidence map will be helpful for informing the next steps to address these critical priorities. In addition, the NIH report identified a series of 'overarching themes' important for future research in this field. These relate to collaboration, innovation, urgency, biobanks, individual-centred care, precision medicine and clinical trials (p. 20).[667]

Limitations

We have produced an evidence map. This summarises what evidence is available and does not summarise what the evidence says. Key limitations relating to this evidence map are:

- Only studies published in 2018 and after are included. The map therefore shows what research has been conducted in the last 5 years, but not prior to this. The inclusion of SRs has provided some insight into the volume of evidence published prior to 2018.
- We applied the data limitation based on year of publication. Some studies will have had relevant reports both pre- and post-2018. We will not have identified and included the reports published prior to 2018.
- We only included studies published in the English language.

- We aimed to identify where there were multiple publications relating to the same study and to merge these together. While we have identified many of these, it was done in an ad hoc manner (during the process of screening and data extraction), and we have not identified them all. Consequently, there will be some double-counting of participants.
- Studies have been categorised to all relevant subtopics. This means that some studies appear multiple times within the map. However, studies are only categorised to one study design.
- Observational studies that had a focus on the exploration of biospecimens were grouped together, and no further attempt to detail the study design was conducted. This means that we have not captured whether these studies are, for example, case-control or cohort studies. This categorisation was a pragmatic decision based on the large volume of studies of this nature and the inconsistencies in terms used by study authors to describe the methodological approach.
- Categorisation of studies to subtopics was sometimes challenging, and our team did not have clinical expertise relating to the ME/CFS. Challenges were faced in relation to studies that reported and discussed risk factors and/or potential risk factors. There were also difficulties in determining whether studies investigating disease-triggering viruses (e.g. COVID-19 and EBV) should be categorised within subtopics relating to comorbidities or risk factors. Distinguishing between the demographic, behavioural/lifestyle and environmental risk factors was also difficult at times. We attempted to minimise errors by having two team members working in pairs to categorise subtopics and to ensure consistency by having one team member who contributed to categorisation of all studies. Where there was uncertainty, we erred on 'over'categorisation, ensuring that studies will be identified in all potentially relevant subtopics. This may mean that, with further scrutiny, some studies are found not to be directly relevant to all subtopics under which they are categorised.
- The use of and reporting of diagnostic criteria used by studies were inconsistent. Many studies reported the use of multiple different criteria, possibly as alternatives or in combination. While our evidence map enables data to be filtered according to the diagnostic criteria used in the study, the complexity of different ways of using and reporting these limits our confidence in these data. Thus, these data are indicative and should not be interpreted as an accurate representation of criteria use in individual studies.
- Extracting and categorising information relating to participant characteristics (age, gender, race/ethnicity and severity) were challenging, with information being reported in a variety of formats and often missing. We attempted to minimise errors by having two people independently extract and categorise data from all studies, with consensus on disagreements reached by involving a third person.
- The quality of the primary studies has not been appraised. This is standard in evidence maps.
- While the quality of SRs was appraised using the AMSTAR2 tool, there are limitations relating to the use of one tool to assess a variety of different types of reviews. In particular, this is limited by the fact that we included a broad range of reviews, including some of which were arguably not designed and presented as 'systematic reviews'. Consequently, many received judgements of low and critically low confidence, indicating problems with quality. However, arguably, one of the problems was that we included narrative-style literature reviews that do not report methods in a way which meets the AMSTAR2 criteria.
- While the quality of SRs was appraised, we did not assess the quality of the evidence within the reviews. It is possible therefore that a 'moderate-confidence' SR could contain primary studies which are not able to support a confident conclusion (e.g. a moderate-confidence review could contain low numbers of primary studies, primary studies with low numbers of participants, heterogeneous studies or studies which have methodological flaws).
- We made a number of changes to our pre-stated protocol (see *Appendix 7*).

Team reflexivity/positionality statement

The authors have varied professional and academic backgrounds, but they neither conducted research relating to ME/CFS nor published any eligible studies, resulting in a low ROB in the conduct of this evidence map. The authors kept a reflexive stance throughout the creation of this map and had no preconceptions of what the review findings would be. The review process and progress were frequently assessed and discussed between authors and stakeholders with collaborative and documented decision-making (see *Report Supplementary Material 3*). No conflicts of interests were declared.

Conclusions

We have produced an interactive evidence map (see *Report Supplementary Material 7*) summarising the topics addressed by research studies published in 2018 onwards. This includes 639 studies. Consideration of the volume of evidence addressing these research priorities can help inform decisions relating to future research. This evidence map can inform strategic plans for future, focused, SRs that will bring together the results of studies which have not previously been robustly synthesised. These in turn will be able to inform plans for priority primary studies.

Evidence relating to ME/CFS is seriously hindered by challenges and inconsistencies relating to the use of and reporting of diagnostic criteria. International agreement and use of shared terminology and clarity around the best practice for use and reporting of diagnostic criteria within clinical practice and research would be beneficial. The data relating to diagnostic criteria within our map are limited by the information available within studies.

It is important to consider research waste in this field. Our evidence map identifies that there have been many studies in the last 5 years which do not address top priorities and that many studies are limited by the poor reporting of basic demographic information. Future studies should be informed by identified research priorities and by syntheses of previous studies.

The ME/CFS JLA PSP[10,11] identified the shared research priorities of people living with ME/CFS, their families, carers and health professionals; we have mapped recent research evidence to these research priorities. We found studies addressing all JLA PSP research priorities, but we found large variations in the volume, nature and quality of research addressing different topics. Details of all research studies addressing different topics and subtopics can be easily downloaded from our evidence map, making this information accessible to people making decisions about future research. This should support efficient planning and development of useful, relevant research studies. This may progress the understanding of the mechanisms of, and effective treatments for, ME/CFS. We strongly believe that it is essential for people making decisions about future research in this field to work collaboratively, building on the findings brought together within this evidence map, to work towards the ultimate goal of improving the lives of people with ME/CFS.

Additional information

CRediT contribution statement

Alex Todhunter-Brown (https://orcid.org/0000-0003-4941-7985): Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization, Supervision, Project administration.

Pauline Campbell (https://orcid.org/0000-0002-5879-5526): Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing – review and editing, Visualization, Supervision.

Cathryn Broderick (https://orcid.org/0000-0003-2891-1394): Methodology, Software, Formal analysis, Investigation, Data curation, Writing – review and editing, Visualization.

Julie Cowie (https://orcid.org/0000-0002-4653-1283): Methodology, Formal analysis, Investigation, Data curation, Writing – review and editing, Visualization.

Bridget Davis (https://orcid.org/0000-0001-6935-0891): Methodology, Investigation, Writing – review and editing, Visualization, Project administration.

Candida Fenton (https://orcid.org/0000-0003-2516-9956): Methodology, Software, Investigation, Data curation, Writing – review and editing, Visualization.

Sarah Markham (https://orcid.org/0000-0002-8755-5935): Conceptualization, Methodology, Project administration.

Ceri Sellers (https://orcid.org/0000-0002-6768-780X): Methodology, Software, Formal analysis, Investigation, Data curation, Writing – review and editing, Visualization.

Katie Thomson (https://orcid.org/0000-0002-2558-2559): Methodology, Formal analysis, Investigation, Data curation, Writing – review and editing, Visualization.

NESSIE Group members

Alex Todhunter-Brown, Jackie Price, Sheila Cameron, Pauline Campbell, Emma France, Rosie Hill, Catriona Keerie, Sarah Markham, Peter Matthews, Gillian Mead, Aileen Neilson, Gerry Stansby, Marlene Stewart, Evropi Theodoratou, Cathryn Broderick, Julie Cowie, Bridget Davis, Candida Fenton, Ceri Sellers, Katie Thomson.

Acknowledgements

We are grateful for the invaluable discussions, comments and feedback from the ME Research Collaborative Patient Advisory Group (MERC PAG) and the ME/CFS Research Working Group, and we thank others who have contributed to this project.

Data-sharing statement

All data requests should be submitted to the corresponding author for consideration. Access to all anonymised data may be granted following review by the NESSIE investigators and completion of a data-sharing agreement.

Ethics statement

This work is a map of available evidence; it involved accessing, processing and analysing data that have already been published and are available to the public. As a result, no patient data were processed; patient consent and/or registration via human research ethics committees were therefore not relevant.

Work on an ethics application to cover PPI activities within all NESSIE projects ran concurrently with the ME/CFS review, coinciding with the start of this 5-year NESSIE project. Our three PPI co-applicants were involved throughout the ethics application, including written input to the protocol, Review Advisory Group role description and consent form. Although ethical approval had not been granted during the ME/CFS review, all PPI works were undertaken according to best practice guidance, including General Data Protection Regulation, and followed the principles set out in the UK Framework for Health and Social Care Research. The Glasgow Caledonian University Nursing and Community Health Research Ethics Committee gave approval for PPI activities in the NESSIE project (HLS/NCH/23/001) on 27 October 2023.

Information governance statement

This work is a map of available evidence; it involved accessing, processing and analysing data that have already been published and are available to the public. As a result, no personal information was processed.

Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/BTBD8846.

Primary conflicts of interest: Alex Todhunter-Brown: None declared.

Pauline Campbell: None declared.

Cathryn Broderick: None declared.

Julie Cowie: None declared.

Bridget Davis: None declared.

Candida Fenton: None declared.

Sarah Markham: HTA General Committee 2022–4.

Ceri Sellers: None declared.

Katie Thomson: None declared.

Department of Health and Social Care disclaimer

This publication presents independent research commissioned by the National Institute for Health and Care Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, MRC, NIHR Coordinating Centre, the Health Technology Assessment programme or the Department of Health and Social Care.

This article was published based on current knowledge at the time and date of publication. NIHR is committed to being inclusive and will continually monitor best practice and guidance in relation to terminology and language to ensure that we remain relevant to our stakeholders.

Publication

NESSIE. *ME/CFS: An Evidence Map of Research Studies and How These Address Key Topics in the JLA PSP Research Priorities (Protocol)*. 2023. https://doi.org/10.17605/OSF.IO/5F3MB

Study registration

The protocol for this study was registered on Open Science Framework: https://doi.org/10.17605/OSF.IO/5F3MB

Funding

This evidence map was conducted by NIHR Evidence Synthesis Scotland InitiativE (NESSIE), which is funded by the NIHR Evidence Synthesis Programme (ESP). NIHR ESP asked NESSIE to conduct this work in a response to a request from the DHSC (Department of Health and Social Care; Science, Research and Evidence Directorate).

This article provided an overview of the research award ME / CFS: An evidence map of research studies and how these address key themes in the JLA PSP research priorities. For more information about this research please view the award page (https://fundingawards.nihr.ac.uk/award/NIHR159926).

About this article

The contractual start date for this research was in April 2023. This article began editorial review in January 2024 and was accepted for publication in December 2024. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The Health Technology Assessment editors and publisher have tried to ensure the accuracy of the authors' article and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this article.

Copyright

List of abbreviations

AMSTAR	A MeaSurement Tool to Assess systematic Reviews
AMSTAR2	A MeaSurement Tool to Assess systematic Reviews 2
CBT	cognitive–behavioural therapy
CCC	Canadian Consensus Criteria 2003
CDC	Centers for Disease Control
CFS	chronic fatigue syndrome
CHM	Chinese herbal medicine
COVID	coronavirus disease
COVID-19	coronavirus disease discovered in 2019
DHSC	Department of Health and Social Care
EBV	Epstein–Barr virus
GET	graded exercise therapy
ICC	International Consensus Criteria 2011
IOM	Institute of Medicine 2015
JLA PSP	James Lind Alliance Priority Setting Partnership
MAs	meta-analyses
MBIs	mind–body interventions
ME	myalgic encephalomyelitis
NESSIE	NIHR Evidence Synthesis Scotland InitiativE
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
OI	orthostatic intolerance
PEM	postexertional malaise
POTS	postural orthostatic tachycardia syndrome
PPI	patient and public involvement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCTs	randomised controlled trials
ROB	risk of bias
SR	systematic reviews

List of supplementary material

Report Supplementary Material 1 Changes/clarifications to data coding for study design and topic
Report Supplementary Material 2 Development of topics and subtopics
Report Supplementary Material 3 Stakeholder involvement in ME/CFS evidence map
Report Supplementary Material 4 Excluded studies with exclusion reasons
Report Supplementary Material 5 Studies with multiple publications
Report Supplementary Material 6 Studies assessed as included but no further data extracted
Report Supplementary Material 7 The evidence map
Report Supplementary Material 8 Table of characteristics of included studies (spreadsheet)
Report Supplementary Material 9 AMSTAR2 risk of bias judgements for each systematic review
Report Supplementary Material 10 Systematic review risk of bias judgement summary
Report Supplementary Material 11 Video describing how to use the evidence map
Report Supplementary Material 12 Transcript of video script describing how to use the evidence map
Report Supplementary Material 13 Narrative summary of evidence addressing JLA PSP research questions

Supplementary material can be found on the NIHR Journals Library report page (https://doi.org/10.3310/BTBD8846).

Supplementary material has been provided by the authors to support the report and any files provided at submission will have been seen by peer reviewers, but not extensively reviewed. Any supplementary material provided at a later stage in the process may not have been peer reviewed.

References

1. World Health Organization. *ICD-11: International Classification of Diseases (11th revision)*. 2022. URL: https://icd.who.int/ (accessed 19 June 2023).
2. Nacul LC, Lacerda EM, Pheby D, Campion P, Molokhia M, Fayyaz S, *et al*. Prevalence of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) in three regions of England: a repeated cross-sectional study in primary care. *BMC Med* 2011;**9**:91. https://doi.org/10.1186/1741-7015-9-91
3. Afari N, Buchwald D. Chronic fatigue syndrome: a review. *Am J Psychiatry* 2003;**160**:221–36. https://doi.org/10.1176/appi.ajp.160.2.221
4. Nacul L, Authier FJ, Scheibenbogen C, Lorusso L, Helland IB, Martin JA, *et al*. European network on myalgic encephalomyelitis/chronic fatigue syndrome (EUROMENE): expert consensus on the diagnosis, service provision, and care of people with ME/CFS in Europe. *Medicina (Kaunas, Lithuania)* 2021;**57**:510. https://doi.org/10.3390/medicina57050510
5. Bretherick A, McGrath S, Devereux-Cooke A, Leary S, Northwood E, Redshaw A, *et al*. Typing myalgic encephalomyelitis by infection at onset: a DecodeME study [version 2; peer review: 1 approved with reservations, 1 not approved]. *NIHR Open Res* 2023;**3**:20. https://doi.org/10.3310/nihropenres.13421.2
6. National Institute for Health and Care Excellence. *Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management*. 2021. URL: www.nice.org.uk/guidance/ng206/resources/myalgic-encephalomyelitis-or-encephalopathy-chronic-fatigue-syndrome-diagnosis-and-management-pdf-66143718094021 (accessed 24 April 2023).
7. Eaton-Fitch N, Johnston SC, Zalewski P, Staines D, Marshall-Gradisnik S. Health-related quality of life in patients with myalgic encephalomyelitis/chronic fatigue syndrome: an Australian cross-sectional study. *Qual Life Res* 2020;**29**:1521–31. https://doi.org/10.1007/s11136-019-02411-6
8. Falk Hvidberg M, Brinth LS, Olesen AV, Petersen KD, Ehlers L. The health-related quality of life for patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *PLOS ONE* 2015;**10**:e0132421. https://doi.org/10.1371/journal.pone.0132421
9. Conroy K, Bhatia S, Islam M, Jason LA. Homebound versus bedridden status among those with myalgic encephalomyelitis/chronic fatigue syndrome. *Healthcare (Basel)* 2021;**9**:106. https://doi.org/10.3390/healthcare9020106
10. Tyson S, Stanley K, Gronlund TA, Leary S, Emmans Dean M, Dransfield C, *et al*. Research priorities for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): the results of a James Lind alliance priority setting exercise. *Fatigue: Biomed Health Behav* 2022;**10**:200–11. https://doi.org/10.1080/21641846.2022.2124775
11. National Institute for Health and Care Excellence James Lind Alliance. *Defining future ME/CFS research 2022: The ME/CFS Priority Setting Partnership*. UK; 2022.
12. Mirin AA, Dimmock ME, Jason LA. Research update: the relation between ME/CFS disease burden and research funding in the USA. *Work* 2020;**66**:277–82. https://doi.org/10.3233/wor-203173
13. Carruthers BM, Jain AK, De Meirleir KL, Peterson DL, Klimas NG, Lerner AM, *et al*. Myalgic encephalomyelitis/chronic fatigue syndrome. *J Chronic Fatigue Syndr* 2003;**11**:7–115. https://doi.org/10.1300/J092v11n01_02
14. Carruthers BM, van de Sande MI, De Meirleir KL, Klimas NG, Broderick G, Mitchell T, *et al*. Myalgic encephalomyelitis: international consensus criteria. *J Intern Med* 2011;**270**:327–38. https://doi.org/10.1111/j.1365-2796.2011.02428.x
15. Committee on the Diagnostic Criteria for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, Board on the Health of Select Populations, Institute of Medicine. *Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness*. USA: National Academies Press; 2015.
16. Sharpe MC, Archard LC, Banatvala JE, Borysiewicz LK, Clare AW, David A, *et al*. A report – chronic fatigue syndrome: guidelines for research. *J R Soc Med* 1991;**84**:118–21. https://doi.org/10.1177/014107689108400224
17. Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. *Ann Intern Med* 1994;**121**:953–9. https://doi.org/10.7326/0003-4819-121-12-199412150-00009
18. White H, Albers B, Gaarder M, Kornør H, Littell J, Marshall Z, *et al*. Guidance for producing a Campbell evidence and gap map. *Campbell Syst Rev* 2020;**16**:e1125. https://doi.org/10.1002/cl2.1125
19. NESSIE. *ME/CFS: An Evidence Map of Research Studies and How These Address Key Themes in the JLA PSP Research Priorities (Protocol)*. 2023. URL: https://osf.io/5f3mb (accessed 14 November 2023).

20. *Evidence-Informed Policy and Practice (EPPI) Centre: What is a Systematic review?* URL: http://eppi.ioe.ac.uk/cms/Default.aspx?tabid=67 (accessed 19 June 2023) .

21. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, *et al*. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med* 2018;**169**:467–73. https://doi.org/10.7326/m18-0850

22. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, *et al*. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 2017;**358**:j4008. https://doi.org/10.1136/bmj.j4008

23. McGuinness LA, Higgins JPT. Risk-of-bias VISualization (robvis): an R package and Shiny web app for visualizing risk-of-bias assessments. *Res Synth Methods* 2020;**12**:55–61. https://doi.org/10.1002/jrsm.1411

24. Digital Solution Foundry and EPPI Centre. *EPPI-Mapper. Version 2.1.0 ed*. London: EPPI Centre, UCL Social Research Institute, University College London; 2022.

25. UK Public Involvement Standards Development Partnership. *UK Standards for Public Involvement*. URL: https://sites.google.com/nihr.ac.uk/pi-standards/home (accessed 19 June 2023).

26. National Institute for Health and Care Excellence. *Guidance on Co-producing a Research Project*. 2021. URL: www.learningforinvolvement.org.uk/content/resource/nihr-guidance-on-co-producing-a-research-project/ (accessed 19 June 2023).

27. *The Statement of Principles for Consumer Involvement in Cochrane*. 2015. URL: https://consumers.cochrane.org/news/statement-principles-consumer-involvement-cochrane (accessed 19 June 2023).

28. Staniszewska S, Brett J, Simera I, Seers K, Mockford C, Goodlad S, *et al*. GRIPP2 reporting checklists: tools to improve reporting of patient and public involvement in research. *BMJ* 2017;**358**:j3453. https://doi.org/10.1136/bmj.j3453

29. Pollock A, Campbell P, Struthers C, Synnot A, Nunn J, Hill S, *et al*. Development of the ACTIVE framework to describe stakeholder involvement in systematic reviews. *J Health Serv Res Policy* 2019;**24**:245–55. https://doi.org/10.1177/1355819619841647

30. Adamson J, Ali S, Santhouse A, Wessely S, Chalder T. Cognitive behavioural therapy for chronic fatigue and chronic fatigue syndrome: outcomes from a specialist clinic in the UK. *J R Soc Med* 2020;**113**:394–402. https://doi.org/10.1177/0141076820951545

31. Ahmed SA, Mewes JC, Vrijhoef H. Assessment of the scientific rigour of randomized controlled trials on the effectiveness of cognitive behavioural therapy and graded exercise therapy for patients with myalgic encephalomyelitis/chronic fatigue syndrome: a systematic review. *J Health Psychol* 2020;**25**:240–55. https://doi.org/10.1177/1359105319847261

32. Al-Ani S, Herra L, Hill A, Nelson I, Yang S, Turner S, *et al*. Differences in dietary intake among healthy volunteers and myalgic encephalomyletitis/chronic fatigue syndrome patients. *J Acad Nutr Diet* 2021;**121**:A124–24-A. https://doi.org/10.1016/j.jand.2021.08.018

33. Al-Rawaf HA, Alghadir AH, Gabr SA. MicroRNAs as biomarkers of pain intensity in patients with chronic fatigue syndrome. *Pain Pract* 2019;**19**:848–60. https://doi.org/10.1111/papr.12817

34. Albers E, Nijhof LN, Berkelbach van der Sprenkel EE, van de Putte EM, Nijhof SL, Knoop H. Effectiveness of internet-based cognitive behavior therapy (fatigue in teenagers on the internet) for adolescents with chronic fatigue syndrome in routine clinical care: observational study. *J Med Internet Res* 2021;**23**:e24839. https://doi.org/10.2196/24839

35. Ali S, Adamczyk L, Burgess M, Chalder T. Psychological and demographic factors associated with fatigue and social adjustment in young people with severe chronic fatigue syndrome/myalgic encephalomyelitis: a preliminary mixed-methods study. *J Behav Med* 2019;**42**:898–910. https://doi.org/10.1007/s10865-019-00010-x

36. Almenar-Perez E, Ovejero T, Sanchez-Fito T, Espejo JA, Nathanson L, Oltra E. Epigenetic components of myalgic encephalomyelitis/chronic fatigue syndrome uncover potential transposable element activation. *Clin Ther* 2019;**41**:675–98. https://doi.org/10.1016/j.clinthera.2019.02.012

37. Almenar-Perez E, Sanchez-Fito T, Ovejero T, Nathanson L, Oltra E. Impact of polypharmacy on candidate biomarker miRNomes for the diagnosis of fibromyalgia and myalgic encephalomyelitis/chronic fatigue syndrome: striking back on treatments. *Pharmaceutics* 2019;**11**:126. https://doi.org/10.3390/pharmaceutics11030126

38. Almenar-Perez E, Sarria L, Nathanson L, Oltra E. Assessing diagnostic value of microRNAs from peripheral blood mononuclear cells and extracellular vesicles in myalgic encephalomyelitis/chronic fatigue syndrome. *Sci Rep* 2020;**10**:2064. https://doi.org/10.1038/s41598-020-58506-5

39. Almutairi B, Langley C, Crawley E, Thai NJ. Using structural and functional MRI as a neuroimaging technique to investigate chronic fatigue syndrome/myalgic encephalopathy: a systematic review. *BMJ Open* 2020;**10**:e031672. https://doi.org/10.1136/bmjopen-2019-031672

40. Altermark N, Plesner A. Austerity and identity formation: how welfare cutbacks condition narratives of sickness. *Sociol Health Illn* 2022;**44**:1270–86. https://doi.org/10.1111/1467-9566.13545

41. Amato ML, Towler BP, Themelis K, Davies KA, Newbury S, Eccles JA, *et al*. Using transcriptomics to investigate the effects of mild inflammation in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and fibromyalgia (FM). *Psychosom Med* 2022;**84**:A110–A1.

42. An C. Sports medicine treatment based on relieving chronic fatigue and sub-health state. *Revista Brasileira de Medicina do Esporte* 2021;**27**:814–7. https://doi.org/10.1590/1517-8692202127082021_0359

43. Anderson E, Parslow R, Hollingworth W, Mills N, Beasant L, Gaunt D, *et al*. Recruiting adolescents with chronic fatigue syndrome/myalgic encephalomyelitis to internet-delivered therapy: internal pilot within a randomized controlled trial. *J Med Internet Res* 2020;**22**:e17768. https://doi.org/10.2196/17768

44. Antcliff D, Keenan AM, Keeley P, Woby S, McGowan L. Testing a newly developed activity pacing framework for chronic pain/fatigue: a feasibility study. *BMJ Open* 2021;**11**:e045398. https://doi.org/10.1136/bmjopen-2020-045398

45. Aoun Sebaiti M, Hainselin M, Gounden Y, Sirbu CA, Sekulic S, Lorusso L, *et al*. Systematic review and meta-analysis of cognitive impairment in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Sci Rep* 2022;**12**:2157. https://doi.org/10.1038/s41598-021-04764-w

46. Apostolou E, Rizwan M, Moustardas P, Sjogren P, Bertilson BC, Bragee B, *et al*. Saliva antibody-fingerprint of reactivated latent viruses after mild/asymptomatic COVID-19 is unique in patients with myalgic-encephalomyelitis/chronic fatigue syndrome. *Front Immunol* 2022;**13**:949787. https://doi.org/10.3389/fimmu.2022.949787

47. Araja D, Berkis U, Lunga A, Murovska M. Shadow burden of undiagnosed myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) on society: retrospective and prospective-in light of COVID-19. *J Clin Med* 2021;**10**:3017. https://doi.org/10.3390/jcm10143017

48. Araja D, Berkis U, Lunga A, Murovska M. POSA63 direct costs of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) in Latvia. *Value Health* 2022;**25**:S45. https://doi.org/10.1016/j.jval.2021.11.208

49. Araja D, Berkis U, Murovska M. CO8 health-related quality of life reported by patients of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Value Health* 2022;**25**:S305. https://doi.org/10.1016/j.jval.2022.04.106

50. Araja D, Brenna E, Hunter RM, Pheby D, Berkis U, Lunga A, Murovska M. Psy44 economic burden of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) to patients: comparative study. *Value Health* 2019;**22**:S909. https://doi.org/10.1016/j.jval.2019.09.2671

51. Ascough C, King H, Serafimova T, Beasant L, Jackson S, Baldock L, *et al*. Interventions to treat pain in paediatric CFS/ME: a systematic review. *BMJ Paediatr Open* 2020;**4**:e000617. https://doi.org/10.1136/bmjpo-2019-000617

52. Asprusten TT, Sulheim D, Fagermoen E, Winger A, Skovlund E, Wyller VB. Systemic exertion intolerance disease diagnostic criteria applied on an adolescent chronic fatigue syndrome cohort: evaluation of subgroup differences and prognostic utility. *BMJ Paediatr Open* 2018;**2**:e000233. https://doi.org/10.1136/bmjpo-2017-000233

53. Azcue N, Gomez-Esteban JC, Acera M, Tijero B, Fernandez T, Ayo-Mentxakatorre N, *et al*. Brain fog of post-COVID-19 condition and chronic fatigue syndrome, same medical disorder? *J Transl Med* 2022;**20**:569. https://doi.org/10.1186/s12967-022-03764-2

54. Bae J, Lin JS. Healthcare utilization in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): analysis of US ambulatory healthcare data, 2000–2009. *Front Pediatr* 2019;**7**:185. https://doi.org/10.3389/fped.2019.00185

55. Baken DM, Harvey ST, Bimler DL, Ross KJ. Stigma in myalgic encephalomyelitis and its association with functioning. *Fatigue: Biomed Health Behav* 2018;**6**:30–40. https://doi.org/10.1080/21641846.2018.1419553

56. Bakken AK, Mengshoel AM, Synnes O, Strand EB. Narratives of change in recovery from severe fatigue – a qualitative study of stories of healing from severe chronic fatigue syndrome/myalgic encephalomyelitis. *Psychosom Med* 2022;**84**:A127.

57. Baklund IH, Dammen T, Moum TA, Kristiansen W, Duarte DS, Castro-Marrero J, *et al*. Evaluating routine blood tests according to clinical symptoms and diagnostic criteria in individuals with

myalgic encephalomyelitis/chronic fatigue syndrome. *J Clin Med* 2021;**10**:3105. https://doi.org/10.3390/jcm10143105

58. Balinas C, Cabanas H, Staines D, Marshall-Gradisnik S. Transient receptor potential melastatin 2 channels are overexpressed in myalgic encephalomyelitis/chronic fatigue syndrome patients. *J Transl Med* 2019;**17**:401. https://doi.org/10.1186/s12967-019-02155-4
59. Balinas C, Eaton-Fitch N, Maksoud R, Staines D, Marshall-Gradisnik S. Impact of life stressors on myalgic encephalomyelitis/chronic fatigue syndrome symptoms: an Australian longitudinal study. *Int J Environ Res Public Health* 2021;**18**:10614. https://doi.org/10.3390/ijerph182010614
60. Balinas C, Nguyen T, Johnston S, Smith P, Staines D, Marshall-Gradisnik S. Investigation of mast cell toll-like receptor 3 in chronic fatigue syndrome/myalgic encephalomyelitis and systemic mastocytosis using the novel application of autoMACS magnetic separation and flow cytometry. *Asian Pac J Allergy Immunol* 2018;**36**:257–64. https://doi.org/10.12932/AP-200517-0086
61. Baraniuk JN, Kern G, Narayan V, Cheema A. Exercise modifies glutamate and other metabolic biomarkers in cerebrospinal fluid from Gulf War illness and myalgic encephalomyelitis/chronic fatigue syndrome. *PLOS ONE* 2021;**16**:e0244116. https://doi.org/10.1371/journal.pone.0244116
62. Barhorst EE, Andrae WE, Rayne TJ, Falvo MJ, Cook DB, Lindheimer JB. Elevated perceived exertion in people with myalgic encephalomyelitis/chronic fatigue syndrome and fibromyalgia: a meta-analysis. *Med Sci Sports Exerc* 2020;**52**:2615–27. https://doi.org/10.1249/MSS.0000000000002421
63. Barnden LR, Shan ZY, Staines DR, Marshall-Gradisnik S, Finegan K, Ireland T, Bhuta S. Hyperintense sensorimotor T1 spin echo MRI is associated with brainstem abnormality in chronic fatigue syndrome. *Neuroimage Clin* 2018;**20**:102–9. https://doi.org/10.1016/j.nicl.2018.07.011
64. Barnden LR, Shan ZY, Staines DR, Marshall-Gradisnik S, Finegan K, Ireland T, Bhuta S. Intra brainstem connectivity is impaired in chronic fatigue syndrome. *Neuroimage Clin* 2019;**24**:102045. https://doi.org/10.1016/j.nicl.2019.102045
65. Bashton D, O'Connor L, Meyer S, Gregorowski A. Tea and cake: an opportunity for young people and their parents/guardians to eat cake and share ideas. *Arch Dis Child* 2019;**104**:A248. https://doi.org/10.1136/archdischild-2019-rcpch.594
66. Bedford FL, Greshake Tzovaras B. Re-analysis of genetic risks for chronic fatigue syndrome from 23andMe data finds few remain. *Front Pediatr* 2021;**9**:590040. https://doi.org/10.3389/fped.2021.590040
67. Bedree H, Sunnquist M, Jason LA. The DePaul symptom questionnaire-2: a validation study. *Fatigue* 2019;**7**:166–79. https://doi.org/10.1080/21641846.2019.1653471
68. Berardi G, Haider S, Janowski A, Joseph LB, Hayashi K, Dailey DL, *et al*. The relation of pain, fatigue, disease impact, and psychological factors with physical function in post-COVID-19 syndrome, fibromyalgia, and chronic fatigue syndrome. *J Pain* 2022;**23**:47. https://doi.org/10.1016/j.jpain.2022.03.180
69. Bermejo-Guerrero L, de Fuenmayor-Fernandez de la Hoz CP, Guerrero-Molina MP, Martin-Jimenez P, Blazquez A, Serrano-Lorenzo P, *et al*. Serum GDF-15 levels accurately differentiate patients with primary mitochondrial myopathy, manifesting with exercise intolerance and fatigue, from patients with chronic fatigue syndrome. *J Clin Med* 2023;**12**:2435. https://doi.org/10.3390/jcm12062435
70. Bernhoff G, Huhmar HM, Rasmussen-Barr E, Bunketorp Kall L. The significance of pain drawing as a screening tool for cervicogenic headache and associated symptoms in chronic fatigue. *J Pain Res* 2022;**15**:2547–56. https://doi.org/10.2147/JPR.S369470
71. Bernhoff G, Rasmussen-Barr E, Bunketorp Kall L. A comparison of health-related factors between patients diagnosed with ME/CFS and patients with a related symptom picture but no ME/CFS diagnosis: a cross-sectional exploratory study. *J Transl Med* 2022;**20**:577. https://doi.org/10.1186/s12967-022-03769-x
72. Bertinat R, Villalobos-Labra R, Hofmann L, Blauensteiner J, Sepulveda N, Westermeier F. Decreased NO production in endothelial cells exposed to plasma from ME/CFS patients. *Vascul Pharmacol* 2022;**143**:106953. https://doi.org/10.1016/j.vph.2022.106953
73. Bileviciute-Ljungar I. Daytime sleepiness in patients with chronic fatigue syndrome. *J Sleep Res* 2018;**27**:e12751. https://doi.org/10.1111/jsr.12751
74. Bileviciute-Ljungar I. Stress-load and it's correlation with infections in patients with myalgic encephalomyelitis/chronic fatigue syndrome. *J Neurol Sci* 2019;**405**:100. https://doi.org/10.1016/j.jns.2019.10.406
75. Bileviciute-Ljungar I, Friberg D. Emotional awareness correlated with number of awakenings from polysomnography in patients with myalgic encephalomyelitis/chronic fatigue syndrome – a pilot study. *Front Psychiatry* 2020;**11**:222. https://doi.org/10.3389/fpsyt.2020.00222

76. Bileviciute-Ljungar I, Maroti D, Bejerot S. Patients with chronic fatigue syndrome do not score higher on the autism-spectrum quotient than healthy controls: comparison with autism spectrum disorder. *Scand J Psychol* 2018;**59**:428–32. https://doi.org/10.1111/sjop.12451

77. Bileviciute-Ljungar I, Maroti D, Friberg D. Alexithymia and emotional awareness are negatively associated with sleep parameters in patients with myalgic encephalomyelitis/chronic fatigue syndrome – an exploratory study. *J Neurol Sci* 2019;**405**:99. https://doi.org/10.1016/j.jns.2019.10.403

78. Bileviciute-Ljungar I, Schult ML, Borg K, Ekholm J. Preliminary ICF core set for patients with myalgic encephalomyelitis/chronic fatigue syndrome in rehabilitation medicine. *J Rehabil Med* 2020;**52**:jrm00074. https://doi.org/10.2340/16501977-2697

79. Blauensteiner J, Bertinat R, Leon LE, Riederer M, Sepulveda N, Westermeier F. Altered endothelial dysfunction-related miRs in plasma from ME/CFS patients. *Sci Rep* 2021;**11**:10604. https://doi.org/10.1038/s41598-021-89834-9

80. Blomberg J, Rizwan M, Bohlin-Wiener A, Elfaitouri A, Julin P, Zachrisson O, *et al*. Antibodies to human herpesviruses in myalgic encephalomyelitis/chronic fatigue syndrome patients. *Front Immunol* 2019;**10**:1946. https://doi.org/10.3389/fimmu.2019.01946

81. Boissoneault J, Letzen J, Lai S, Robinson ME, Staud R. Static and dynamic functional connectivity in patients with chronic fatigue syndrome: use of arterial spin labelling fMRI. *Clin Physiol Funct Imaging* 2018;**38**:128–37. https://doi.org/10.1111/cpf.12393

82. Boissoneault J, Letzen J, Robinson M, Staud R. Cerebral blood flow and heart rate variability predict fatigue severity in patients with chronic fatigue syndrome. *Brain Imaging Behav* 2019;**13**:789–97. https://doi.org/10.1007/s11682-018-9897-x

83. Bond J, Nielsen T, Hodges L. Effects of post-exertional malaise on markers of arterial stiffness in individuals with myalgic encephalomyelitis/chronic fatigue syndrome. *Int J Environ Res Public Health* 2021;**18**:2366. https://doi.org/10.3390/ijerph18052366

84. Boneva RS, Lin JS, Wieser F, Nater UM, Ditzen B, Taylor RN, Unger ER. Endometriosis as a comorbid condition in chronic fatigue syndrome (CFS): secondary analysis of data from a CFS case-control study. *Front Pediatr* 2019;**7**:195. https://doi.org/10.3389/fped.2019.00195

85. Bonilla H, Hampton D, Marques de Menezes EG, Deng X, Montoya JG, Anderson J, Norris PJ. Comparative analysis of extracellular vesicles in patients with severe and mild myalgic encephalomyelitis/chronic fatigue syndrome. *Front Immunol* 2022;**13**:841910. https://doi.org/10.3389/fimmu.2022.841910

86. Bouquet J, Li T, Gardy JL, Kang X, Stevens S, Stevens J, *et al*. Whole blood human transcriptome and virome analysis of ME/CFS patients experiencing post-exertional malaise following cardiopulmonary exercise testing. *PLOS ONE* 2019;**14**:e0212193. https://doi.org/10.1371/journal.pone.0212193

87. Bourke JH, Wodehouse T, Clark LV, Constantinou E, Kidd BL, Langford R, *et al*. Central sensitisation in chronic fatigue syndrome and fibromyalgia; a case control study. *J Psychosom Res* 2021;**150**:110624. https://doi.org/10.1016/j.jpsychores.2021.110624

88. Bozzini S, Albergati A, Capelli E, Lorusso L, Gazzaruso C, Pelissero G, Falcone C. Cardiovascular characteristics of chronic fatigue syndrome. *Biomed Rep* 2018;**8**:26–30. https://doi.org/10.3892/br.2017.1024

89. Braamse A, Voss H, Nikolaus S, Wearden A, Knoop H. The role of partners' fatigue and the patient-partner relationship in the outcome of cognitive behavioural therapy for chronic fatigue syndrome. *J Psychosom Res* 2020;**135**:110133. https://doi.org/10.1016/j.jpsychores.2020.110133

90. Bragee B, Michos A, Drum B, Fahlgren M, Szulkin R, Bertilson BC. Signs of intracranial hypertension, hypermobility, and craniocervical obstructions in patients with myalgic encephalomyelitis/chronic fatigue syndrome. *Front Neurol* 2020;**11**:828. https://doi.org/10.3389/fneur.2020.00828

91. Bram AD, Gottschalk KA, Leeds WM. Emotional regulation in women with chronic fatigue syndrome and depression: internal representations and adaptive defenses. *J Am Psychoanal Assoc* 2018;**66**:701–41. https://doi.org/10.1177/0003065118798043

92. Bram AD, Gottschalk KA, Leeds WM. Chronic fatigue syndrome and the somatic expression of emotional distress: applying the concept of illusory mental health to address the controversy. *J Clin Psychol* 2019;**75**:116–31. https://doi.org/10.1002/jclp.22692

93. Brellier F, Pujades-Rodriguez M, Powell E, Mudie K, Mattos L, Nacul L, *et al*. Incidence of Lyme disease in the United Kingdom and association with fatigue: a population-based, historical cohort study. *PLOS ONE* 2022;**17**:e0265765. https://doi.org/10.1371/journal.pone.0265765

94. Brenna E, Araja D, Pheby DFH. Comparative survey of people with ME/CFS in Italy, Latvia, and the UK: a report on behalf of the socioeconomics working group of the European ME/CFS research network (EUROMENE). *Medicina (Kaunas)* 2021;**57**:300. https://doi.org/10.3390/medicina57030300

95. Brewer G, Stratton K. Living with chronic fatigue syndrome during lockdown and a global pandemic. *Fatigue: Biomed Health Behav* 2020;**8**:144–55. https://doi.org/10.1080/21641846.2020.1827503

96. Brigden A, Beasant L, Gaunt D, Hollingworth W, Mills N, Solomon-Moore E, *et al*. Results of the feasibility phase of the managed activity graded exercise in teenagers and pre-adolescents (MAGENTA) randomised controlled trial of treatments for chronic fatigue syndrome/myalgic encephalomyelitis. *Pilot Feasibility Stud* 2019;**5**:151. https://doi.org/10.1186/s40814-019-0525-3

97. Brigden A, Parslow RM, Gaunt D, Collin SM, Jones A, Crawley E. Defining the minimally clinically important difference of the SF-36 physical function subscale for paediatric CFS/ME: triangulation using three different methods. *Health Qual Life Outcomes* 2018;**16**:202. https://doi.org/10.1186/s12955-018-1028-2

98. Brigden A, Shaw A, Anderson E, Crawley E. Chronic fatigue syndrome/myalgic encephalomyelitis in children aged 5 to 11 years: a qualitative study. *Clin Child Psychol Psychiatry* 2021;**26**:18–32. https://doi.org/10.1177/1359104520964528

99. Brittain E, Muirhead N, Finlay AY, Vyas J. Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): major impact on lives of both patients and family members. *Medicina (Kaunas)* 2021;**57**:43. https://doi.org/10.3390/medicina57010043

100. Broadbent S, Coetzee S, Beavers R. Effects of a short-term aquatic exercise intervention on symptoms and exercise capacity in individuals with chronic fatigue syndrome/myalgic encephalomyelitis: a pilot study. *Eur J Appl Physiol* 2018;**118**:1801–10. https://doi.org/10.1007/s00421-018-3913-0

101. Brodwall EM, Pedersen M, Asprusten TT, Wyller VBB. Pain in adolescent chronic fatigue following Epstein-Barr virus infection. *Scand J Pain* 2020;**20**:765–73. https://doi.org/10.1515/sjpain-2020-0031

102. Brown A, Jason LA. Meta-analysis investigating post-exertional malaise between patients and controls. *J Health Psychol* 2020;**25**:2053–71. https://doi.org/10.1177/1359105318784161

103. Brown AE, Dibnah B, Fisher E, Newton JL, Walker M. Pharmacological activation of AMPK and glucose uptake in cultured human skeletal muscle cells from patients with ME/CFS. *Biosci Rep* 2018;**38**:29. https://doi.org/10.1042/BSR20180242

104. Bulut A, Bulut A. The prevalence of chronic fatigue syndrome in emergency healthcare professionals and the associated factors. *Int J Caring Sci* 2018;**11**:868–75.

105. Bynke A, Julin P, Gottfries CG, Heidecke H, Scheibenbogen C, Bergquist J. Autoantibodies to beta-adrenergic and muscarinic cholinergic receptors in myalgic encephalomyelitis (ME) patients – a validation study in plasma and cerebrospinal fluid from two Swedish cohorts. *Brain Behav Immun Health* 2020;**7**:100107. https://doi.org/10.1016/j.bbih.2020.100107

106. Calvo N, Pueyo N, Gutierrez F, Ferrer M, Castro-Marrero J, Alegre J, *et al*. Dimensional personality assessment among a chronic fatigue syndrome (CFS) sample with personality inventory for DSM-5 (PID-5). *Actas Esp Psiquiatr* 2018;**46**:125–32.

107. Cambras T, Castro-Marrero J, Zaragoza MC, Diez-Noguera A, Alegre J. Circadian rhythm abnormalities and autonomic dysfunction in patients with chronic fatigue syndrome/myalgic encephalomyelitis. *PLOS ONE* 2018;**13**:e0198106. https://doi.org/10.1371/journal.pone.0198106

108. Cambras T, Zeron-Rugerio MF, Diez-Noguera A, Zaragoza MC, Domingo JC, Sanmartin-Sentanes R, *et al*. Skin temperature circadian rhythms and dysautonomia in myalgic encephalomyelitis/chronic fatigue syndrome: the role of endothelin-1 in the vascular tone dysregulation. *Int J Mol Sci* 2023;**24**:4835. https://doi.org/10.3390/ijms24054835

109. Campagne J, Fornasieri I, Andreani B, Eginard M, de Korwin JD. Separating patients with SEID from those with CFS in the French ME/CFS association, with some thoughts on nomenclature. *Diagnostics (Basel)* 2022;**12**:1095. https://doi.org/10.3390/diagnostics12051095

110. Campbell R, Vansteenkiste M, Delesie L, Tobback E, Mariman A, Vogelaers D, Mouratidis A. Reciprocal associations between daily need-based experiences, energy, and sleep in chronic fatigue syndrome. *Health Psychol* 2018;**37**:1168–78. https://doi.org/10.1037/hea0000621

111. Campen C, Rowe PC, Visser FC. Orthostatic symptoms and reductions in cerebral blood flow in long-haul COVID-19 patients: similarities with myalgic encephalomyelitis/chronic fatigue syndrome. *Medicina (Kaunas)* 2021;**58**:24. https://doi.org/10.3390/medicina58010028

112. Capdevila L, Castro-Marrero J, Alegre J, Ramos-Castro J, Escorihuela RM. Analysis of gender differences in HRV of patients with myalgic encephalomyelitis/chronic fatigue syndrome using mobile-health technology. *Sensors (Basel)* 2021;**21**:3746. https://doi.org/10.3390/s21113746

113. Carr E, Vitoratou S, Chalder T, Goldsmith K. Discernment of mediator and outcome measurement

in the PACE trial. *J Psychosom Res* 2021;**149**:110595. https://doi.org/10.1016/j.jpsychores.2021.110595

114. Carr MJ, Ashcroft DM, White PD, Kapur N, Webb RT. Prevalence of comorbid mental and physical illnesses and risks for self-harm and premature death among primary care patients diagnosed with fatigue syndromes. *Psychol Med* 2020;**50**:1156–63. https://doi.org/10.1017/S0033291719001065

115. Carroll S, Chalder T, Hemingway C, Heyman I, Bear H, Sweeney L, Moss-Morris R. Adolescent and parent factors related to fatigue in paediatric multiple sclerosis and chronic fatigue syndrome: a comparative study. *Eur J Paediatr Neurol* 2019;**23**:70–80. https://doi.org/10.1016/j.ejpn.2018.10.006

116. Cash A, Kaufman DL. Oxaloacetate treatment for mental and physical fatigue in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and long-COVID fatigue patients: a non-randomized controlled clinical trial. *J Transl Med* 2022;**20**:295. https://doi.org/10.1186/s12967-022-03488-3

117. Casson S, Jones MD, Cassar J, Kwai N, Lloyd AR, Barry BK, Sandler CX. The effectiveness of activity pacing interventions for people with chronic fatigue syndrome: a systematic review and meta-analysis. *Disabil Rehabil* 2022;**45**:3788–802. https://doi.org/10.1080/09638288.2022.2135776

118. Castro-Marrero J, Domingo JC, Cordobilla B, Ferrer R, Giralt M, Sanmartin-Sentanes R, Alegre-Martín J. Does coenzyme Q10 plus selenium supplementation ameliorate clinical outcomes by modulating oxidative stress and inflammation in individuals with myalgic encephalomyelitis/chronic fatigue syndrome? *Antioxid Redox Signal* 2022;**36**:729–39. https://doi.org/10.1089/ars.2022.0018

119. Castro-Marrero J, Faro M, Zaragoza MC, Aliste L, de Sevilla TF, Alegre J. Unemployment and work disability in individuals with chronic fatigue syndrome/myalgic encephalomyelitis: a community-based cross-sectional study from Spain. *BMC Public Health* 2019;**19**:840. https://doi.org/10.1186/s12889-019-7225-z

120. Castro-Marrero J, Segundo MJ, Lacasa M, Martinez-Martinez A, Sentanes RS, Alegre-Martin J. Effect of dietary coenzyme Q10 Plus NADH supplementation on fatigue perception and health-related quality of life in individuals with myalgic encephalomyelitis/chronic fatigue syndrome: a prospective, randomized, double-blind, placebo-controlled trial. *Nutrients* 2021;**13**:2658. https://doi.org/10.3390/nu13082658

121. Castro-Marrero J, Serrano-Pertierra E, Oliveira-Rodriguez M, Zaragoza MC, Martinez-Martinez A, Blanco-Lopez MDC, Alegre J. Circulating extracellular vesicles as potential biomarkers in chronic fatigue syndrome/myalgic encephalomyelitis: an exploratory pilot study. *J Extracell Vesicles* 2018;**7**:1453730. https://doi.org/10.1080/20013078.2018.1453730

122. Castro-Marrero J, Zacares M, Almenar-Perez E, Alegre-Martin J, Oltra E. Complement component C1q as a potential diagnostic tool for myalgic encephalomyelitis/chronic fatigue syndrome subtyping. *J Clin Med* 2021;**10**:4171. https://doi.org/10.3390/jcm10184171

123. Castro-Marrero J, Zaragoza MC, Domingo JC, Martinez-Martinez A, Alegre J, von Schacky C. Low omega-3 index and polyunsaturated fatty acid status in patients with chronic fatigue syndrome/myalgic encephalomyelitis. *Prostaglandins Leukot Essent Fatty Acids* 2018;**139**:20–4. https://doi.org/10.1016/j.plefa.2018.11.006

124. Castro-Marrero J, Zaragoza MC, Gonzalez-Garcia S, Aliste L, Saez-Francas N, Romero O, *et al*. Poor self-reported sleep quality and health-related quality of life in patients with chronic fatigue syndrome/myalgic encephalomyelitis. *J Sleep Res* 2018;**27**:e12703. https://doi.org/10.1111/jsr.12703

125. Chan A, Truong A, Farhadian B, Willett T, Silverman M, Tran P, *et al*. Chronic fatigue symptoms in children with abrupt early-onset OCD And/or PANS. *Arthritis Rheumatol* 2020;**72**:1–338. https://doi.org/10.1002/art.41304

126. Chandan JS, Thomas T, Raza K, Bradbury-Jones C, Taylor J, Bandyopadhyay S, Nirantharakumar K. Intimate partner violence and the risk of developing fibromyalgia and chronic fatigue syndrome. *J Interpers Violence* 2021;**36**:NP12279–98. https://doi.org/10.1177/0886260519888515

127. Chapman N, Broadbent S, Coutts R. Acceptance, fatigue severity and self-reported physical activity in individuals with chronic fatigue syndrome/myalgic encephalomyelitis. *Fatigue: Biomed Health Behav* 2019;**7**:102–15. https://doi.org/10.1080/21641846.2019.1629760

128. Chaves-Filho AJM, Macedo DS, de Lucena DF, Maes M. Shared microglial mechanisms underpinning depression and chronic fatigue syndrome and their comorbidities. *Behav Brain Res* 2019;**372**:111975. https://doi.org/10.1016/j.bbr.2019.111975

129. Che X, Brydges CR, Yu Y, Price A, Joshi S, Roy A, *et al*. Metabolomic evidence for peroxisomal dysfunction in myalgic encephalomyelitis/chronic fatigue syndrome. *Int J Mol Sci* 2022;**23**:7906. https://doi.org/10.3390/ijms23147906

130. Cheema AK, Sarria L, Bekheit M, Collado F, Almenar-Perez E, Martin-Martinez E, *et al*. Unravelling myalgic encephalomyelitis/chronic fatigue syndrome (ME/

CFS): gender-specific changes in the microRNA expression profiling in ME/CFS. *J Cell Mol Med* 2020;**24**:5865–77. https://doi.org/10.1111/jcmm.15260

131. Chen C, Yip HT, Leong KH, Yao WC, Hung CL, Su CH, *et al*. Presence of depression and anxiety with distinct patterns of pharmacological treatments before the diagnosis of chronic fatigue syndrome: a population-based study in Taiwan. *J Transl Med* 2023;**21**:98. https://doi.org/10.1186/s12967-023-03886-1

132. Chen CS, Cheng HM, Chen HJ, Tsai SY, Kao CH, Lin HJ, *et al*. Dry eye syndrome and the subsequent risk of chronic fatigue syndrome – a prospective population-based study in Taiwan. *Oncotarget* 2018;**9**:30694–703. https://doi.org/10.18632/oncotarget.25544

133. Chen S-s, Liu R, Wu B, Chen S, Guo F, Xue X-l, Wang J. Acupuncture on back-shu points of five zang for chronic fatigue syndrome: a randomized control trial. *World J Acupunct Moxibustion* 2018;**28**:237–41. https://doi.org/10.1016/j.wjam.2018.12.007

134. Cheshire A, Ridge D, Clark L, White P. Guided graded exercise self-help for chronic fatigue syndrome: patient experiences and perceptions. *Disabil Rehabil* 2020;**42**:368–77. https://doi.org/10.1080/09638288.2018.1499822

135. Chirumbolo S, Valdenassi L, Franzini M, Pandolfi S, Ricevuti G, Tirelli U. Male vs. Female Differences in Responding to Oxygen–Ozone Autohemotherapy (O2-O3-AHT) in Patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). *J Clin Med* 2021;**11**:173. https://doi.org/10.3390/jcm11010173

136. Christensen B, Davenport TE, Stevens S, Van Ness JM, Stevens J, Snell CR. Cardiopulmonary exercise test performance in myalgic encephalomyelitis/chronic fatigue syndrome: systematic review and meta-analysis. *Cardiopulm Phys Ther J* 2020;**31**:e1–11. https://doi.org/10.1097/cpt.0000000000000136

137. Chu L, Valencia IJ, Garvert DW, Montoya JG. Deconstructing post-exertional malaise in myalgic encephalomyelitis/chronic fatigue syndrome: a patient-centered, cross-sectional survey. *PLOS ONE* 2018;**13**:e0197811. https://doi.org/10.1371/journal.pone.0197811

138. Clague-Baker N, Bull M, Leslie K, Hilliard N. Survey of people with myalgic encephalomyelitis (ME) to explore their use and experiences of physiotherapy services in the UK. *Physiotherapy* 2021;**113**:e101–2. https://doi.org/10.1016/j.physio.2021.10.079

139. Clague-Baker N, Davenport TE, Madi M, Dickinson K, Leslie K, Bull M, Hilliard N. An international survey of experiences and attitudes towards pacing using a heart rate monitor for people with myalgic encephalomyelitis/chronic fatigue syndrome. *Work* 2023;**74**:1225–34. https://doi.org/10.3233/WOR-220512

140. Clark C, Holttum S. 'A life I can cope with'. An alternative model of cognitive behavioural therapy (CBT) for CFS/ME. *Health Expect* 2022;**25**:91–102. https://doi.org/10.1111/hex.13326

141. Clark JE, Davidson SL, Maclachlan L, Newton JL, Watson S. Rethinking childhood adversity in chronic fatigue syndrome. *Fatigue* 2018;**6**:20–9. https://doi.org/10.1080/21641846.2018.1384095

142. Clark JE, Ng WF, Rushton S, Watson S, Newton JL. Network structure underpinning (dys)homeostasis in chronic fatigue syndrome; preliminary findings. *PLOS ONE* 2019;**14**:e0213724. https://doi.org/10.1371/journal.pone.0213724

143. Clark LV, McCrone P, Pesola F, Vergara-Williamson M, White PD. Guided graded exercise self-help for chronic fatigue syndrome: long term follow up and cost-effectiveness following the GETSET trial. *J Psychosom Res* 2021;**146**:110484. https://doi.org/10.1016/j.jpsychores.2021.110484

144. Clery P, Linney C, Parslow R, Starbuck J, Laffan A, Leveret J, Crawley E. The importance of school in the management of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): issues identified by adolescents and their families. *Health Soc Care Community* 2022;**30**:e5234–44. https://doi.org/10.1111/hsc.13942

145. Clery P, Royston A, Driver K, Bailey J, Crawley E, Loades M. What treatments work for anxiety and depression in children and adolescents with chronic fatigue syndrome? An updated systematic review. *BMJ Open* 2022;**12**:e051358. https://doi.org/10.1136/bmjopen-2021-051358

146. Cliff JM, King EC, Lee JS, Sepulveda N, Wolf AS, Kingdon C, *et al*. Cellular Immune function in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Front Immunol* 2019;**10**:796. https://doi.org/10.3389/fimmu.2019.00796

147. Close S, Marshall-Gradisnik S, Byrnes J, Smith P, Nghiem S, Staines D. The economic impacts of myalgic encephalomyelitis/chronic fatigue syndrome in an Australian cohort. *Front Public Health* 2020;**8**:420. https://doi.org/10.3389/fpubh.2020.00420

148. Cochrane M, Mitchell E, Hollingworth W, Crawley E, Trepel D. Cost-effectiveness of interventions for chronic fatigue syndrome or myalgic encephalomyelitis: a systematic review of economic evaluations. *Appl Health Econ Health Policy*

2021;**19**:473–86. https://doi.org/10.1007/s40258-021-00635-7

149. Collard SS, Murphy J. Management of chronic fatigue syndrome/myalgic encephalomyelitis in a pediatric population: a scoping review. *J Child Health Care* 2020;**24**:411–31. https://doi.org/10.1177/1367493519864747

150. Collin SM, Heron J, Nikolaus S, Knoop H, Crawley E. Chronic fatigue syndrome (CFS/ME) symptom-based phenotypes and 1-year treatment outcomes in two clinical cohorts of adult patients in the UK and the Netherlands. *J Psychosom Res* 2018;**104**:29–34. https://doi.org/10.1016/j.jpsychores.2017.11.007

151. Collin SM, Norris T, Deere KC, Jago R, Ness AR, Crawley E. Physical activity at age 11 years and chronic disabling fatigue at ages 13 and 16 years in a UK birth cohort. *Arch Dis Child* 2018;**103**:586–91. https://doi.org/10.1136/archdischild-2017-314138

152. Collin SM, Norris T, Gringras P, Blair PS, Tilling K, Crawley E. Childhood sleep and adolescent chronic fatigue syndrome (CFS/ME): evidence of associations in a UK birth cohort. *Sleep Med* 2018;**46**:26–36. https://doi.org/10.1016/j.sleep.2018.01.005

153. Collin SM, Norris T, Joinson C, Loades ME, Lewis G, Stansfeld SA, Crawley E. Depressive symptoms at age 9–13 and chronic disabling fatigue at age 16: a longitudinal study. *J Adolesc* 2019;**75**:123–9. https://doi.org/10.1016/j.adolescence.2019.07.014

154. Comella P, Beckmann N, Hoffman G, Schadt E. Machine learning classifiers implicate B cell activation in chronic fatigue syndrome [Abstracts from the 52nd European Society of Human Genetics (ESHG) Conference: Posters]. *Eur J Hum Genet* 2019;**27**:1174–813. https://doi.org/10.1038/s41431-019-0494-2

155. Comhaire F. Treating patients suffering from myalgic encephalopathy/chronic fatigue syndrome (ME/CFS) with sodium dichloroacetate: an open-label, proof-of-principle pilot trial. *Med Hypotheses* 2018;**114**:45–8. https://doi.org/10.1016/j.mehy.2018.03.002

156. Comhaire F. Why do some ME/CFS patients benefit from treatment with sodium dichloroacetate, but others do not? *Med Hypotheses* 2018;**120**:65–7. https://doi.org/10.1016/j.mehy.2018.08.014

157. Conroy KE, Islam MF, Jason LA. Evaluating case diagnostic criteria for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): toward an empirical case definition. *Disabil Rehabil* 2023;**45**:840–7. https://doi.org/10.1080/09638288.2022.2043462

158. Cook DB, VanRiper S, Dougherty RJ, Lindheimer JB, Falvo MJ, Chen Y, *et al*.; MCAM Study Group. Cardiopulmonary, metabolic, and perceptual responses during exercise in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): a multi-site clinical assessment of ME/CFS (MCAM) sub-study. *PLOS ONE* 2022;**17**:e0265315. https://doi.org/10.1371/journal.pone.0265315

159. Corbitt M, Campagnolo N, Staines D, Marshall-Gradisnik S. A systematic review of probiotic interventions for gastrointestinal symptoms and irritable bowel syndrome in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). *Probiotics Antimicrob Proteins* 2018;**10**:466–77. https://doi.org/10.1007/s12602-018-9397-8

160. Corbitt M, Eaton-Fitch N, Staines D, Cabanas H, Marshall-Gradisnik S. A systematic review of cytokines in chronic fatigue syndrome/myalgic encephalomyelitis/systemic exertion intolerance disease (CFS/ME/SEID). *BMC Neurol* 2019;**19**:207. https://doi.org/10.1186/s12883-019-1433-0

161. Cotler J, Holtzman C, Dudun C, Jason LA. A brief questionnaire to assess post-exertional malaise. *Diagnostics (Basel)* 2018;**8**:66. https://doi.org/10.3390/diagnostics8030066

162. Cotler J, Katz BZ, Reurts-Post C, Vermeulen R, Jason LA. A hierarchical logistic regression predicting rapid respiratory rates from post-exertional malaise. *Fatigue* 2020;**8**:205–13. https://doi.org/10.1080/21641846.2020.1845287

163. Cournoyer J, Salmun G. Attenuated fat oxidation rates in ME/CFS patients. *Med Sci Sports Exerc* 2018;**50**:824. https://doi.org/10.1249/01.mss.0000538712.91111.69

164. Cox BS, Alharshawi K, Mena-Palomo I, Lafuse WP, Ariza ME. EBV/HHV-6A dUTPases contribute to myalgic encephalomyelitis/chronic fatigue syndrome pathophysiology by enhancing TFH cell differentiation and extrafollicular activities. *JCI Insight* 2022;**7**:08. https://doi.org/10.1172/jci.insight.158193

165. Crawley EM, Gaunt DM, Garfield K, Hollingworth W, Sterne JAC, Beasant L, *et al*. Clinical and cost-effectiveness of the lightning process in addition to specialist medical care for paediatric chronic fatigue syndrome: randomised controlled trial. *Arch Dis Child* 2018;**103**:155–64. https://doi.org/10.1136/archdischild-2017-313375

166. Creed F. Psychiatric disorders and the onset of self-reported fibromyalgia and chronic fatigue syndrome: the lifelines cohort study. *Front Psychiatry* 2023;**14**:1120250. https://doi.org/10.3389/fpsyt.2023.1120250

167. Crosby LD, Kalanidhi S, Bonilla A, Subramanian A, Ballon JS, Bonilla H. Off label use of Aripiprazole

shows promise as a treatment for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): a retrospective study of 101 patients treated with a low dose of Aripiprazole. *J Transl Med* 2021;**19**:50. https://doi.org/10.1186/s12967-021-02721-9

168. Cusa C, Venturini L, Capelli E, Lorusso L, Romeo M, Falcone C, *et al*. Treatment of fibromyalgia. Probiotics can be a useful therapy in chronic fatigue syndrome patients. *Clin Exp Rheumatol* 2019;**37**:S140.

169. Daniels J, Parker H, Salkovskis PM. Prevalence and treatment of chronic fatigue syndrome/myalgic encephalomyelitis and co-morbid severe health anxiety. *Int J Clin Health Psychol* 2020;**20**:10–9. https://doi.org/10.1016/j.ijchp.2019.11.003

170. Danilenko OV, Gavrilova NY, Churilov LP. Chronic fatigue exhibits heterogeneous autoimmunity characteristics which reflect etiology. *Pathophysiology* 2022;**29**:187–99. https://doi.org/10.3390/pathophysiology29020016

171. Das S, Taylor K, Kozubek J, Sardell J, Gardner S. Genetic risk factors for ME/CFS identified using combinatorial analysis. *J Transl Med* 2022;**20**:598. https://doi.org/10.1186/s12967-022-03815-8

172. Davenport TE, Lehnen M, Stevens SR, VanNess JM, Stevens J, Snell CR. Chronotropic intolerance: an overlooked determinant of symptoms and activity limitation in myalgic encephalomyelitis/chronic fatigue syndrome? *Front Pediatr* 2019;**7**:82. https://doi.org/10.3389/fped.2019.00082

173. De Bellis A, Bellastella G, Pernice V, Cirillo P, Longo M, Maio A, *et al*. Hypothalamic-pituitary autoimmunity and related impairment of hormone secretions in chronic fatigue syndrome. *J Clin Endocrinol Metab* 2021;**106**:e5147–55. https://doi.org/10.1210/clinem/dgab429

174. De Meirleir KL, Mijatovic T, Subramanian K, Schlauch KA, Lombardi VC. Evaluation of four clinical laboratory parameters for the diagnosis of myalgic encephalomyelitis. *J Transl Med* 2018;**16**:322. https://doi.org/10.1186/s12967-018-1696-z

175. de Orleans Casagrande P, Coimbra DR, de Souza LC, Andrade A. Effects of yoga on depressive symptoms, anxiety, sleep quality, and mood in patients with rheumatic diseases: systematic review and meta-analysis. *PM R* 2023;**15**:899–915. https://doi.org/10.1002/pmrj.12867

176. de Vega WC, Erdman L, Vernon SD, Goldenberg A, McGowan PO. Integration of DNA methylation & health scores identifies subtypes in myalgic encephalomyelitis/chronic fatigue syndrome. *Epigenomics* 2018;**10**:539–57. https://doi.org/10.2217/epi-2017-0150

177. De Venter M, Illegems J, Van Royen R, Sabbe BGC, Moorkens G, Van Den Eede F. The relationship between childhood trauma and the response to group cognitive-behavioural therapy for chronic fatigue syndrome. *Front Psychiatry* 2020;**11**:536. https://doi.org/10.3389/fpsyt.2020.00536

178. Deumer US, Varesi A, Floris V, Savioli G, Mantovani E, Lopez-Carrasco P, *et al*. Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): an overview. *J Clin Med* 2021;**10**:4786. https://doi.org/10.3390/jcm10204786

179. Devendorf AR, McManimen SL, Jason LA. Suicidal ideation in non-depressed individuals: the effects of a chronic, misunderstood illness. *J Health Psychol* 2020;**25**:2106–17. https://doi.org/10.1177/1359105318785450

180. Devendorf AR, Rown AA, Jason LA. Patients' hopes for recovery from myalgic encephalomyelitis and chronic fatigue syndrome: toward a 'recovery in' framework. *Chronic Illn* 2020;**16**:307–21. https://doi.org/10.1177/1742395318815965

181. Dibnah B, Traianos E, Tarn J, Lendrem D, Ng WF. Investigating the role of TGF-B and fatigue in chronic fatigue syndrome. *Ann Rheum Dis* 2019;**78**:1495. https://doi.org/10.1136/annrheumdis-2019-eular.4690

182. Do Campo J, Taylor V. Spironolactone as treatment for chronic fatigue syndrome in patients with positive Epstein Bar virus serology. *Intern Med J* 2020;**50**:19. https://doi.org/10.1111/imj.11_14849

183. Do C. Clinical improvement in patients with ME/CFs with synergistic effect of colchicine and spironolactone targeting inhibition of inflammasome activity. *Intern Med J* 2022;**52**:13. https://doi.org/10.1111/imj.23_15766

184. Domingo JC, Cordobilla B, Ferrer R, Giralt M, Alegre-Martin J, Castro-Marrero J. Are circulating fibroblast growth factor 21 and N-terminal prohormone of brain natriuretic peptide promising novel biomarkers in myalgic encephalomyelitis/chronic fatigue syndrome? *Antioxid Redox Signal* 2021;**34**:1420–7. https://doi.org/10.1089/ars.2020.8230

185. Domingues TD, Grabowska AD, Lee JS, Ameijeiras-Alonso J, Westermeier F, Scheibenbogen C, *et al*. Herpesviruses serology distinguishes different subgroups of patients from the United Kingdom myalgic encephalomyelitis/chronic fatigue syndrome biobank. *Front Med (Lausanne)* 2021;**8**:686736. https://doi.org/10.3389/fmed.2021.686736

186. Donnachie E, Schneider A, Mehring M, Enck P. Incidence of irritable bowel syndrome and chronic fatigue following GI infection: a population-level study using routinely collected claims data. *Gut*

2018;**67**:1078–86. https://doi.org/10.1136/gutjnl-2017-313713

187. Preez D, Corbitt M, Cabanas H, Eaton N, Staines D, Marshall-Gradisnik S. A systematic review of enteric dysbiosis in chronic fatigue syndrome/myalgic encephalomyelitis. *Syst Rev* 2018;**7**:241. https://doi.org/10.1186/s13643-018-0909-0

188. Preez D, Eaton-Fitch N, Cabanas H, Staines D, Marshall-Gradisnik S. Characterization of IL-2 stimulation and TRPM7 pharmacomodulation in NK cell cytotoxicity and channel co-localization with PIP(2) in myalgic encephalomyelitis/chronic fatigue syndrome patients. *Int J Environ Res Public Health* 2021;**18**:12. https://doi.org/10.3390/ijerph182211879

189. Duvignaud A, Fianu A, Bertolotti A, Jaubert J, Michault A, Poubeau P, *et al*. Rheumatism and chronic fatigue, the two facets of post-chikungunya disease: the TELECHIK cohort study on Reunion island. *Epidemiol Infect* 2018;**146**:633–41. https://doi.org/10.1017/S0950268818000031

190. Eaton-Fitch N, du P, Cabanas H, Staines D, Marshall-Gradisnik S. A systematic review of natural killer cells profile and cytotoxic function in myalgic encephalomyelitis/chronic fatigue syndrome. *Syst Rev* 2019;**8**:279. https://doi.org/10.1186/s13643-019-1202-6

191. Eccles JA, Thompson B, Themelis K, Amato ML, Stocks R, Pound A, *et al*. Beyond bones: the relevance of variants of connective tissue (hypermobility) to fibromyalgia, ME/CFS and controversies surrounding diagnostic classification: an observational study. *Clin Med (Lond)* 2021;**21**:53–8. https://doi.org/10.7861/clinmed.2020-0743

192. Eguchi A, Fukuda S, Kuratsune H, Nojima J, Nakatomi Y, Watanabe Y, Feldstein AE. Identification of actin network proteins, talin-1 and filamin-A, in circulating extracellular vesicles as blood biomarkers for human myalgic encephalomyelitis/chronic fatigue syndrome. *Brain Behav Immun* 2020;**84**:106–14. https://doi.org/10.1016/j.bbi.2019.11.015

193. Ekberg KM, Torres C, Jason LA. Parent-child discrepancies in health-related quality of life of children and adolescents with myalgic encephalomyelitis/chronic fatigue syndrome. *Qual Life Res* 2021;**30**:3443–8. https://doi.org/10.1007/s11136-021-02919-w

194. El-Mokadem John FK, DiMarco K, Kelley Thomas M, Duffield L. Three principles/innate health: the efficacy of psycho-spiritual mental health education for people with chronic fatigue syndrome. *Spiritual Clin Pract* 2020;**10**(4):289–303. https://doi.org/10.1037/scp0000232

195. Elliott MK, Jason LA. Risk factors for suicidal ideation in a chronic illness. *Death Stud* 2023;**47**:827–35. https://doi.org/10.1080/07481187.2022.2132551

196. Eriksen W. ME/CFS, case definition, and serological response to Epstein-Barr virus. A systematic literature review. *Fatigue: Biomed Health Behav* 2018;**6**:220–34. https://doi.org/10.1080/21641846.2018.1503125

197. Esfandyarpour R, Kashi A, Nemat-Gorgani M, Wilhelmy J, Davis RW. A nanoelectronics-blood-based diagnostic biomarker for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Proc Natl Acad Sci U S A* 2019;**116**:10250–7. https://doi.org/10.1073/pnas.1901274116

198. Espinosa P, Urra JM. Decreased expression of the CD57 molecule in T lymphocytes of patients with chronic fatigue syndrome. *Mol Neurobiol* 2019;**56**:6581–5. https://doi.org/10.1007/s12035-019-1549-7

199. Estevez-Lopez F, Mudie K, Wang-Steverding X, Bakken IJ, Ivanovs A, Castro-Marrero J, *et al*. Systematic review of the epidemiological burden of myalgic encephalomyelitis/chronic fatigue syndrome across Europe: current evidence and EUROMENE research recommendations for epidemiology. *J Clin Med* 2020;**9**:1557. https://doi.org/10.3390/jcm9051557

200. Eyskens JB, Illegems J, De Nil L, Nijs J, Kampen JK, Moorkens G. Assessing chronic fatigue syndrome: self-reported physical functioning and correlations with physical testing. *J Bodyw Mov Ther* 2019;**23**:598–603. https://doi.org/10.1016/j.jbmt.2019.03.006

201. Falaguera-Vera FJ, Garcia-Escudero M, Bonastre-Ferez J, Zacares M, Oltra E. Pressure point thresholds and ME/CFS comorbidity as indicators of patient's response to manual physiotherapy in fibromyalgia. *Int J Environ Res Public Health* 2020;**17**:8044. https://doi.org/10.3390/ijerph17218044

202. Fang Y, Yue BW, Ma HB, Yuan YP. Acupuncture and moxibustion for chronic fatigue syndrome: a systematic review and network meta-analysis. *Medicine (Baltim)* 2022;**101**:e29310. https://doi.org/10.1097/MD.0000000000029310

203. Fatt SJ, Beilharz JE, Joubert M, Wilson C, Lloyd AR, Vollmer-Conna U, Cvejic E. Parasympathetic activity is reduced during slow-wave sleep, but not resting wakefulness, in patients with chronic fatigue syndrome. *J Clin Sleep Med* 2020;**16**:19–28. https://doi.org/10.5664/jcsm.8114

204. Fatt SJ, Cvejic E, Lloyd AR, Vollmer-Conna U, Beilharz JE. The invisible burden of chronic fatigue in the community: a narrative review. *Curr*

Rheumatol Rep 2019;**21**:5. https://doi.org/10.1007/s11926-019-0804-2

205. Fernie BA, Aoun A, Kollmann J, Spada MM, Nikcevic AV. Transcultural, transdiagnostic, and concurrent validity of a revised metacognitions about symptoms control scale. *Clin Psychol Psychother* 2019;**26**:471–82. https://doi.org/10.1002/cpp.2367
206. Finkelmeyer A, He J, Maclachlan L, Blamire AM, Newton JL. Intracranial compliance is associated with symptoms of orthostatic intolerance in chronic fatigue syndrome. *PLOS ONE* 2018;**13**:e0200068. https://doi.org/10.1371/journal.pone.0200068
207. Finkelmeyer A, He J, Maclachlan L, Watson S, Gallagher P, Newton JL, Blamire AM. Grey and white matter differences in chronic fatigue syndrome – a voxel-based morphometry study. *Neuroimage Clin* 2018;**17**:24–30. https://doi.org/10.1016/j.nicl.2017.09.024
208. Fluge O, Rekeland IG, Lien K, Thurmer H, Borchgrevink PC, Schafer C, *et al*. B-Lymphocyte depletion in patients with myalgic encephalomyelitis/chronic fatigue syndrome: a randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 2019;**170**:585–93. https://doi.org/10.7326/M18-1451
209. Franklin JD, Atkinson G, Atkinson JM, Batterham AM. Peak oxygen uptake in chronic fatigue syndrome/myalgic encephalomyelitis: a meta-analysis. *Int J Sports Med* 2019;**40**:77–87. https://doi.org/10.1055/a-0802-9175
210. Franklin John D, Graham M. Repeated maximal exercise tests of peak oxygen consumption in people with myalgic encephalomyelitis/chronic fatigue syndrome: a systematic review and meta-analysis. *Fatigue: Biomed Health Behav* 2022;**10**:119–35. https://doi.org/10.1080/21641846.2022.2108628
211. Freitag H, Szklarski M, Lorenz S, Sotzny F, Bauer S, Philippe A, *et al*. Autoantibodies to vasoregulative G-protein-coupled receptors correlate with symptom severity, autonomic dysfunction and disability in myalgic encephalomyelitis/chronic fatigue syndrome. *J Clin Med* 2021;**10**:3675. https://doi.org/10.3390/jcm10163675
212. Friedberg F, Adamowicz JL, Bruckenthal P, Milazzo M, Ramjan S, Quintana D. Nonimprovement in chronic fatigue syndrome: relation to activity patterns, uplifts and hassles, and autonomic dysfunction. *Psychosom Med* 2022;**84**:669–78. https://doi.org/10.1097/PSY.0000000000001082
213. Friedberg F, Adamowicz JL, Bruckenthal P, Milazzo M, Ramjan S, Zhang X, Yang J. Sex differences in post-exercise fatigue and function in myalgic encephalomyelitis/chronic fatigue syndrome. *Sci Rep* 2023;**13**:5442. https://doi.org/10.1038/s41598-023-32581-w
214. Friedberg F, Choi D. Hydrogen water as a treatment for myalgic encephalomyelitis/chronic fatigue syndrome: a pilot randomized trial. *Fatigue: Biomed Health Behav* 2022;**10**:26–39. https://doi.org/10.1080/21641846.2022.2038519
215. Froehlich L, Hattesohl DB, Cotler J, Jason LA, Scheibenbogen C, Behrends U. Causal attributions and perceived stigma for myalgic encephalomyelitis/chronic fatigue syndrome. *J Health Psychol* 2022;**27**:2291–304. https://doi.org/10.1177/13591053211027631
216. Fujii H, Sato W, Kimura Y, Matsuda H, Ota M, Maikusa N, *et al*. Altered structural brain networks related to adrenergic/muscarinic receptor autoantibodies in chronic fatigue syndrome. *J Neuroimaging* 2020;**30**:822–7. https://doi.org/10.1111/jon.12751
217. Gaglio CL, Islam MF, Cotler J, Jason LA. Orthostatic intolerance and neurocognitive impairment in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Epidemiol Methods* 2022;**11**:20210033. https://doi.org/10.1515/em-2021-0033
218. Galeoto G, Sansoni J, Valenti D, Mollica R, Valente D, Parente M, Servadio A. The effect of physiotherapy on fatigue and physical functioning in chronic fatigue syndrome patients: a systematic review. *Clin Ter* 2018;**169**:e184–8. https://doi.org/10.7417/T.2018.2076
219. Garner R, Baraniuk JN. Orthostatic intolerance in chronic fatigue syndrome. *J Transl Med* 2019;**17**:185. https://doi.org/10.1186/s12967-019-1935-y
220. Geraghty K, Hann M, Kurtev S. Myalgic encephalomyelitis/chronic fatigue syndrome patients' reports of symptom changes following cognitive behavioural therapy, graded exercise therapy and pacing treatments: analysis of a primary survey compared with secondary surveys. *J Health Psychol* 2019;**24**:1318–33. https://doi.org/10.1177/1359105317726152
221. Geraghty KJ, Blease C. Myalgic encephalomyelitis/chronic fatigue syndrome and the biopsychosocial model: a review of patient harm and distress in the medical encounter. *Disabil Rehabil* 2019;**41**:3092–102. https://doi.org/10.1080/09638288.2018.1481149
222. Germain A, Barupal DK, Levine SM, Hanson MR. Comprehensive circulatory metabolomics in ME/CFS reveals disrupted metabolism of acyl lipids and steroids. *Metabolites* 2020;**10**:34. https://doi.org/10.3390/metabo10010034
223. Germain A, Giloteaux L, Moore GE, Levine SM, Chia JK, Keller BA, *et al*. Plasma metabolomics reveals

disrupted response and recovery following maximal exercise in myalgic encephalomyelitis/chronic fatigue syndrome. *JCI Insight* 2022;**7**:09. https://doi.org/10.1172/jci.insight.157621

224. Germain A, Ruppert D, Levine SM, Hanson MR. Prospective biomarkers from plasma metabolomics of myalgic encephalomyelitis/chronic fatigue syndrome implicate redox imbalance in disease symptomatology. *Metabolites* 2018;**8**:90. https://doi.org/10.3390/metabo8040090
225. Ghali A, Richa P, Lacout C, Gury A, Beucher AB, Homedan C, *et al*. Epidemiological and clinical factors associated with post-exertional malaise severity in patients with myalgic encephalomyelitis/chronic fatigue syndrome. *J Transl Med* 2020;**18**:246. https://doi.org/10.1186/s12967-020-02419-4
226. Giloteaux L, Li J, Hornig M, Lipkin WI, Ruppert D, Hanson MR. Proteomics and cytokine analyses distinguish myalgic encephalomyelitis/chronic fatigue syndrome cases from controls. *J Transl Med* 2023;**21**:322. https://doi.org/10.1186/s12967-023-04179-3
227. Giloteaux L, O'Neal A, Castro-Marrero J, Levine SM, Hanson MR. Cytokine profiling of extracellular vesicles isolated from plasma in myalgic encephalomyelitis/chronic fatigue syndrome: a pilot study. *J Transl Med* 2020;**18**:387. https://doi.org/10.1186/s12967-020-02560-0
228. Glass KA, Germain A, Huang YV, Hanson MR. Urine metabolomics exposes anomalous recovery after maximal exertion in female ME/CFS patients. *Int J Mol Sci* 2023;**24**:3685. https://doi.org/10.3390/ijms24043685
229. Gleason KD, Stoothoff J, McClellan D, McManimen S, Thorpe T, Katz BZ, Jason LA. Operationalizing substantial reduction in functioning among young adults with chronic fatigue syndrome. *Int J Behav Med* 2018;**25**:448–55. https://doi.org/10.1007/s12529-018-9732-1
230. Godlewska BR, Williams S, Emir UE, Chen C, Sharpley AL, Goncalves AJ, *et al*. Neurochemical abnormalities in chronic fatigue syndrome: a pilot magnetic resonance spectroscopy study at 7 Tesla. *Psychopharmacology (Berl)* 2022;**239**:163–71. https://doi.org/10.1007/s00213-021-05986-6
231. Gomez-Mora E, Carrillo J, Urrea V, Rigau J, Alegre J, Cabrera C, *et al*. Impact of long-term cryopreservation on blood immune cell markers in myalgic encephalomyelitis/chronic fatigue syndrome: implications for biomarker discovery. *Front Immunol* 2020;**11**:582330. https://doi.org/10.3389/fimmu.2020.582330
232. Gonzalez-Cebrian A, Almenar-Perez E, Xu J, Yu T, Huang WE, Gimenez-Orenga K, *et al*. Diagnosis of myalgic encephalomyelitis/chronic fatigue syndrome with partial least squares discriminant analysis: relevance of blood extracellular vesicles. *Front Med (Lausanne)* 2022;**9**:842991. https://doi.org/10.3389/fmed.2022.842991
233. Gotaas ME, Stiles TC, Bjorngaard JH, Borchgrevink PC, Fors EA. Cognitive behavioral therapy improves physical function and fatigue in mild and moderate chronic fatigue syndrome: a consecutive randomized controlled trial of standard and short interventions. *Front Psychiatry* 2021;**12**:580924. https://doi.org/10.3389/fpsyt.2021.580924
234. Gottschalk G, Peterson D, Knox K, Maynard M, Whelan RJ, Roy A. Elevated ATG13 in serum of patients with ME/CFS stimulates oxidative stress response in microglial cells via activation of receptor for advanced glycation end products (RAGE). *Mol Cell Neurosci* 2022;**120**:103731. https://doi.org/10.1016/j.mcn.2022.103731
235. Goudman L, Mouraux A, Daenen L, Nijs J, Cras P, Roussel N, *et al*. Does motor cortex engagement during movement preparation differentially inhibit nociceptive processing in patients with chronic whiplash associated disorders, chronic fatigue syndrome and healthy controls? An experimental study. *J Clin Med* 2020;**9**:1520. https://doi.org/10.3390/jcm9051520
236. Gravelsina S, Nora-Krukle Z, Vilmane A, Svirskis S, Vecvagare K, Krumina A, Murovska M. Potential of activin B as a clinical biomarker in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Biomolecules* 2021;**11**:1189. https://doi.org/10.3390/biom11081189
237. Gravelsina S, Vilmane A, Svirskis S, Rasa-Dzelzkaleja S, Nora-Krukle Z, Vecvagare K, *et al*. Biomarkers in the diagnostic algorithm of myalgic encephalomyelitis/chronic fatigue syndrome. *Front Immunol* 2022;**13**:928945. https://doi.org/10.3389/fimmu.2022.928945
238. Groven N, Fors EA, Reitan SK. Patients with fibromyalgia and chronic fatigue syndrome show increased hsCRP compared to healthy controls. *Brain Behav Immun* 2019;**81**:172–7. https://doi.org/10.1016/j.bbi.2019.06.010
239. Gunther OP, Gardy JL, Stafford P, Fluge O, Mella O, Tang P, *et al*. Immunosignature analysis of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Mol Neurobiol* 2019;**56**:4249–57. https://doi.org/10.1007/s12035-018-1354-8
240. Guo C, Che X, Briese T, Ranjan A, Allicock O, Yates RA, *et al*. Deficient butyrate-producing capacity in the gut microbiome is associated with bacterial network disturbances and fatigue symptoms in ME/

CFS. *Cell Host Microbe* 2023;**31**:288–304.e8. https://doi.org/10.1016/j.chom.2023.01.004

241. Gurjar D, Singh P. Chronic fatigue syndrome in post COVID-19 patients: a community based study in North India. *Indian J Psychiatry* 2023;**65**:S114.

242. Haffke M, Freitag H, Rudolf G, Seifert M, Doehner W, Scherbakov N, *et al*. Endothelial dysfunction and altered endothelial biomarkers in patients with post-COVID-19 syndrome and chronic fatigue syndrome (ME/CFS). *J Transl Med* 2022;**20**:138. https://doi.org/10.1186/s12967-022-03346-2

243. Haghighi S, Forsmark S, Zachrisson O, Carlsson A, Nilsson MKL, Carlsson ML, *et al*. Open-label study with the monoamine stabilizer (-)-OSU6162 in myalgic encephalomyelitis/chronic fatigue syndrome. *Brain Behav* 2021;**11**:e02040. https://doi.org/10.1002/brb3.2040

244. Haider S, Janowski AJ, Lesnak JB, Hayashi K, Dailey DL, Chimenti R, *et al*. A comparison of pain, fatigue, and function between post-COVID-19 condition, fibromyalgia, and chronic fatigue syndrome: a survey study. *Pain* 2023;**164**:385–401. https://doi.org/10.1097/j.pain.0000000000002711

245. Haig-Ferguson A, Loades M, Whittle C, Read R, Higson-Sweeney N, Beasant L, *et al*. 'It's not one size fits all'; the use of videoconferencing for delivering therapy in a Specialist Paediatric Chronic Fatigue Service. *Internet Interv* 2019;**15**:43–51. https://doi.org/10.1016/j.invent.2018.12.003

246. Haines C, Loades M, Davis C. Illness perceptions in adolescents with chronic fatigue syndrome and other physical health conditions: application of the common sense model. *Clin Child Psychol Psychiatry* 2019;**24**:546–63. https://doi.org/10.1177/1359104519829796

247. Hajdarevic R, Lande A, Mehlsen J, Rydland A, Sosa DD, Strand EB, *et al*. Genetic association study in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) identifies several potential risk loci. *Brain Behav Immun* 2022;**102**:362–9. https://doi.org/10.1016/j.bbi.2022.03.010

248. Hajdarevic R, Lande A, Rekeland I, Rydland A, Strand EB, Sosa DD, *et al*. Fine mapping of the major histocompatibility complex (MHC) in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) suggests involvement of both HLA class I and class II loci. *Brain Behav Immun* 2021;**98**:101–9. https://doi.org/10.1016/j.bbi.2021.08.219

249. Hanevik K, Saghaug C, Aaland M, Morch K, Langeland N. No difference in serum levels of B-cell activating receptor and antibodies against cytolethal distending toxin B and flagellin in post-infectious irritable bowel syndrome and chronic fatigue syndrome after Giardia infection. *JGH Open* 2022;**6**:185–8. https://doi.org/10.1002/jgh3.12724

250. Harland MR, Parslow RM, Anderson N, Byrne D, Crawley E. Paediatric chronic fatigue syndrome patients' and parents' perceptions of recovery. *BMJ Paediatr Open* 2019;**3**:e000525. https://doi.org/10.1136/bmjpo-2019-000525

251. Hartle M, Bateman L, Vernon Suzanne D. Dissecting the nature of post-exertional malaise. *Fatigue: Biomed Health Behav* 2021;**9**:33–44. https://doi.org/10.1080/21641846.2021.1905415

252. Hartwig J, Sotzny F, Bauer S, Heidecke H, Riemekasten G, Dragun D, *et al*. IgG stimulated beta2 adrenergic receptor activation is attenuated in patients with ME/CFS. *Brain Behav Immun Health* 2020;**3**:100047. https://doi.org/10.1016/j.bbih.2020.100047

253. Heald A, Barber L, Jones HL, Farman S, Walther A. Service based comparison of group cognitive behavior therapy to waiting list control for chronic fatigue syndrome with regard to symptom reduction and positive psychological dimensions. *Medicine (Baltim)* 2019;**98**:e16720. https://doi.org/10.1097/MD.0000000000016720

254. Helliwell AM, Sweetman EC, Stockwell PA, Edgar CD, Chatterjee A, Tate WP. Changes in DNA methylation profiles of myalgic encephalomyelitis/chronic fatigue syndrome patients reflect systemic dysfunctions. *Clin Epigenetics* 2020;**12**:167. https://doi.org/10.1186/s13148-020-00960-z

255. Hendrix J, Polli A, Ickamns K, Creta M, Bakusic J, Ghosh M, *et al*. The relation between cortisol and anxiety in patients with myalgic encephalomyelitis/chronic fatigue syndrome and healthy people. *Pain Pract* 2022;**22**:8–64. https://doi.org/10.1111/papr.13128

256. Herane-Vives A, Papadopoulos A, de Angel V, Chua KC, Soto L, Chalder T, *et al*. Cortisol levels in chronic fatigue syndrome and atypical depression measured using hair and saliva specimens. *J Affect Disord* 2020;**267**:307–14. https://doi.org/10.1016/j.jad.2020.01.146

257. Herrera S, de Vega WC, Ashbrook D, Vernon SD, McGowan PO. Genome-epigenome interactions associated with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Epigenetics* 2018;**13**:1174–90. https://doi.org/10.1080/15592294.2018.1549769

258. Hiremath S, Doukrou M, Flannery H, Carey C, Gregorowski A, Ward J, *et al*. Key features of a multi-disciplinary hospital-based rehabilitation program for children and adolescents with moderate to severe myalgic encephalomyelitis/chronic fatigue syndrome ME/CFS. *Int J Environ Res Public*

Health 2022;**19**:13608. https://doi.org/10.3390/ijerph192013608

259. Hodges L, Nielsen T, Cochrane D, Baken D. The physiological time line of post-exertional malaise in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Transl Sports Med* 2020;**3**:243–9. https://doi.org/10.1002/tsm2.133

260. Hodges LD, Nielsen T, Baken D. Physiological measures in participants with chronic fatigue syndrome, multiple sclerosis and healthy controls following repeated exercise: a pilot study. *Clin Physiol Funct Imaging* 2018;**38**:639–44. https://doi.org/10.1111/cpf.12460

261. Hoel F, Hoel A, Pettersen IK, Rekeland IG, Risa K, Alme K, *et al*. A map of metabolic phenotypes in patients with myalgic encephalomyelitis/chronic fatigue syndrome. *JCI Insight* 2021;**6**:23. https://doi.org/10.1172/jci.insight.149217

262. Holden S, Maksoud R, Eaton-Fitch N, Cabanas H, Staines D, Marshall-Gradisnik S. A systematic review of mitochondrial abnormalities in myalgic encephalomyelitis/chronic fatigue syndrome/systemic exertion intolerance disease. *J Transl Med* 2020;**18**:290. https://doi.org/10.1186/s12967-020-02452-3

263. Holder KG, Vemulapalli V, Daines B, Kankam A, Galvan B, Nambiar R. Post-COVID myalgic encephalomyelitis in chronic heart disease patient: a case series. *J Investig Med* 2022;**70**:475. https://doi.org/10.1136/jim-2022-SRMC.40

264. Holtzman CS, Bhatia S, Cotler J, Jason LA. Assessment of post-exertional malaise (PEM) in patients with myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS): a patient-driven survey. *Diagnostics (Basel)* 2019;**9**:26. https://doi.org/10.3390/diagnostics9010026

265. Honan CA, Venettacci R, Turner J, Ahuja K, Lim E. Cognitive fatigue in chronic fatigue syndrome: comparisons with individuals with multiple sclerosis and healthy individuals. *Brain Impairment* 2019;**20**:289–376. https://doi.org/10.1017/BrImp.2019.29

266. Huber KA, Sunnquist M, Jason LA. Latent class analysis of a heterogeneous international sample of patients with myalgic encephalomyelitis/chronic fatigue syndrome. *Fatigue* 2018;**6**:163–78. https://doi.org/10.1080/21641846.2018.1494530

267. Hughes AM, Hirsch CR, Nikolaus S, Chalder T, Knoop H, Moss-Morris R. Cross-cultural study of information processing biases in chronic fatigue syndrome: comparison of Dutch and UK chronic fatigue patients. *Int J Behav Med* 2018;**25**:49–54. https://doi.org/10.1007/s12529-017-9682-z

268. Hulens M, Bruyninckx F, Dankaerts W, Rasschaert R, De Mulder P, Stalmans I, *et al*. High prevalence of perineural cysts in patients with fibromyalgia and chronic fatigue syndrome. *Pain Med* 2021;**22**:883–90. https://doi.org/10.1093/pm/pnaa410

269. Hulens M, Dankaerts W, Rasschaert R, Bruyninckx F, De Mulder P, Bervoets C. The link between empty sella syndrome, fibromyalgia, and chronic fatigue syndrome: the role of increased cerebrospinal fluid pressure. *J Pain Res* 2023;**16**:205–19. https://doi.org/10.2147/JPR.S394321

270. Huth TK, Eaton-Fitch N, Staines D, Marshall-Gradisnik S. A systematic review of metabolomic dysregulation in chronic fatigue syndrome/myalgic encephalomyelitis/systemic exertion intolerance disease (CFS/ME/SEID). *J Transl Med* 2020;**18**:198. https://doi.org/10.1186/s12967-020-02356-2

271. Hviid A, Thorsen NM, Valentiner-Branth P, Frisch M, Molbak K. Association between quadrivalent human papillomavirus vaccination and selected syndromes with autonomic dysfunction in Danish females: population based, self-controlled, case series analysis. *BMJ* 2020;**370**:m2930. https://doi.org/10.1136/bmj.m2930

272. Hyland ME, Bacon AM, Lanario JW, Davies AF. Symptom frequency and development of a generic functional disorder symptom scale suitable for use in studies of patients with irritable bowel syndrome, fibromyalgia syndrome or chronic fatigue syndrome. *Chronic Dis Transl Med* 2019;**5**:129–38. https://doi.org/10.1016/j.cdtm.2019.05.003

273. Ingman T, Smakowski A, Goldsmith K, Chalder T. A systematic literature review of randomized controlled trials evaluating prognosis following treatment for adults with chronic fatigue syndrome. *Psychol Med* 2022;**52**:2917–29. https://doi.org/10.1017/S0033291722002471

274. Jacob L, Haro JM, Kostev K. Associations of physical and psychiatric conditions with chronic fatigue syndrome in Germany: an exploratory case-control study. *Psychol Med* 2022;**52**:780–6. https://doi.org/10.1017/S0033291720002470

275. Jakel B, Kedor C, Grabowski P, Wittke K, Thiel S, Scherbakov N, *et al*. Hand grip strength and fatigability: correlation with clinical parameters and diagnostic suitability in ME/CFS. *J Transl Med* 2021;**19**:159. https://doi.org/10.1186/s12967-021-02774-w

276. Jammes Y, Adjriou N, Kipson N, Criado C, Charpin C, Rebaudet S, *et al*. Altered muscle membrane potential and redox status differentiates two subgroups of patients with chronic fatigue syndrome. *J Transl Med* 2020;**18**:173. https://doi.org/10.1186/s12967-020-02341-9

277. Jammes Y, Stavris C, Charpin C, Rebaudet S, Lagrange G, Retornaz F. Maximal handgrip strength can predict maximal physical performance in patients with chronic fatigue. *Clin Biomech (Bristol)* 2020;**73**:162–5. https://doi.org/10.1016/j.clinbiomech.2020.01.003

278. Janse A, Bleijenberg G, Knoop H. Prediction of long-term outcome after cognitive behavioral therapy for chronic fatigue syndrome. *J Psychosom Res* 2019;**121**:93–9. https://doi.org/10.1016/j.jpsychores.2019.03.017

279. Janse A, van Dam A, Pijpers C, Wiborg JF, Bleijenberg G, Tummers M, *et al*. Implementation of stepped care for patients with chronic fatigue syndrome in community-based mental health care: outcomes at post-treatment and long-term follow-up. *Behav Cogn Psychother* 2019;**47**:548–58. https://doi.org/10.1017/S1352465819000110

280. Janse A, Worm-Smeitink M, Bleijenberg G, Donders R, Knoop H. Efficacy of web-based cognitive-behavioural therapy for chronic fatigue syndrome: randomised controlled trial. *Br J Psychiatry* 2018;**212**:112–8. https://doi.org/10.1192/bjp.2017.22

281. Jason LA, Conroy KE, Furst J, Vasan K, Katz BZ. Pre-illness data reveals differences in multiple metabolites and metabolic pathways in those who do and do not recover from infectious mononucleosis. *Mol Omics* 2022;**18**:662–5. https://doi.org/10.1039/d2mo00124a

282. Jason LA, Cotler J, Islam MF, Sunnquist M, Katz BZ. Risks for developing myalgic encephalomyelitis/chronic fatigue syndrome in college students following infectious mononucleosis: a prospective cohort study. *Clin Infect Dis* 2021;**73**:e3740–6. https://doi.org/10.1093/cid/ciaa1886

283. Jason LA, Dorri JA. ME/CFS and post-exertional malaise among patients with long COVID. *Neurol Int* 2022;**15**:1–11. https://doi.org/10.3390/neurolint15010001

284. Jason LA, Gaglio CL, Furst J, Islam M, Sorenson M, Conroy KE, Katz BZ. Cytokine network analysis in a community-based pediatric sample of patients with myalgic encephalomyelitis/chronic fatigue syndrome. *Chronic Illn* 2023;**19**:571–80. https://doi.org/10.1177/17423953221101606

285. Jason LA, Islam M, Conroy K, Cotler J, Torres C, Johnson M, Mabie B. COVID-19 symptoms over time: comparing long-haulers to ME/CFS. *Fatigue* 2021;**9**:59–68. https://doi.org/10.1080/21641846.2021.1922140

286. Jason LA, Kalns J, Richarte A, Katz BZ, Torres C. Saliva fatigue biomarker index as a marker for severe myalgic encephalomyelitis/chronic fatigue syndrome in a community based sample. *Fatigue* 2021;**9**:189–95. https://doi.org/10.1080/21641846.2021.1994222

287. Jason LA, Katz BZ, Sunnquist M, Torres C, Cotler J, Bhatia S. The prevalence of pediatric myalgic encephalomyelitis/chronic fatigue syndrome in a community-based sample. *Child Youth Care Forum* 2020;**49**:563–79. https://doi.org/10.1007/s10566-019-09543-3

288. Jason LA, McManimen SL, Sunnquist M, Holtzman CS. Patient perceptions of post exertional malaise. *Fatigue: Biomed Health Behav* 2018;**6**:92–105. https://doi.org/10.1080/21641846.2018.1453265

289. Jason LA, Yoo S, Bhatia S. Patient perceptions of infectious illnesses preceding myalgic encephalomyelitis/chronic fatigue syndrome. *Chronic Illn* 2022;**18**:901–10. https://doi.org/10.1177/17423953211043106

290. Jason Leonard A, Cotler J, Islam Mohammed F, Furst J, Sorenson M, Katz Ben Z. Cytokine networks analysis uncovers further differences between those who develop myalgic encephalomyelitis/chronic fatigue syndrome following infectious mononucleosis. *Fatigue: Biomed Health Behav* 2021;**9**:45–57. https://doi.org/10.1080/21641846.2021.1915131

291. Jason Leonard A, Johnson M, Torres C. Pediatric post-acute sequelae of SARS-CoV-2 infection. *Fatigue: Biomed Health Behav* 2023;**11**:55–65. https://doi.org/10.1080/21641846.2022.2162764

292. Jeffrey MG, Nathanson L, Aenlle K, Barnes ZM, Baig M, Broderick G, *et al*. Treatment avenues in myalgic encephalomyelitis/chronic fatigue syndrome: a split-gender pharmacogenomic study of gene-expression modules. *Clin Ther* 2019;**41**:815–35.e6. https://doi.org/10.1016/j.clinthera.2019.01.011

293. Johnson M, Torres C, Watts-Rich H, Jason L. Adults with ME/CFS report surprisingly high rates of youth symptoms: a qualitative analysis of patient blog commentary. *Work* 2023;**74**:1241–51. https://doi.org/10.3233/WOR-220484

294. Jones A, Smakowski A, Hughes A, David Anthony S, Chalder T. Illness-related cognition, distress and adjustment in functional stroke symptoms, vascular stroke, and chronic fatigue syndrome. *Eur J Health Psychol* 2022;**29**:145–55. https://doi.org/10.1027/2512-8442/a000093

295. Jones LS, Anderson E, Loades M, Barnes R, Crawley E. Can linguistic analysis be used to identify whether adolescents with a chronic illness are depressed? *Clin Psychol Psychother* 2020;**27**:179–92. https://doi.org/10.1002/cpp.2417

296. Jonsjo MA, Olsson GL, Wicksell RK, Alving K, Holmstrom L, Andreasson A. The role of low-grade inflammation in ME/CFS (myalgic encephalomyelitis/

chronic fatigue syndrome) – associations with symptoms. *Psychoneuroendocrinology* 2020;**113**:104578. https://doi.org/10.1016/j.psyneuen.2019.104578

297. Jonsjö MA, Åström J, Jones MP, Karshikoff B, Lodin K, Holmström L, *et al*. Patients with ME/CFS (myalgic encephalomyelitis/chronic fatigue syndrome) and chronic pain report similar level of sickness behavior as individuals injected with bacterial endotoxin at peak inflammation. *Brain Behav Immun Health* 2020;**2**:100028. https://doi.org/10.1016/j.bbih.2019.100028
298. Jonsjö Martin A, Wicksell Rikard K, Holmström L, Andreasson A, Olsson Gunnar L. Acceptance & commitment therapy for ME/CFS (chronic fatigue syndrome) – a feasibility study. *J Contextual Behav Sci* 2019;**12**:89–97. https://doi.org/10.1016/j.jcbs.2019.02.008
299. Joseph P, Arevalo C, Oliveira RKF, Faria-Urbina M, Felsenstein D, Oaklander AL, Systrom DM. Insights from invasive cardiopulmonary exercise testing of patients with myalgic encephalomyelitis/chronic fatigue syndrome. *Chest* 2021;**160**:642–51. https://doi.org/10.1016/j.chest.2021.01.082
300. Joseph P, Pari R, Miller S, Warren A, Stovall MC, Squires J, *et al*. Neurovascular dysregulation and acute exercise intolerance in myalgic encephalomyelitis/chronic fatigue syndrome: a randomized, placebo-controlled trial of pyridostigmine. *Chest* 2022;**162**:1116–26. https://doi.org/10.1016/j.chest.2022.04.146
301. Josev EK, Malpas CB, Seal ML, Scheinberg A, Lubitz L, Rowe K, Knight SJ. Resting-state functional connectivity, cognition, and fatigue in response to cognitive exertion: a novel study in adolescents with chronic fatigue syndrome. *Brain Imaging Behav* 2020;**14**:1815–30. https://doi.org/10.1007/s11682-019-00119-2
302. Joung JY, Lee JS, Cho JH, Lee DS, Ahn YC, Son CG. The efficacy and safety of myelophil, an ethanol extract mixture of astragali radix and salviae radix, for chronic fatigue syndrome: a randomized clinical trial. *Front Pharmacol* 2019;**10**:991. https://doi.org/10.3389/fphar.2019.00991
303. Kalfas M, Smakowski A, Hirsch C, Simiao F, Chalder T. Generalized worry in patients with chronic fatigue syndrome following cognitive behavioral therapy: a prospective cohort study in secondary care. *Behav Ther* 2022;**53**:828–42. https://doi.org/10.1016/j.beth.2022.01.004
304. Kemp J, Sunnquist M, Jason LA, Newton JL. Autonomic dysfunction in myalgic encephalomyelitis and chronic fatigue syndrome: comparing self-report and objective measures. *Clin Auton Res* 2019;**29**:475–7. https://doi.org/10.1007/s10286-019-00615-x
305. Kendler KS, Rosmalen JGM, Ohlsson H, Sundquist J, Sundquist K. A distinctive profile of family genetic risk scores in a Swedish national sample of cases of fibromyalgia, irritable bowel syndrome, and chronic fatigue syndrome compared to rheumatoid arthritis and major depression. *Psychol Med* 2023;**53**:3879–86. https://doi.org/10.1017/S0033291722000526
306. Kenyon JN, Coe S, Izadi H. A retrospective outcome study of 42 patients with chronic fatigue syndrome, 30 of whom had irritable bowel syndrome. Half were treated with oral approaches, and half were treated with Faecal Microbiome Transplantation. *Hum Microbiome J* 2019;**13**:100061. https://doi.org/10.1016/j.humic.2019.100061
307. Kesler B. Quality of life among entrepreneurs with chronic fatigue syndrome. *Diss Abstr Int: Section B: Sci Eng* 2018;**79**.
308. Keynejad RC, Fenby E, Pick S, Moss-Morris R, Hirsch C, Chalder T, *et al*. Attentional processing and interpretative bias in functional neurological disorder. *Psychosom Med* 2020;**82**:586–92. https://doi.org/10.1097/PSY.0000000000000821
309. Khanpour A, Karkhaneh M, Stein E, Punja S, Junqueira DR, Kuzmyn T, *et al*. Systematic review of mind-body interventions to treat myalgic encephalomyelitis/chronic fatigue syndrome. *Medicina (Kaunas)* 2021;**57**:24. https://doi.org/10.3390/medicina57070652
310. Kielland A, Liu J, Jason LA. Do diagnostic criteria for ME matter to patient experience with services and interventions? Key results from an online RDS survey targeting fatigue patients in Norway. *J Health Psychol* 2023;**28**:1189–203. https://doi.org/10.1177/13591053231169191
311. Kim DY, Lee JS, Park SY, Kim SJ, Son CG. Systematic review of randomized controlled trials for chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). *J Transl Med* 2020;**18**:7:101069. https://doi.org/10.1186/s12967-019-02196-9
312. Kim TH, Kim DH, Kang Jung W. Medicinal herbs for managing fatigue symptoms in patients with idiopathic chronic fatigue: a PRISMA compliant updated systematic review and meta-analysis of randomized controlled trials based on the GRADE approach. *Eur J Integr Med* 2020;**35**. https://doi.org/10.1016/j.eujim.2020.101069
313. Kimura Y, Sato N, Ota M, Shigemoto Y, Morimoto E, Enokizono M, *et al*. Brain abnormalities in myalgic encephalomyelitis/chronic fatigue syndrome: evaluation by diffusional kurtosis imaging and neurite orientation dispersion and density imaging. *J Magn Reson Imaging* 2019;**49**:818–24. https://doi.org/10.1002/jmri.26247

314. King E, Beynon M, Chalder T, Sharpe M, White PD. Patterns of daytime physical activity in patients with chronic fatigue syndrome. *J Psychosom Res* 2020;**135**:110154. https://doi.org/10.1016/j.jpsychores.2020.110154

315. Kingdon CC, Bowman EW, Curran H, Nacul L, Lacerda EM. Functional status and well-being in people with myalgic encephalomyelitis/chronic fatigue syndrome compared with people with multiple sclerosis and healthy controls. *PharmacoEcon Open* 2018;**2**:381–92. https://doi.org/10.1007/s41669-018-0071-6

316. Kitami T, Fukuda S, Kato T, Yamaguti K, Nakatomi Y, Yamano E, *et al*. Deep phenotyping of myalgic encephalomyelitis/chronic fatigue syndrome in Japanese population. *Sci Rep* 2020;**10**:19933. https://doi.org/10.1038/s41598-020-77105-y

317. Klaver-Krol EG, Hermens HJ, Vermeulen RC, Klaver MM, Luyten H, Henriquez NR, Zwarts MJ. Chronic fatigue syndrome: abnormally fast muscle fiber conduction in the membranes of motor units at low static force load. *Clin Neurophysiol* 2021;**132**:967–74. https://doi.org/10.1016/j.clinph.2020.11.043

318. Klebek L, Sunnquist M, Jason LA. Differentiating post-polio syndrome from myalgic encephalomyelitis and chronic fatigue syndrome. *Fatigue* 2019;**7**:196–206. https://doi.org/10.1080/21641846.2019.1687117

319. Knight S, Elders S, Rodda J, Harvey A, Lubitz L, Rowe K, *et al*. Epidemiology of paediatric chronic fatigue syndrome in Australia. *Arch Dis Child* 2019;**104**:733–8. https://doi.org/10.1136/archdischild-2018-316450

320. Ko C, Lucassen P, van der Linden B, Ballering A, Olde Hartman T. Stigma perceived by patients with functional somatic syndromes and its effect on health outcomes – a systematic review. *J Psychosom Res* 2022;**154**:110715. https://doi.org/10.1016/j.jpsychores.2021.110715

321. Kraaij V, Bik J, Garnefski N. Cognitive and behavioral coping in people with chronic fatigue syndrome: an exploratory study searching for intervention targets for depressive symptoms. *J Health Psychol* 2019;**24**:1878–83. https://doi.org/10.1177/1359105317707259

322. Krabbe SH, Mengshoel AM, Schroder B, Sveen U, Groven KS. Bodies in lockdown: young women's narratives of falling severely ill with ME/CFS during childhood and adolescence. *Health Care Women Int* 2023;**44**:1155–77. https://doi.org/10.1080/07399332.2022.2043862

323. Krumina A, Vecvagare K, Svirskis S, Gravelsina S, Nora-Krukle Z, Gintere S, Murovska M. Clinical profile and aspects of differential diagnosis in patients with ME/CFS from Latvia. *Medicina (Kaunas)* 2021;**57**:958. https://doi.org/10.3390/medicina57090958

324. Kujawski S, Bach AM, Slomko J, Pheby DFH, Murovska M, Newton JL, Zalewski P. Changes in the allostatic response to whole-body cryotherapy and static-stretching exercises in chronic fatigue syndrome patients vs. healthy individuals. *J Clin Med* 2021;**10**:2795. https://doi.org/10.3390/jcm10132795

325. Kujawski S, Cossington J, Slomko J, Dawes H, Strong JW, Estevez-Lopez F, *et al*. Prediction of discontinuation of structured exercise programme in chronic fatigue syndrome patients. *J Clin Med* 2020;**9**:3436–12. https://doi.org/10.3390/jcm9113436

326. Kujawski S, Slomko J, Hodges L, Pheby DFH, Murovska M, Newton JL, Zalewski P. Post-exertional malaise may be related to central blood pressure, sympathetic activity and mental fatigue in chronic fatigue syndrome patients. *J Clin Med* 2021;**10**:2327. https://doi.org/10.3390/jcm10112327

327. Kujawski S, Slomko J, Newton JL, Eaton-Fitch N, Staines DR, Marshall-Gradisnik S, Zalewski P. Network analysis of symptoms co-occurrence in chronic fatigue syndrome. *Int J Environ Res Public Health* 2021;**18**:10736. https://doi.org/10.3390/ijerph182010736

328. Kuo CF, Shi L, Lin CL, Yao WC, Chen HT, Lio CF, *et al*. How peptic ulcer disease could potentially lead to the lifelong, debilitating effects of chronic fatigue syndrome: an insight. *Sci Rep* 2021;**11**:7520. https://doi.org/10.1038/s41598-021-87018-z

329. Lacerda EM, Geraghty K, Kingdon CC, Palla L, Nacul L. A logistic regression analysis of risk factors in ME/CFS pathogenesis. *BMC Neurol* 2019;**19**:275. https://doi.org/10.1186/s12883-019-1468-2

330. Lacerda EM, McDermott C, Kingdon CC, Butterworth J, Cliff JM, Nacul L. Hope, disappointment and perseverance: reflections of people with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and multiple sclerosis participating in biomedical research. A qualitative focus group study. *Health Expect* 2019;**22**:373–84. https://doi.org/10.1111/hex.12857

331. Lande A, Fluge O, Strand EB, Flam ST, Sosa DD, Mella O, *et al*. Human leukocyte antigen alleles associated with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Sci Rep* 2020;**10**:5267. https://doi.org/10.1038/s41598-020-62157-x

332. Larun L, Brurberg KG, Odgaard-Jensen J, Price JR. Exercise therapy for chronic fatigue syndrome. *Cochrane Database Syst Rev* 2019;**10**:CD003200. https://doi.org/10.1002/14651858.CD003200.pub8

333. Lechner J, Schmidt M, von Baehr V, Schick F. Undetected jawbone marrow defects as inflammatory and degenerative signaling pathways: chemokine RANTES/CCL5 as a possible link between the jawbone and systemic interactions? *J Inflamm Res* 2021;**14**:1603–12. https://doi.org/10.2147/JIR.S307635

334. Lee J, Vernon SD, Jeys P, Ali W, Campos A, Unutmaz D, *et al*. Hemodynamics during the 10-minute NASA Lean Test: evidence of circulatory decompensation in a subset of ME/CFS patients. *J Transl Med* 2020;**18**:314. https://doi.org/10.1186/s12967-020-02481-y

335. Lee J, Wall P, Kimler C, Bateman L, Vernon SD. Clinically accessible tools for documenting the impact of orthostatic intolerance on symptoms and function in ME/CFS. *Work* 2020;**66**:257–63. https://doi.org/10.3233/WOR-203169

336. Lee JS, Lacerda EM, Nacul L, Kingdon CC, Norris J, O'Boyle S, *et al*. Salivary DNA loads for human herpesviruses 6 and 7 are correlated with disease phenotype in myalgic encephalomyelitis/chronic fatigue syndrome. *Front Med (Lausanne)* 2021;**8**:656692. https://doi.org/10.3389/fmed.2021.656692

337. Leem JH, Jeon HE, Nam H, Kim HC, Joa KL. A 2-day cardiopulmonary exercise test in chronic fatigue syndrome patients who were exposed to humidifier disinfectants. *Environ Anal Health Toxicol* 2022;**37**:e2022033–0. https://doi.org/10.5620/eaht.2022033

338. Leong KH, Yip HT, Kuo CF, Tsai SY. Treatments of chronic fatigue syndrome and its debilitating comorbidities: a 12-year population-based study. *J Transl Med* 2022;**20**:268. https://doi.org/10.1186/s12967-022-03461-0

339. Li M, Shu Q, Huang H, Bo W, Wang L, Wu H. Associations of occupational stress, workplace violence, and organizational support on chronic fatigue syndrome among nurses. *J Adv Nurs* 2020;**76**:1151–61. https://doi.org/10.1111/jan.14312

340. Li X, Julin P, Li TQ. Limbic perfusion is reduced in patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Tomography* 2021;**7**:675–87. https://doi.org/10.3390/tomography7040056

341. Li Y, Wu K, Hu X, Xu T, Li Z, Zhang Y, Li K. Altered effective connectivity of resting-state networks by Tai Chi Chuan in chronic fatigue syndrome patients: a multivariate granger causality study. *Front Neurol* 2022;**13**:858833. https://doi.org/10.3389/fneur.2022.858833

342. Lidbury BA, Kita B, Richardson AM, Lewis DP, Privitera E, Hayward S, *et al*. Rethinking ME/CFS diagnostic reference intervals via machine learning, and the utility of activin B for defining symptom severity. *Diagnostics (Basel)* 2019;**9**:79. https://doi.org/10.3390/diagnostics9030079

343. Lien K, Johansen B, Veierod MB, Haslestad AS, Bohn SK, Melsom MN, *et al*. Abnormal blood lactate accumulation during repeated exercise testing in myalgic encephalomyelitis/chronic fatigue syndrome. *Physiol Rep* 2019;**7**:e14138. https://doi.org/10.14814/phy2.14138

344. Liljebo T, Jonsjo M, Andreasson A. Comparison of energy- and macronutrient intake in patient with myalgic encephalomyelitis/chronic fatigue syndrome and healthy controls – a pilot study. *Neuroimmunomodulation* 2022;**29**:22.

345. Lim EJ, Ahn YC, Jang ES, Lee SW, Lee SH, Son CG. Systematic review and meta-analysis of the prevalence of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). *J Transl Med* 2020;**18**:100. https://doi.org/10.1186/s12967-020-02269-0

346. Lim EJ, Kang EB, Jang ES, Son CG. The prospects of the two-day cardiopulmonary exercise test (CPET) in ME/CFS patients: a meta-analysis. *J Clin Med* 2020;**9**:4040–13. https://doi.org/10.3390/jcm9124040

347. Lim EJ, Lee JS, Lee EJ, Jeong SJ, Park HY, Ahn YC, Son CG. Nationwide epidemiological characteristics of chronic fatigue syndrome in South Korea. *J Transl Med* 2021;**19**:502. https://doi.org/10.1186/s12967-021-03170-0

348. Lim EJ, Son CG. Prevalence of chronic fatigue syndrome (CFS) in Korea and Japan: a meta-analysis. *J Clin Med* 2021;**10**(15):3204. https://doi.org/10.3390/jcm10153204

349. Loades Maria E, Rimes Katharine A, Lievesley K, Ali S, Chalder T. Illness beliefs of adolescents with CFS and their parents: the perceived causes of illness and beliefs about recovery. *Int J Adolesc Med Health* 2020;**32**:1–4.

350. Loades ME, Chalder T, Smakowski A, Rimes KA. Anticipation of and response to exercise in adolescents with CFS: an experimental study. *J Psychosom Res* 2021;**146**:110490. https://doi.org/10.1016/j.jpsychores.2021.110490

351. Loades ME, Read R, Smith L, Higson-Sweeney NT, Laffan A, Stallard P, *et al*. How common are depression and anxiety in adolescents with chronic fatigue syndrome (CFS) and how should we screen for these mental health co-morbidities? A clinical cohort study. *Eur Child Adolesc Psychiatry* 2021;**30**:1733–43. https://doi.org/10.1007/s00787-020-01646-w

352. Loades ME, Rimes K, Lievesley K, Ali S, Chalder T. Cognitive and behavioural responses to symptoms in adolescents with chronic fatigue syndrome: a case-control study nested within a cohort. *Clin Child Psychol Psychiatry* 2019;**24**:564–79. https://doi.org/10.1177/1359104519835583

353. Loades ME, Rimes KA, Ali S, Chalder T. Depressive symptoms in adolescents with chronic fatigue syndrome (CFS): are rates higher than in controls and do depressive symptoms affect outcome? *Clin Child Psychol Psychiatry* 2019;**24**:580–92. https://doi.org/10.1177/1359104519838584

354. Loades ME, Rimes KA, Ali S, Lievesley K, Chalder T. The presence of co-morbid mental health problems in a cohort of adolescents with chronic fatigue syndrome. *Clin Child Psychol Psychiatry* 2018;**23**:398–408. https://doi.org/10.1177/1359104517736357

355. Loades ME, Rimes KA, Ali S, Lievesley K, Chalder T. Does fatigue and distress in a clinical cohort of adolescents with chronic fatigue syndrome correlate with fatigue and distress in their parents? *Child Care Health Dev* 2019;**45**:129–37. https://doi.org/10.1111/cch.12626

356. Loades ME, Vitoratou S, Rimes KA, Ali S, Chalder T. Psychometric properties of the cognitive and behavioural responses questionnaire (CBRQ) in adolescents with chronic fatigue syndrome. *Behav Cogn Psychother* 2020;**48**:160–71. https://doi.org/10.1017/S1352465819000390

357. Loades ME, Vitoratou S, Rimes KA, Chalder T. Assessing functioning in adolescents with chronic fatigue syndrome: psychometric properties and factor structure of the School and Social Adjustment Scale and the Physical Functioning Subscale of the SF36. *Behav Cogn Psychother* 2020;**48**:546–56. https://doi.org/10.1017/S1352465820000193

358. Loiacono B, Sunnquist M, Nicholson L, Jason LA. Activity measurement in pediatric chronic fatigue syndrome. *Chronic Illn* 2022;**18**:268–76. https://doi.org/10.1177/1742395320949613

359. Luo L, Zhang Y, Huang T, Zhou F, Xiong C, Liu Y, *et al*. A description of the current status of chronic fatigue syndrome and associated factors among university students in Wuhan, China. *Front Psychiatry* 2022;**13**:1047014. https://doi.org/10.3389/fpsyt.2022.1047014

360. Lupo GFD, Rocchetti G, Lucini L, Lorusso L, Manara E, Bertelli M, *et al*. Potential role of microbiome in chronic fatigue syndrome/myalgic encephalomyelits (CFS/ME). *Sci Rep* 2021;**11**:7043. https://doi.org/10.1038/s41598-021-86425-6

361. Lutz L, Rohrhofer J, Zehetmayer S, Stingl M, Untersmayr E. Evaluation of Immune Dysregulation in an Austrian Patient Cohort Suffering from Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Biomolecules* 2021;**11**:1359. https://doi.org/10.3390/biom11091359

362. Lynn M, Maclachlan L, Finkelmeyer A, Clark J, Locke J, Todryk S, *et al*. Reduction of glucocorticoid receptor function in chronic fatigue syndrome. *Mediators Inflamm* 2018;**2018**:3972104. https://doi.org/10.1155/2018/3972104

363. Maeda KI, Islam MF, Conroy KE, Jason L. Health outcomes of sensory hypersensitivities in myalgic encephalomyelitis/chronic fatigue syndrome and multiple sclerosis. *Psychol Health Med* 2023;**28**:3052–63. https://doi.org/10.1080/13548506.2023.2195670

364. Maksoud R, Balinas C, Holden S, Cabanas H, Staines D, Marshall-Gradisnik S. A systematic review of nutraceutical interventions for mitochondrial dysfunctions in myalgic encephalomyelitis/chronic fatigue syndrome. *J Transl Med* 2021;**19**:81. https://doi.org/10.1186/s12967-021-02742-4

365. Maksoud R, du P, Eaton-Fitch N, Thapaliya K, Barnden L, Cabanas H, *et al*. A systematic review of neurological impairments in myalgic encephalomyelitis/chronic fatigue syndrome using neuroimaging techniques. *PLOS ONE* 2020;**15**:e0232475. https://doi.org/10.1371/journal.pone.0232475

366. Malfliet A, Pas R, Brouns R, De Win J, Hatem SM, Meeus M, *et al*. Cerebral blood flow and heart rate variability in chronic fatigue syndrome: a randomized cross-over study. *Pain Physician* 2018;**21**:E13–24.

367. Maltsev D. A comparative study of valaciclovir, valganciclovir, and artesunate efficacy in reactivated HHV-6 and HHV-7 infections associated with chronic fatigue syndrome/myalgic encephalomyelitis. *Microbiol Immunol* 2022;**66**:193–9. https://doi.org/10.1111/1348-0421.12966

368. Mandarano AH, Giloteaux L, Keller BA, Levine SM, Hanson MR. Eukaryotes in the gut microbiota in myalgic encephalomyelitis/chronic fatigue syndrome. *PeerJ* 2018;**6**:e4282. https://doi.org/10.7717/peerj.4282

369. Mandarano AH, Maya J, Giloteaux L, Peterson DL, Maynard M, Gottschalk CG, Hanson MR. Myalgic encephalomyelitis/chronic fatigue syndrome patients exhibit altered T cell metabolism and cytokine associations. *J Clin Invest* 2020;**130**:1491–505. https://doi.org/10.1172/JCI132185

370. Maness C, Saini P, Bliwise DL, Olvera V, Rye DB, Trotti LM. Systemic exertion intolerance disease/chronic

fatigue syndrome is common in sleep centre patients with hypersomnolence: a retrospective pilot study. *J Sleep Res* 2019;**28**:e12689. https://doi.org/10.1111/jsr.12689

371. Maroti D, Bileviciute-Ljungar I. Similarities and differences between health-related quality of life in patients with exhaustion syndrome and chronic fatigue syndrome. *Fatigue: Biomed Health Behav* 2018;**6**:208–19. https://doi.org/10.1080/21641846.2018.1515583

372. Martin M, Alexeeva I. Greater specificity of activity memories in chronic fatigue syndrome/myalgic encephalomyelitis: implications for exercise-based treatment. *Ment Health Phys Act* 2018;**14**:19–30. https://doi.org/10.1016/j.mhpa.2017.12.003

373. Mateo LJ, Chu L, Stevens S, Stevens J, Snell CR, Davenport T, VanNess JM. Post-exertional symptoms distinguish myalgic encephalomyelitis/chronic fatigue syndrome subjects from healthy controls. *Work* 2020;**66**:265–75. https://doi.org/10.3233/WOR-203168

374. Matsui T, Hara K, Iwata M, Hojo S, Shitara N, Endo Y, *et al*. Possible involvement of the autonomic nervous system in cervical muscles of patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *BMC Musculoskelet Disord* 2021;**22**:419. https://doi.org/10.1186/s12891-021-04293-7

375. May M, Milrad SF, Perdomo DM, Czaja SJ, Fletcher MA, Jutagir DR, *et al*. Post-exertional malaise is associated with greater symptom burden and psychological distress in patients diagnosed with chronic fatigue syndrome. *J Psychosom Res* 2020;**129**:109893. https://doi.org/10.1016/j.jpsychores.2019.109893

376. May M, Milrad SF, Perdomo DM, Czaja SJ, Fletcher MA, Jutagir DR, *et al*. Videoconferenced group cognitive behavioral stress management improves symptoms in ME/CFS patients presenting with elevated post-exertional malaise. *Psychosom Med* 2022;**84**:A134.

377. Maya J, Leddy SM, Gottschalk CG, Peterson DL, Hanson MR. Altered fatty acid oxidation in lymphocyte populations of myalgic encephalomyelitis/chronic fatigue syndrome. *Int J Mol Sci* 2023;**24**:2010. https://doi.org/10.3390/ijms24032010

378. McCourt A, Maile E, Gregorowski A, Hargreaves D, Segal T. Characteristics of a patient population attending a specialist outpatient service for chronic fatigue syndrome. *Arch Dis Child* 2019;**104**:A242. https://doi.org/10.1136/archdischild-2019-rcpch.580

379. McGregor NR, Armstrong CW, Lewis DP, Gooley PR. Post-exertional malaise is associated with hypermetabolism, hypoacetylation and purine metabolism deregulation in ME/CFS cases. *Diagnostics (Basel)* 2019;**9**:70. https://doi.org/10.3390/diagnostics9030070

380. McKay PG, Walker H, Martin CR, Fleming M. Exploratory study into the relationship between the symptoms of chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) and fibromyalgia (FM) using a quasiexperimental design. *BMJ Open* 2021;**11**:e041947. https://doi.org/10.1136/bmjopen-2020-041947

381. McManimen S, McClellan D, Stoothoff J, Gleason K, Jason LA. Dismissing chronic illness: a qualitative analysis of negative health care experiences. *Health Care Women Int* 2019;**40**:241–58. https://doi.org/10.1080/07399332.2018.1521811

382. McManimen SL, McClellan D, Stoothoff J, Jason LA. Effects of unsupportive social interactions, stigma, and symptoms on patients with myalgic encephalomyelitis and chronic fatigue syndrome. *J Community Psychol* 2018;**46**:959–71. https://doi.org/10.1002/jcop.21984

383. McManimen SL, Sunnquist ML, Jason LA. Deconstructing post-exertional malaise: an exploratory factor analysis. *J Health Psychol* 2019;**24**:188–98. https://doi.org/10.1177/1359105316664139

384. McWhorter KL, Parks CL, D'Aloisio AA, Rojo-Wissar DM, Sandler DP, Jackson CL. Traumatic childhood experiences, poor sleep and chronic fatigue syndrome among adult women. *Sleep* 2018;**41**:A108.

385. Mehalick ML, Schmaling KB, Sabath DE, Buchwald DS. Longitudinal associations of lymphocyte subsets with clinical outcomes in chronic fatigue syndrome. *Fatigue* 2018;**6**:80–91. https://doi.org/10.1080/21641846.2018.1426371

386. Melvin A, Lacerda E, Dockrell HM, O'Rahilly S, Nacul L. Circulating levels of GDF15 in patients with myalgic encephalomyelitis/chronic fatigue syndrome. *J Transl Med* 2019;**17**:409. https://doi.org/10.1186/s12967-019-02153-6

387. Meng XD, Guo HR, Zhang QY, Li X, Chen Y, Li MY, *et al*. The effectiveness of cupping therapy on chronic fatigue syndrome: a single-blind randomized controlled trial. *Complement Ther Clin Pract* 2020;**40**:101210. https://doi.org/10.1016/j.ctcp.2020.101210

388. Mengshoel AM, Helland IB, Meeus M, Castro-Marrero J, Pheby D, Bolle Strand E. Patients' experiences and effects of non-pharmacological treatment for myalgic encephalomyelitis/chronic fatigue syndrome – a scoping mixed methods review. *Int J Qual Stud Health Well-being* 2020;**15**:1764830. https://doi.org/10.1080/17482631.2020.1764830

389. Metselaar PI, Mendoza-Maldonado L, Li Y, Yim AYFL, Abarkan I, Henneman P, *et al*. Recursive ensemble feature selection provides a robust mRNA expression signature for myalgic encephalomyelitis/chronic fatigue syndrome. *Sci Rep* 2021;**11**:4541. https://doi.org/10.1038/s41598-021-83660-9

390. Milivojevic M, Che X, Bateman L, Cheng A, Garcia BA, Hornig M, *et al*. Plasma proteomic profiling suggests an association between antigen driven clonal B cell expansion and ME/CFS. *PLOS ONE* 2020;**15**:e0236148. https://doi.org/10.1371/journal.pone.0236148

391. Milrad Sara F. Couple-based stress management intervention and chronic fatigue syndrome (CFS) biopsychological processes. *Diss Abstr Int: Section B: Sci Eng* 2018;**79**.

392. Milrad SF, Hall DL, Jutagir DR, Lattie EG, Czaja SJ, Perdomo DM, *et al*. Depression, evening salivary cortisol and inflammation in chronic fatigue syndrome: a psychoneuroendocrinological structural regression model. *Int J Psychophysiol* 2018;**131**:124–30. https://doi.org/10.1016/j.ijpsycho.2017.09.009

393. Milrad SF, Hall DL, Jutagir DR, Lattie EG, Czaja SJ, Perdomo DM, *et al*. Relationship satisfaction, communication self-efficacy, and chronic fatigue syndrome-related fatigue. *Soc Sci Med* 2019;**237**:112392. https://doi.org/10.1016/j.socscimed.2019.112392

394. Missailidis D, Annesley SJ, Allan CY, Sanislav O, Lidbury BA, Lewis DP, Fisher P. An isolated complex V inefficiency and dysregulated mitochondrial function in immortalized lymphocytes from ME/CFS patients. *Int J Mol Sci* 2020;**21**:06. https://doi.org/10.3390/ijms21031074

395. Missailidis D, Sanislav O, Allan CY, Annesley SJ, Fisher PR. Cell-based blood biomarkers for myalgic encephalomyelitis/chronic fatigue syndrome. *Int J Mol Sci* 2020;**21**:08. https://doi.org/10.3390/ijms21031142

396. Missailidis D, Sanislav O, Allan CY, Smith PK, Annesley SJ, Fisher PR. Dysregulated provision of oxidisable substrates to the mitochondria in ME/CFS lymphoblasts. *Int J Mol Sci* 2021;**22**:2046. https://doi.org/10.3390/ijms22042046

397. Miwa K. Oral minocycline therapy improves symptoms of myalgic encephalomyelitis, especially in the initial disease stage. *Intern Med* 2021;**60**:2577–84. https://doi.org/10.2169/internalmedicine.6082-20

398. Miwa K, Inoue Y. Paradigm shift to disequilibrium in the genesis of orthostatic intolerance in patients with myalgic encephalomyelitis and chronic fatigue syndrome. *Int J Cardiol Hypertens* 2020;**5**:100032. https://doi.org/10.1016/j.ijchy.2020.100032

399. Mohamed AZ, Andersen T, Radovic S, Del Fante P, Kwiatek R, Calhoun V, *et al*. Objective sleep measures in chronic fatigue syndrome patients: a systematic review and meta-analysis. *Sleep Med Rev* 2023;**69**:101771. https://doi.org/10.1016/j.smrv.2023.101771

400. Moncorps F, Jouet E, Bayen S, Fornasieri I, Renet S, Las-Vergnas O, Messaadi N. Specifics of chronic fatigue syndrome coping strategies identified in a French flash survey during the COVID-19 containment. *Health Soc Care Community* 2022;**30**:1–10. https://doi.org/10.1111/hsc.13376

401. Moneghetti KJ, Skhiri M, Contrepois K, Kobayashi Y, Maecker H, Davis M, *et al*. Value of circulating cytokine profiling during submaximal exercise testing in myalgic encephalomyelitis/chronic fatigue syndrome. *Sci Rep* 2018;**8**:2779. https://doi.org/10.1038/s41598-018-20941-w

402. Montoya JG, Anderson JN, Adolphs DL, Bateman L, Klimas N, Levine SM, *et al*. KPAX002 as a treatment for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): a prospective, randomized trial. *Int J Clin Exp Med* 2018;**11**:2890–900.

403. Monzon-Nomdedeu MB, Morten KJ, Oltra E. Induced pluripotent stem cells as suitable sensors for fibromyalgia and myalgic encephalomyelitis/chronic fatigue syndrome. *World J Stem Cells* 2021;**13**:1134–50. https://doi.org/10.4252/wjsc.v13.i8.1134

404. Moore GE, Keller BA, Stevens J, Mao X, Stevens SR, Chia JK, *et al*. Recovery from exercise in persons with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Medicina (Kaunas)* 2023;**59**:571. https://doi.org/10.3390/medicina59030571

405. Moore Y, Serafimova T, Anderson N, King H, Richards A, Brigden A, *et al*. Recovery from chronic fatigue syndrome: a systematic review-heterogeneity of definition limits study comparison. *Arch Dis Child* 2021;**106**:1087–94. https://doi.org/10.1136/archdischild-2020-320196

406. Morehouse S, Schaible K, Williams O, Herlache-Pretzer E, Webster S. Impacts of online support groups on quality of life, and perceived anxiety and depression in those with ME/CFS: a survey. *Fatigue: Biomed Health Behav* 2021;**9**:113–22. https://doi.org/10.1080/21641846.2021.1950406

407. Morris MC, Cooney KE, Sedghamiz H, Abreu M, Collado F, Balbin EG, *et al*. Leveraging prior knowledge of endocrine immune regulation in the therapeutically relevant phenotyping of women with chronic fatigue syndrome. *Clin Ther* 2019;**41**:656–74.e4. https://doi.org/10.1016/j.clinthera.2019.03.002

408. Morrison KR, Reynolds N, Todd J, Paterson J, Mowat C, Groome M. Is fatigue common in inflammatory

bowel disease and is it a separate entity? *United European Gastroenterol J* 2018;**6**:A433–A4. https://doi.org/10.1177/2050640618792819

409. Moslehi R, Kumar A, Dzutsev A. Increased risks of cancer and autoimmune disease among the first-degree relatives of patients with myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS). *Cancer Res* 2022;**82**:34. https://doi.org/10.1158/1538-7445.Am2022-34
410. Mozhgani SH, Rajabi F, Qurbani M, Erfani Y, Yaslianifard S, Moosavi A, *et al*. Human herpesvirus 6 infection and risk of chronic fatigue syndrome: a systematic review and meta-analysis. *Intervirology* 2022;**65**:49–57. https://doi.org/10.1159/000517930
411. Mueller C, Lin JC, Sheriff S, Maudsley AA, Younger JW. Evidence of widespread metabolite abnormalities in myalgic encephalomyelitis/chronic fatigue syndrome: assessment with whole-brain magnetic resonance spectroscopy. *Brain Imaging Behav* 2020;**14**:562–72. https://doi.org/10.1007/s11682-018-0029-4
412. Muller AE, Tveito K, Bakken IJ, Flottorp SA, Mjaaland S, Larun L. Potential causal factors of CFS/ME: a concise and systematic scoping review of factors researched. *J Transl Med* 2020;**18**:484. https://doi.org/10.1186/s12967-020-02665-6
413. Murga I, Aranburu L, Gargiulo PA, Gómez Esteban, JC, Lafuente JV. Clinical heterogeneity in ME/CFS. A way to understand long-COVID19 fatigue. *Front Psychiatry* 2021;**12**:735784. https://doi.org/10.3389/fpsyt.2021.735784
414. Murray R, Turner L. Using communities of practice theory to understand the crisis of identity in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). *Chronic Illn* 2023;**19**:56–64. https://doi.org/10.1177/17423953211064989
415. Nacul L, de Barros B, Kingdon CC, Cliff JM, Clark TG, Mudie K, *et al*. Evidence of clinical pathology abnormalities in people with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) from an analytic cross-sectional study. *Diagnostics (Basel)* 2019;**9**:41. https://doi.org/10.3390/diagnostics9020041
416. Nagy-Szakal D, Barupal DK, Lee B, Che X, Williams BL, Kahn EJR, *et al*. Insights into myalgic encephalomyelitis/chronic fatigue syndrome phenotypes through comprehensive metabolomics. *Sci Rep* 2018;**8**:10056. https://doi.org/10.1038/s41598-018-28477-9
417. Natelson BH, Brunjes DL, Mancini D. Chronic fatigue syndrome and cardiovascular disease: JACC state-of-the-art review. *J Am Coll Cardiol* 2021;**78**:1056–67. https://doi.org/10.1016/j.jacc.2021.06.045
418. Natelson BH, Lin JS, Lange G, Khan S, Stegner A, Unger ER. The effect of comorbid medical and psychiatric diagnoses on chronic fatigue syndrome. *Ann Med* 2019;**51**:371–8. https://doi.org/10.1080/07853890.2019.1683601
419. Neale FK, Segal TY, Hargreaves DS. Prevalence and correlates of low mood, poor quality of life and high symptom impact in adolescents attending a tertiary service for chronic fatigue syndrome/myalgic encephalomyelitis. *Arch Dis Child* 2018;**103**:A5–6. https://doi.org/10.1136/archdischild-2018-rcpch.13
420. Nelson MJ, Bahl JS, Buckley JD, Thomson RL, Davison K. Evidence of altered cardiac autonomic regulation in myalgic encephalomyelitis/chronic fatigue syndrome: a systematic review and meta-analysis. *Medicine (Baltim)* 2019;**98**:e17600. https://doi.org/10.1097/MD.0000000000017600
421. Nelson MJ, Buckley JD, Thomson RL, Clark D, Kwiatek R, Davison K. Diagnostic sensitivity of 2-day cardiopulmonary exercise testing in myalgic encephalomyelitis/chronic fatigue syndrome. *J Transl Med* 2019;**17**:80. https://doi.org/10.1186/s12967-019-1836-0
422. Nelson T, Zhang LX, Guo H, Nacul L, Song X. Brainstem abnormalities in myalgic encephalomyelitis/chronic fatigue syndrome: a scoping review and evaluation of magnetic resonance imaging findings. *Front Neurol* 2021;**12**:769511. https://doi.org/10.3389/fneur.2021.769511
423. Nepotchatykh E, Caraus I, Elremaly W, Leveau C, Elbakry M, Godbout C, *et al*. Circulating microRNA expression signatures accurately discriminate myalgic encephalomyelitis from fibromyalgia and comorbid conditions. *Sci Rep* 2023;**13**:1896. https://doi.org/10.1038/s41598-023-28955-9
424. Nepotchatykh E, Elremaly W, Caraus I, Godbout C, Leveau C, Chalder L, *et al*. Profile of circulating microRNAs in myalgic encephalomyelitis and their relation to symptom severity, and disease pathophysiology. *Sci Rep* 2020;**10**:19620. https://doi.org/10.1038/s41598-020-76438-y
425. Newberry F, Hsieh SY, Wileman T, Carding SR. Does the microbiome and virome contribute to myalgic encephalomyelitis/chronic fatigue syndrome? *Clin Sci (Lond)* 2018;**132**:523–42. https://doi.org/10.1042/CS20171330
426. Nguyen CB, Kumar S, Zucknick M, Kristensen VN, Gjerstad J, Nilsen H, Wyller VB. Associations between clinical symptoms, plasma norepinephrine and deregulated immune gene networks in subgroups of adolescent with chronic fatigue syndrome. *Brain Behav Immun* 2019;**76**:82–96. https://doi.org/10.1016/j.bbi.2018.11.008
427. Nilsson I, Palmer J, Apostolou E, Gottfries CG, Rizwan M, Dahle C, Rosén A. Metabolic dysfunction in

myalgic encephalomyelitis/chronic fatigue syndrome not due to anti-mitochondrial antibodies. *Front Med (Lausanne)* 2020;**7**:108. https://doi.org/10.3389/fmed.2020.00108

428. Nilsson MKL, Zachrisson O, Gottfries CG, Matousek M, Peilot B, Forsmark S, *et al*. A randomised controlled trial of the monoaminergic stabiliser (-)-OSU6162 in treatment of myalgic encephalomyelitis/chronic fatigue syndrome. *Acta Neuropsychiatr* 2018;**30**:148–57. https://doi.org/10.1017/neu.2017.35
429. Nkiliza A, Parks M, Cseresznye A, Oberlin S, Evans JE, Darcey T, *et al*. Sex-specific plasma lipid profiles of ME/CFS patients and their association with pain, fatigue, and cognitive symptoms. *J Transl Med* 2021;**19**:370. https://doi.org/10.1186/s12967-021-03035-6
430. Nunes JM, Kruger A, Proal A, Kell DB, Pretorius E. The occurrence of hyperactivated platelets and fibrinaloid microclots in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Pharmaceuticals (Basel)* 2022;**15**:931. https://doi.org/10.3390/ph15080931
431. Nyland M, Naess H, Lode K, Figved N, Nyland H. Disability and risk factors for unemployment in chronic fatigue syndrome: a comparison with multiple sclerosis. *Fatigue: Biomed Health Behav* 2019;**7**:127–40. https://doi.org/10.1080/21641846.2019.1652417
432. O'Connor K, Sunnquist M, Nicholson L, Jason LA, Newton JL, Strand EB. Energy envelope maintenance among patients with myalgic encephalomyelitis and chronic fatigue syndrome: implications of limited energy reserves. *Chronic Illn* 2019;**15**:51–60. https://doi.org/10.1177/1742395317746470
433. O'Donnell NA, McCourt A, Segal T. A cohort study of whether parental separation and lack of contact with a parent predicts disease severity at diagnosis in young peoples chronic fatigue syndrome/myalgic encephalomyelitis. *Arch Dis Child* 2020;**105**:A188. https://doi.org/10.1136/archdischild-2020-rcpch.449
434. O'Higgins CM, Dukic S, Rice A, Connor BO, Cuffe S, Hanrahan E, *et al*. Corticomuscular coherence in pre-treatment cancer-related fatigue vs chronic fatigue syndrome [Abstracts of the MASCC/ISOO Annual Meeting 2018]. *Support Care Cancer* 2018;**26**:39–364. https://doi.org/10.1007/s00520-018-4193-2
435. Oie MG, Rodo ASB, Bolgen MS, Pedersen M, Asprusten TT, Wyller VBB. Subjective and objective cognitive function in adolescent with chronic fatigue following Epstein-Barr virus infection. *J Psychosom Res* 2022;**163**:111063. https://doi.org/10.1016/j.jpsychores.2022.111063
436. Oka T, Tanahashi T, Sudo N, Lkhagvasuren B, Yamada Y. Changes in fatigue, autonomic functions, and blood biomarkers due to sitting isometric yoga in patients with chronic fatigue syndrome. *Biopsychosoc Med* 2018;**12**:3. https://doi.org/10.1186/s13030-018-0123-2
437. Oka T, Yamada Y. Effects of recumbent isometric yoga on patients with myalgic encephalpmyelitis/chronic fatigue syndrome: a randomized, controlled trial. *Psychosom Med* 2019;**81**:A1–A213. https://doi.org/10.1097/psy.0000000000000699
438. Oka T, Yamada Y, Lkhagvasuren B, Nakao M, Nakajima R, Kanou M, *et al*. Clinical effects of wasabi extract containing 6-MSITC on myalgic encephalomyelitis/chronic fatigue syndrome: an open-label trial. *Biopsychosoc Med* 2022;**16**:26. https://doi.org/10.1186/s13030-022-00255-0
439. Oliveira CR, Jason LA, Unutmaz D, Bateman L, Vernon SD. Improvement of Long COVID symptoms over one year. *Front Med (Lausanne)* 2022;**9**:1065620. https://doi.org/10.3389/fmed.2022.1065620
440. Orji N, Campbell JA, Wills K, Hensher M, Palmer AJ, Rogerson M, *et al*. Prevalence of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) in Australian primary care patients: only part of the story? *BMC Public Health* 2022;**22**:1516. https://doi.org/10.1186/s12889-022-13929-9
441. Pajediene E, Bileviciute-Ljungar I, Friberg D. Sleep patterns among patients with chronic fatigue: a polysomnography-based study. *Clin Respir J* 2018;**12**:1389–97. https://doi.org/10.1111/crj.12667
442. Palacios N, Molsberry S, Fitzgerald KC, Komaroff AL. Different risk factors distinguish myalgic encephalomyelitis/chronic fatigue syndrome from severe fatigue. *Sci Rep* 2023;**13**:2469. https://doi.org/10.1038/s41598-023-29329-x
443. Palombo T, Campos A, Vernon SD, Roundy S. Accurate and objective determination of myalgic encephalomyelitis/chronic fatigue syndrome disease severity with a wearable sensor. *J Transl Med* 2020;**18**:423. https://doi.org/10.1186/s12967-020-02583-7
444. Park HY, Jeon HJ, Bang YR, Yoon IY. Multidimensional comparison of cancer-related fatigue and chronic fatigue syndrome: the role of psychophysiological markers. *Psychiatry Investig* 2019;**16**:71–9. https://doi.org/10.30773/pi.2018.10.26
445. Parslow RM, Anderson N, Byrne D, Haywood KL, Shaw A, Crawley E. Development of a conceptual framework to underpin a health-related quality of life outcome measure in paediatric chronic fatigue syndrome/myalgic encephalopathy (CFS/ME): prioritisation through card ranking. *Qual Life Res*

2020;**29**:1169–81. https://doi.org/10.1007/s11136-019-02399-z

446. Pednekar DD, Amin MR, Azgomi HF, Aschbacher K, Crofford LJ, Faghih RT. Characterization of cortisol dysregulation in fibromyalgia and chronic fatigue syndromes: a state-space approach. *IEEE Trans Biomed Eng* 2020;**67**:3163–72. https://doi.org/10.1109/TBME.2020.2978801

447. Pereira G, Gillies H, Chanda S, Corbett M, Vernon SD, Milani T, Bateman L. Acute corticotropin-releasing factor receptor type 2 agonism results in sustained symptom improvement in myalgic encephalomyelitis/chronic fatigue syndrome. *Front Syst Neurosci* 2021;**15**:698240. https://doi.org/10.3389/fnsys.2021.698240

448. Perez M, Jaundoo R, Hilton K, Del Alamo A, Gemayel K, Klimas NG, *et al*. Genetic predisposition for immune system, hormone, and metabolic dysfunction in myalgic encephalomyelitis/chronic fatigue syndrome: a pilot study. *Front Pediatr* 2019;**7**:206. https://doi.org/10.3389/fped.2019.00206

449. Pheby DFH, Araja D, Berkis U, Brenna E, Cullinan J, de Korwin JD, *et al*. A literature review of GP knowledge and understanding of ME/CFS: a report from the socioeconomic working group of the European network on ME/CFS (EUROMENE). *Medicina (Kaunas)* 2020;**57**:7. https://doi.org/10.3390/medicina57010007

450. Pifarré F, Rosselló L, Hileno R, Palmi J, Bañeres L, Planas A, Prat JA. The use of oxygen as a possible screening biomarker for the diagnosis of chronic fatigue. *Apunts Sports Medicine* 2022;**57**:100379. https://doi.org/10.1016/j.apunsm.2022.100379

451. Pilkington K, Ridge DT, Igwesi-Chidobe CN, Chew-Graham CA, Little P, Babatunde O, *et al*. A relational analysis of an invisible illness: a meta-ethnography of people with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and their support needs. *Soc Sci Med* 2020;**265**:113369. https://doi.org/10.1016/j.socscimed.2020.113369

452. Polli A, Van Oosterwijck J, Meeus M, Lambrecht L, Nijs J, Ickmans K. Exercise-induce hyperalgesia, complement system and elastase activation in myalgic encephalomyelitis/chronic fatigue syndrome – a secondary analysis of experimental comparative studies. *Scand J Pain* 2019;**19**:183–92. https://doi.org/10.1515/sjpain-2018-0075

453. Polli A, Van Oosterwijck J, Nijs J, Marusic U, De Wandele I, Paul L, *et al*. Relationship between exercise-induced oxidative stress changes and parasympathetic activity in chronic fatigue syndrome: an observational study in patients and healthy subjects. *Clin Ther* 2019;**41**:641–55. https://doi.org/10.1016/j.clinthera.2018.12.012

454. Polo O, Pesonen P, Tuominen E. Low-dose naltrexone in the treatment of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Fatigue: Biomed Health Behav* 2019;**7**:207–17. https://doi.org/10.1080/21641846.2019.1692770

455. Priou S, Viani N, Vernugopan V, Tytherleigh C, Hassan FA, Dutta R, *et al*. Clinical history segment extraction from chronic fatigue syndrome assessments to model disease trajectories. *Stud Health Technol Inform* 2020;**270**:98–102. https://doi.org/10.3233/SHTI200130

456. Proulx-Cabana S, Segal TY, Gregorowski A, Hargreaves D, Flannery H. Virtual consultations: young people and their parents' experience. *Adolesc Health Med Ther* 2021;**12**:37–43. https://doi.org/10.2147/AHMT.S292977

457. Provenzano D, Washington SD, Baraniuk JN. A machine learning approach to the differentiation of functional magnetic resonance imaging data of chronic fatigue syndrome (CFS) from a sedentary control. *Front Comput Neurosci* 2020;**14**:2. https://doi.org/10.3389/fncom.2020.00002

458. Raanes EFW, Stiles TC. Associations between psychological and immunological variables in chronic fatigue syndrome/myalgic encephalomyelitis: a systematic review. *Front Psychiatry* 2021;**12**:716320. https://doi.org/10.3389/fpsyt.2021.716320

459. Raijmakers RPH, Jansen AFM, Keijmel SP, ter Horst R, Roerink ME, Novakovic B, *et al*. A possible role for mitochondrial-derived peptides humanin and MOTS-c in patients with Q fever fatigue syndrome and chronic fatigue syndrome. *J Transl Med* 2019;**17**:157. https://doi.org/10.1186/s12967-019-1906-3

460. Raijmakers RPH, Koeken V, Jansen AFM, Keijmel SP, Roerink ME, Joosten LAB, *et al*. Cytokine profiles in patients with Q fever fatigue syndrome. *J Infect* 2019;**78**:349–57. https://doi.org/10.1016/j.jinf.2019.01.006

461. Raijmakers RPH, Roerink ME, Jansen AFM, Keijmel SP, Gacesa R, Li Y, *et al*. Multi-omics examination of Q fever fatigue syndrome identifies similarities with chronic fatigue syndrome. *J Transl Med* 2020;**18**:448. https://doi.org/10.1186/s12967-020-02585-5

462. Rajeevan MS, Murray J, Oakley L, Lin JS, Unger ER. Association of chronic fatigue syndrome with premature telomere attrition. *J Transl Med* 2018;**16**:44. https://doi.org/10.1186/s12967-018-1414-x

463. Ramirez-Morales R, Bermudez-Benitez E, Martinez-Martinez LA, Martinez-Lavin M. Clinical overlap

between fibromyalgia and myalgic encephalomyelitis. A systematic review and meta-analysis. *Autoimmun Rev* 2022;**21**:103129. https://doi.org/10.1016/j.autrev.2022.103129

464. Rasa S, Chapenko S, Skuja S, Roga S, Logina I, Krumina A, *et al*. Implication of HHV-6 and HHV-7 infection in the pathogenesis of neurological disorders. *J Neuroimmune Pharmacol* 2018;**13**:1–102. https://doi.org/10.1007/s11481-018-9786-5
465. Rasa-Dzelzkaleja S, Krumina A, Capenko S, Nora-Krukle Z, Gravelsina S, Vilmane A, *et al*.; VirA project. The persistent viral infections in the development and severity of myalgic encephalomyelitis/chronic fatigue syndrome. *J Transl Med* 2023;**21**:33. https://doi.org/10.1186/s12967-023-03887-0
466. Rasouli O, Fors EA, Vasseljen O, Stensdotter AK. A concurrent cognitive task does not perturb quiet standing in fibromyalgia and chronic fatigue syndrome. *Pain Res Manag* 2018;**2018**:9014232. https://doi.org/10.1155/2018/9014232
467. Rauwerda N, Kuut TA, Braamse AM, Csorba I, Nieuwkerk P, Van Straten A, *et al*. Insomnia and sleep characteristics in post COVID-19 related fatigue. *J Sleep Res* 2022;**31**:P439. https://doi.org/10.1111/jsr.13740
468. Rekeland IG, Fluge O, Alme K, Risa K, Sorland K, Mella O, *et al*. Rituximab serum concentrations and anti-rituximab antibodies during B-cell depletion therapy for myalgic encephalopathy/chronic fatigue syndrome. *Clin Ther* 2019;**41**:806–14. https://doi.org/10.1016/j.clinthera.2018.10.019
469. Rekeland IG, Fossa A, Lande A, Ktoridou-Valen I, Sorland K, Holsen M, *et al*. Intravenous cyclophosphamide in myalgic encephalomyelitis/chronic fatigue syndrome. An open-label phase II study. *Front Med (Lausanne)* 2020;**7**:162. https://doi.org/10.3389/fmed.2020.00162
470. Rekeland IG, Sorland K, Bruland O, Risa K, Alme K, Dahl O, *et al*. Activity monitoring and patient-reported outcome measures in myalgic encephalomyelitis/chronic fatigue syndrome patients. *PLOS ONE* 2022;**17**:e0274472. https://doi.org/10.1371/journal.pone.0274472
471. Retornaz F, Rebaudet S, Stavris C, Jammes Y. Long-term neuromuscular consequences of SARS-Cov-2 and their similarities with myalgic encephalomyelitis/chronic fatigue syndrome: results of the retrospective CoLGEM study. *J Transl Med* 2022;**20**:429. https://doi.org/10.1186/s12967-022-03638-7
472. Ricevuti G, Franzini M, Valdenassi L. Treatment of fibromyalgia oxygen ozone therapy to control astenia and pain in fibromyalgia and chronic fatigue syndrome. *Clin Exp Rheumatol* 2019;**37**:S140.
473. Richardson AM, Lewis DP, Kita B, Ludlow H, Groome NP, Hedger MP, *et al*. Weighting of orthostatic intolerance time measurements with standing difficulty score stratifies ME/CFS symptom severity and analyte detection. *J Transl Med* 2018;**16**:97. https://doi.org/10.1186/s12967-018-1473-z
474. Rivas JL, Palencia T, Fernandez G, Garcia M. Association of T and NK cell phenotype with the diagnosis of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Front Immunol* 2018;**9**:1028. https://doi.org/10.3389/fimmu.2018.01028
475. Robertson D, Mansfield K, Dennis H, Wilson C, Kumar Y. Prognosis for childhood CFS is excellent. *Arch Dis Child* 2019;**104**:A58. https://doi.org/10.1136/archdischild-2019-rcpch.138
476. Robinson LJ, Gallagher P, Watson S, Pearce R, Finkelmeyer A, Maclachlan L, Newton JL. Impairments in cognitive performance in chronic fatigue syndrome are common, not related to co-morbid depression but do associate with autonomic dysfunction. *PLOS ONE* 2019;**14**:e0210394. https://doi.org/10.1371/journal.pone.0210394
477. Rodrigues LS, da Silva Nali LH, Leal COD, Sabino EC, Lacerda EM, Kingdon CC, *et al*. HERV-K and HERV-W transcriptional activity in myalgic encephalomyelitis/chronic fatigue syndrome. *Auto Immun Highlights* 2019;**10**:12. https://doi.org/10.1186/s13317-019-0122-8
478. Roerink ME, Roerink S, Skoluda N, van der Schaaf ME, Hermus A, van der Meer JWM, *et al*. Hair and salivary cortisol in a cohort of women with chronic fatigue syndrome. *Horm Behav* 2018;**103**:1–6. https://doi.org/10.1016/j.yhbeh.2018.05.016
479. Roerink ME, van der Schaaf ME, Hawinkels L, Raijmakers RPH, Knoop H, Joosten LAB, *et al*. Pitfalls in cytokine measurements – plasma TGF-β1 in chronic fatigue syndrome. *Neth J Med* 2018;**76**:310–3.
480. Roma M, Marden CL, Flaherty MAK, Jasion SE, Cranston EM, Rowe PC. Impaired health-related quality of life in adolescent myalgic encephalomyelitis/chronic fatigue syndrome: the impact of core symptoms. *Front Pediatr* 2019;**7**:26. https://doi.org/10.3389/fped.2019.00026
481. Roman P, Carrillo-Trabalon F, Sanchez-Labraca N, Canadas F, Estevez AF, Cardona D. Are probiotic treatments useful on fibromyalgia syndrome or chronic fatigue syndrome patients? A systematic review. *Benef Microbes* 2018;**9**:603–11. https://doi.org/10.3920/BM2017.0125
482. Roor JJ, Dandachi-FitzGerald B, Peters MJV, Knoop H, Ponds R. Performance validity and outcome of cognitive behavior therapy in patients with chronic fatigue

syndrome. *J Int Neuropsychol Soc* 2022;**28**:473–82. https://doi.org/10.1017/S1355617721000643

483. Roor JJ, Knoop H, Dandachi-FitzGerald B, Peters MJV, Bleijenberg G, Ponds R. Feedback on underperformance in patients with chronic fatigue syndrome: the impact on subsequent neuropsychological test performance. *Appl Neuropsychol Adult* 2020;**27**:188–96. https://doi.org/10.1080/23279095.2018.1519509

484. Rosenberg M, Bar-Shalita T, Weiss M, Rahav G, Avrech B. Associations between daily routines and social support among women with chronic fatigue syndrome. *Scand J Occup Ther* 2023;**30**:1037–46. https://doi.org/10.1080/11038128.2023.2200580

485. Rowe KS. Long term follow up of young people with chronic fatigue syndrome attending a pediatric outpatient service. *Front Pediatr* 2019;**7**:21. https://doi.org/10.3389/fped.2019.00021

486. Rowe PC, Marden CL, Flaherty MAK, Jasion SE, Cranston EM, Fontaine KR, Violand RL. Two-year follow-up of impaired range of motion in chronic fatigue syndrome. *J Pediatr* 2018;**200**:249–53.e1. https://doi.org/10.1016/j.jpeds.2018.05.012

487. Royston AP, Rai M, Brigden A, Burge S, Segal TY, Crawley EM. Severe myalgic encephalomyelitis/chronic fatigue syndrome in children and young people: a British Paediatric Surveillance Unit study. *Arch Dis Child* 2023;**108**:230–5. https://doi.org/10.1136/archdischild-2022-324319

488. Rozenfeld I, Renesca V, Nunez Maria V. Nutritional themes in care for patients with myalgic encephalomyelitis/chronic fatigue syndrome. *Eur J Integr Med* 2021;**48**:101935. https://doi.org/10.1016/j.eujim.2021.101935

489. Ruiz-Núñez B, Tarasse R, Vogelaar EF, Janneke Dijck-Brouwer, DA, Muskiet FAJ. Higher prevalence of 'low T3 syndrome' in patients with chronic fatigue syndrome: a case-control study. *Front Endocrinol (Lausanne)* 2018;**9**:97. https://doi.org/10.3389/fendo.2018.00097

490. Russell A, Hepgul N, Nikkheslat N, Borsini A, Zajkowska Z, Moll N, *et al*. Persistent fatigue induced by interferon-alpha: a novel, inflammation-based, proxy model of chronic fatigue syndrome. *Psychoneuroendocrinology* 2019;**100**:276–85. https://doi.org/10.1016/j.psyneuen.2018.11.032

491. Ryabkova VA, Gavrilova NY, Fedotkina TV, Churilov LP, Shoenfeld Y. Myalgic encephalomyelitis/chronic fatigue syndrome and post-COVID syndrome: a common neuroimmune ground? *Diagnostics (Basel)* 2022;**13**:66. https://doi.org/10.3390/diagnostics13010066

492. Ryan EG, Vitoratou S, Goldsmith KA, Chalder T. Psychometric properties and factor structure of a long and shortened version of the cognitive and behavioural responses questionnaire. *Psychosom Med* 2018;**80**:230–7. https://doi.org/10.1097/PSY.0000000000000536

493. Safadi JM, Quinton AMG, Lennox BR, Burnet PWJ, Minichino A. Gut dysbiosis in severe mental illness and chronic fatigue: a novel trans-diagnostic construct? A systematic review and meta-analysis. *Mol Psychiatry* 2022;**27**:141–53. https://doi.org/10.1038/s41380-021-01032-1

494. Saha AK, Schmidt BR, Wilhelmy J, Nguyen V, Abugherir A, Do JK, *et al*. Red blood cell deformability is diminished in patients with chronic fatigue syndrome. *Clin Hemorheol Microcirc* 2019;**71**:113–6. https://doi.org/10.3233/CH-180469

495. Sahbai S, Kauv P, Abrivard M, Blanc-Durand P, Aoun-Sebati M, Emsen B, *et al*. Multi-parametric cerebral 18F-FDG PET/MRI in patients referred for chronic fatigue. *Eur J Nucl Med Mol Imaging* 2018;**46**:531–2. https://doi.org/10.1007/s00259-018-4148-3

496. Sandler CX, Cvejic E, Valencia BM, Li H, Hickie IB, Lloyd AR. Predictors of chronic fatigue syndrome and mood disturbance after acute infection. *Front Neurol* 2022;**13**:935442. https://doi.org/10.3389/fneur.2022.935442

497. Sarter L, Heider J, Kirchner L, Schenkel S, Witthoft M, Rief W, Kleinstäuber M. Cognitive and emotional variables predicting treatment outcome of cognitive behavior therapies for patients with medically unexplained symptoms: a meta-analysis. *J Psychosom Res* 2021;**146**:110486. https://doi.org/10.1016/j.jpsychores.2021.110486

498. Sato W, Ono H, Matsutani T, Nakamura M, Shin I, Amano K, *et al*. Skewing of the B cell receptor repertoire in myalgic encephalomyelitis/chronic fatigue syndrome. *Brain Behav Immun* 2021;**95**:245–55. https://doi.org/10.1016/j.bbi.2021.03.023

499. Scartozzi S, Sunnquist M, Jason LA. Myalgic encephalomyelitis and chronic fatigue syndrome case definitions: effects of requiring a substantial reduction in functioning. *Fatigue* 2019;**7**:59–68. https://doi.org/10.1080/21641846.2019.1600825

500. Scheibenbogen C, Loebel M, Freitag H, Krueger A, Bauer S, Antelmann M, *et al*. Immunoadsorption to remove ß2 adrenergic receptor antibodies in chronic fatigue syndrome CFS/ME. *PLOS ONE* 2018;**13**:e0193672. https://doi.org/10.1371/journal.pone.0193672

501. Scheibenbogen C, Sotzny F, Hartwig J, Bauer S, Freitag H, Wittke K, *et al*. Tolerability and efficacy of s.c. IgG self-treatment in ME/CFS patients with IgG/

IgG subclass deficiency: a proof-of-concept study. *J Clin Med* 2021;**10**:2420. https://doi.org/10.3390/jcm10112420

502. Scherbakov N, Szklarski M, Hartwig J, Sotzny F, Lorenz S, Meyer A, *et al*. Peripheral endothelial dysfunction in myalgic encephalomyelitis/chronic fatigue syndrome. *ESC Heart Fail* 2020;**7**:1064–71. https://doi.org/10.1002/ehf2.12633

503. Schmaling KB, Fales JL, McPherson S. Longitudinal outcomes associated with significant other responses to chronic fatigue and pain. *J Health Psychol* 2020;**25**:692–702. https://doi.org/10.1177/1359105317731824

504. Schovsbo SU, Mollehave LT, Petersen MW, Ahrendt B, Eliasen M, Pedersen SB, *et al*. Association between infections and functional somatic disorders: a cross-sectional population-based cohort study. *BMJ Open* 2022;**12**:e066037. https://doi.org/10.1136/bmjopen-2022-066037

505. Schultz KR, Katz BZ, Bockian NR, Jason LA. Associations between autonomic and orthostatic self-report and physician ratings of orthostatic intolerance in youth. *Clin Ther* 2019;**41**:633–40. https://doi.org/10.1016/j.clinthera.2019.02.010

506. Sepulveda N, Malato J, Sotzny F, Grabowska AD, Fonseca A, Cordeiro C, *et al*. Revisiting IgG antibody reactivity to Epstein-Barr virus in myalgic encephalomyelitis/chronic fatigue syndrome and its potential application to disease diagnosis. *Front Med (Lausanne)* 2022;**9**:921101. https://doi.org/10.3389/fmed.2022.921101

507. Serafimova T, Ascough C, Parslow RM, Crawley E. Experiences of pain in paediatric chronic fatigue syndrome/myalgic encephalomyelitis: a single-centre qualitative study. *BMJ Paediatr Open* 2022;**6**:e001201. https://doi.org/10.1136/bmjpo-2021-001201

508. Serafimova T, Loades M, Gaunt D, Crawley E. Who should we ask about mental health symptoms in adolescents with CFS/ME? Parent-child agreement on the revised children's anxiety and depression scale. *Clin Child Psychol Psychiatry* 2021;**26**:367–80. https://doi.org/10.1177/1359104521994880

509. Serrador JM, Quigley KS, Zhao C, Findley T, Natelson BH. Balance deficits in chronic fatigue syndrome with and without fibromyalgia. *NeuroRehabilitation* 2018;**42**:235–46. https://doi.org/10.3233/NRE-172245

510. Sevel LS, Boissoneault J, Letzen JE, Robinson ME, Staud R. Structural brain changes versus self-report: machine-learning classification of chronic fatigue syndrome patients. *Exp Brain Res* 2018;**236**:2245–53. https://doi.org/10.1007/s00221-018-5301-8

511. Shabahang R, Sheykhangafshe F, Aruguete M, Hossienkhanzadeh A. Beliefs about sharing illness experiences in chronic fatigue syndrome: the role of interpersonal trust and personality. *Health Psychol Rep* 2020;**8**:435–44. https://doi.org/10.5114/hpr.2020.99395

512. Shan ZY, Barnden LR, Kwiatek RA, Bhuta S, Hermens DF, Lagopoulos J. Neuroimaging characteristics of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): a systematic review. *J Transl Med* 2020;**18**:335. https://doi.org/10.1186/s12967-020-02506-6

513. Shan ZY, Finegan K, Bhuta S, Ireland T, Staines DR, Marshall-Gradisnik SM, Barnden LR. Brain function characteristics of chronic fatigue syndrome: a task fMRI study. *Neuroimage Clin* 2018;**19**:279–86. https://doi.org/10.1016/j.nicl.2018.04.025

514. Shan ZY, Finegan K, Bhuta S, Ireland T, Staines DR, Marshall-Gradisnik SM, Barnden LR. Decreased connectivity and increased blood oxygenation level dependent complexity in the default mode network in individuals with chronic fatigue syndrome. *Brain Connect* 2018;**8**:33–9. https://doi.org/10.1089/brain.2017.0549

515. Shea Meredith G, Parks Jordan K, Byrd MT, Bergstrom Larry R, Johnson Bruce D, Wheatley-Guy Courtney M. Post exertional malaise in chronic fatigue patients with high widespread pain score. *Med Sci Sports Exerc* 2022;**54**:604. https://doi.org/10.1249/01.mss.0000882640.56534.fe

516. Shi J, Shen J, Xie J, Zhi J, Xu Y. Chronic fatigue syndrome in Chinese middle-school students. *Medicine (Baltim)* 2018;**97**:e9716. https://doi.org/10.1097/MD.0000000000009716

517. Shikova E, Reshkova V, Kumanova capital AC, Raleva S, Alexandrova D, Capo N, *et al*. Cytomegalovirus, Epstein-Barr virus, and human herpesvirus-6 infections in patients with myalgic encephalomyelitis/chronic fatigue syndrome. *J Med Virol* 2020;**92**:3682–8. https://doi.org/10.1002/jmv.25744

518. Shin S, Park SJ, Hwang M. Effectiveness a herbal medicine (Sipjeondaebo-tang) on adults with chronic fatigue syndrome: a randomized, double-blind, placebo-controlled trial. *Integr Med Res* 2021;**10**:100664. https://doi.org/10.1016/j.imr.2020.100664

519. Shungu D. Anti-glutamatergic property of n-acetylcysteine (NAC) documented in vivo in the human brain using proton magnetic resonance spectroscopy. *J Neurol Sci* 2021;**429**:118333. https://doi.org/10.1016/j.jns.2021.118333

520. Simila WA, Halsteinli V, Helland IB, Suvatne C, Elmi H, Ro TB. Health-related quality of life in Norwegian adolescents living with chronic fatigue syndrome.

Health Qual Life Outcomes 2020;**18**:170. https://doi.org/10.1186/s12955-020-01430-z

521. Simila WA, Nost TH, Helland IB, Ro TB. Factors related to educational adaptations and social life at school experienced by young people with CFS/ME: a qualitative study. *BMJ Open* 2021;**11**:e051094. https://doi.org/10.1136/bmjopen-2021-051094

522. Singh S, Stafford P, Schlauch KA, Tillett RR, Gollery M, Johnston SA, *et al*. Humoral immunity profiling of subjects with myalgic encephalomyelitis using a random peptide microarray differentiates cases from controls with high specificity and sensitivity. *Mol Neurobiol* 2018;**55**:633–41. https://doi.org/10.1007/s12035-016-0334-0

523. Sirois FM, Hirsch JK. Self-compassion and adherence in five medical samples: the role of stress. *Mindfulness (N Y)* 2019;**10**:46–54. https://doi.org/10.1007/s12671-018-0945-9

524. Sivertsen B, Hysing M, Harvey AG, Petrie KJ. The epidemiology of insomnia and sleep duration across mental and physical health: the SHoT study. *Front Psychol* 2021;**12**:662572. https://doi.org/10.3389/fpsyg.2021.662572

525. Slomko J, Estevez-Lopez F, Kujawski S, Zawadka-Kunikowska M, Tafil-Klawe M, Klawe JJ, *et al*. Autonomic phenotypes in chronic fatigue syndrome (CFS) are associated with illness severity: a cluster analysis. *J Clin Med* 2020;**9**:2531–15. https://doi.org/10.3390/jcm9082531

526. Slomko J, Newton JL, Kujawski S, Tafil-Klawe M, Klawe J, Staines D, *et al*. Prevalence and characteristics of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) in Poland: a cross-sectional study. *BMJ Open* 2019;**9**:e023955. https://doi.org/10.1136/bmjopen-2018-023955

527. Smakowski A, Adamson J, Turner T, Chalder T. Graded exercise therapy for patients with chronic fatigue syndrome in secondary care – a benchmarking study. *Disabil Rehabil* 2022;**44**:5878–86. https://doi.org/10.1080/09638288.2021.1949049

528. Smith L, Crawley E, Riley M, McManus M, Loades ME. Exploring anhedonia in adolescents with chronic fatigue syndrome (CFS): a mixed-methods study. *Clin Child Psychol Psychiatry* 2021;**26**:855–69. https://doi.org/10.1177/13591045211005515

529. Solomon-Moore E, Jago R, Beasant L, Brigden A, Crawley E. Physical activity patterns among children and adolescents with mild-to-moderate chronic fatigue syndrome/myalgic encephalomyelitis. *BMJ Paediatr Open* 2019;**3**:e000425. https://doi.org/10.1136/bmjpo-2018-000425

530. Sommerfelt K, Schei T, Angelsen A. Severe and very severe myalgic encephalopathy/chronic fatigue syndrome ME/CFS in Norway: symptom burden and access to care. *J Clin Med* 2023;**12**:1487. https://doi.org/10.3390/jcm12041487

531. Sorg AL, Becht S, Jank M, Armann J, von Both U, Hufnagel M, *et al*. Association of SARS-CoV-2 seropositivity with myalgic encephalomyelitis and/or chronic fatigue syndrome among children and adolescents in Germany. *JAMA Netw Open* 2022;**5**:e2233454. https://doi.org/10.1001/jamanetworkopen.2022.33454

532. Staud R, Boissoneault J, Craggs JG, Lai S, Robinson ME. Task related cerebral blood flow changes of patients with chronic fatigue syndrome: an arterial spin labeling study. *Fatigue* 2018;**6**:63–79. https://doi.org/10.1080/21641846.2018.1453919

533. Steiner S, Becker SC, Hartwig J, Sotzny F, Lorenz S, Bauer S, *et al*. Autoimmunity-related risk variants in PTPN22 and CTLA4 are associated with ME/CFS with infectious onset. *Front Immunol* 2020;**11**:578. https://doi.org/10.3389/fimmu.2020.00578

534. Steinsvik EK, Hausken T, Fluge O, Mella O, Gilja OH. Gastric dysmotility and gastrointestinal symptoms in myalgic encephalomyelitis/chronic fatigue syndrome. *Scand J Gastroenterol* 2023;**58**:718–25. https://doi.org/10.1080/00365521.2023.2173533

535. Stevelink SAM, Fear NT, Hotopf M, Chalder T. Factors associated with work status in chronic fatigue syndrome. *Occup Med (Lond)* 2019;**69**:453–8. https://doi.org/10.1093/occmed/kqz108

536. Stocks RA, Themelis K, Cipinova ZC, Shah-Goodwin L, Barrit A, Critchley HD, *et al*. Baseline fatigue severity predicts inflammation induced autonomic hyperactivity and pain sensitivity in fibromyalgia and ME/CFS. *Psychosom Med* 2019;**81**:A1–A213. https://doi.org/10.1097/psy.0000000000000699

537. Strand EB, Mengshoel AM, Sandvik L, Helland IB, Abraham S, Nes LS. Pain is associated with reduced quality of life and functional status in patients with myalgic encephalomyelitis/chronic fatigue syndrome. *Scand J Pain* 2019;**19**:61–72. https://doi.org/10.1515/sjpain-2018-0095

538. Strand Elin B, Castro-Marrero J, Helland I, Alegre J, Mengshoel Anne M. Pain and depression are associated with more anxiety in ME/CFS: a cross-sectional cohort study between Norway and Spain. *Clin Med Insights Psychiatry* 2020;**11**:1–8. https://doi.org/10.1177/1179557320941478

539. Strassheim VJ, Sunnquist M, Jason LA, Newton JL. Defining the prevalence and symptom burden of those with self-reported severe chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME): a

two-phase community pilot study in the North East of England. *BMJ Open* 2018;**8**:e020775. https://doi.org/10.1136/bmjopen-2017-020775

540. Strawbridge R, Sartor ML, Scott F, Cleare AJ. Inflammatory proteins are altered in chronic fatigue syndrome – a systematic review and meta-analysis. *Neurosci Biobehav Rev* 2019;**107**:69–83. https://doi.org/10.1016/j.neubiorev.2019.08.011

541. Strayer DR, Young D, Mitchell WM. Effect of disease duration in a randomized Phase III trial of rintatolimod, an immune modulator for myalgic encephalomyelitis/chronic fatigue syndrome. *PLOS ONE* 2020;**15**:e0240403. https://doi.org/10.1371/journal.pone.0240403

542. Stubhaug B, Lier HO, Assmus J, Rongve A, Kvale G. A 4-day mindfulness-based cognitive behavioral intervention program for CFS/ME. An open study, with 1-year follow-up. *Front Psychiatry* 2018;**9**:720. https://doi.org/10.3389/fpsyt.2018.00720

543. Stussman B, Williams A, Snow J, Gavin A, Scott R, Nath A, Walitt B. Characterization of post-exertional malaise in patients with myalgic encephalomyelitis/chronic fatigue syndrome. *Front Neurol* 2020;**11**:1025. https://doi.org/10.3389/fneur.2020.01025

544. Su J, Thapaliya K, Eaton-Fitch N, Marshall-Gradisnik S, Barnden L. Connectivity between salience and default mode networks and subcortical nodes distinguishes between two classes of myalgic encephalomyelitis/chronic fatigue syndrome. *Brain Connect* 2023;**13**:164–73. https://doi.org/10.1089/brain.2022.0049

545. Sung AP, Tang JJ, Guglielmo MJ, Smith-Gagen J, Bateman L, Navarrete-Galvan L, *et al*. Antibody-dependent cell-mediated cytotoxicity (ADCC) in familial myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Fatigue* 2020;**8**:226–44. https://doi.org/10.1080/21641846.2021.1876613

546. Sung WS, Kang HR, Jung CY, Park SS, Lee SH, Kim EJ. Efficacy of Korean red ginseng (Panax ginseng) for middle-aged and moderate level of chronic fatigue patients: a randomized, double-blind, placebo-controlled trial. *Complement Ther Med* 2020;**48**:102246. https://doi.org/10.1016/j.ctim.2019.102246

547. Sunnquist M, Jason LA. A reexamination of the cognitive behavioral model of chronic fatigue syndrome. *J Clin Psychol* 2018;**74**:1234–45. https://doi.org/10.1002/jclp.22593

548. Sunnquist M, Lazarus S, Jason LA. The development of a short form of the DePaul symptom questionnaire. *Rehabil Psychol* 2019;**64**:453–62. https://doi.org/10.1037/rep0000285

549. Surian AA, Baraniuk JN. Systemic hyperalgesia in females with gulf war illness, chronic fatigue syndrome and fibromyalgia. *Sci Rep* 2020;**10**:5751. https://doi.org/10.1038/s41598-020-62771-9

550. Sweetman E, Kleffmann T, Edgar C, de Lange M, Vallings R, Tate W. A SWATH-MS analysis of myalgic encephalomyelitis/chronic fatigue syndrome peripheral blood mononuclear cell proteomes reveals mitochondrial dysfunction. *J Transl Med* 2020;**18**:365. https://doi.org/10.1186/s12967-020-02533-3

551. Sweetman E, Ryan M, Edgar C, MacKay A, Vallings R, Tate W. Changes in the transcriptome of circulating immune cells of a New Zealand cohort with myalgic encephalomyelitis/chronic fatigue syndrome. *Int J Immunopathol Pharmacol* 2019;**33**:1–8. https://doi.org/10.1177/2058738418820402

552. Szklarski M, Freitag H, Lorenz S, Becker SC, Sotzny F, Bauer S, *et al*. Delineating the association between soluble CD26 and autoantibodies against G-protein coupled receptors, immunological and cardiovascular parameters identifies distinct patterns in post-infectious vs. non-infection-triggered myalgic encephalomyelitis/chronic fatigue syndrome. *Front Immunol* 2021;**12**:644548. https://doi.org/10.3389/fimmu.2021.644548

553. Tack M, Tuller David M, Struthers C. Bias caused by reliance on patient-reported outcome measures in non-blinded randomized trials: an in-depth look at exercise therapy for chronic fatigue syndrome. *Fatigue: Biomed Health Behav* 2020;**8**:181–92. https://doi.org/10.1080/21641846.2020.1848262

554. Teitelbaum J, Goudie S. An open-label, pilot trial of HRG80 red ginseng in chronic fatigue syndrome, fibromyalgia, and post-viral fatigue. *Pharmaceuticals (Basel)* 2021;**15**:43. https://doi.org/10.3390/ph15010043

555. Teitelbaum J, Morello G, Goudie S. Nutritional intervention in chronic fatigue syndrome and fibromyalgia (CFS/FMS) a unique porcine serum polypeptide nutritional supplement. *Open Pain J* 2020;**13**:52–8. https://doi.org/10.2174/1876386302013010052

556. Teodoro T, Edwards MJ, Isaacs JD. A unifying theory for cognitive abnormalities in functional neurological disorders, fibromyalgia and chronic fatigue syndrome: systematic review. *J Neurol Neurosurg Psychiatry* 2018;**89**:1308–19. https://doi.org/10.1136/jnnp-2017-317823

557. Terman JM, Awsumb JM, Cotler J, Jason LA. Confirmatory factor analysis of a myalgic encephalomyelitis and chronic fatigue syndrome stigma scale. *J Health Psychol* 2020;**25**:2352–61. https://doi.org/10.1177/1359105318796906

558. Thapaliya K, Marshall-Gradisnik S, Barth M, Eaton-Fitch N, Barnden L. Brainstem volume changes in myalgic encephalomyelitis/chronic fatigue syndrome and long COVID patients. *Front Neurosci* 2023;**17**:1125208. https://doi.org/10.3389/fnins.2023.1125208

559. Thapaliya K, Marshall-Gradisnik S, Staines D, Barnden L. Mapping of pathological change in chronic fatigue syndrome using the ratio of T1- and T2-weighted MRI scans. *Neuroimage Clin* 2020;**28**:102366. https://doi.org/10.1016/j.nicl.2020.102366

560. Thapaliya K, Marshall-Gradisnik S, Staines D, Barnden L. Diffusion tensor imaging reveals neuronal microstructural changes in myalgic encephalomyelitis/chronic fatigue syndrome. *Eur J Neurosci* 2021;**54**:6214–28. https://doi.org/10.1111/ejn.15413

561. Thapaliya K, Marshall-Gradisnik S, Staines D, Su J, Barnden L. Alteration of cortical volume and thickness in myalgic encephalomyelitis/chronic fatigue syndrome. *Front Neurosci* 2022;**16**:848730. https://doi.org/10.3389/fnins.2022.848730

562. Thapaliya K, Staines D, Marshall-Gradisnik S, Su J, Barnden L. Volumetric differences in hippocampal subfields and associations with clinical measures in myalgic encephalomyelitis/chronic fatigue syndrome. *J Neurosci Res* 2022;**100**:1476–86. https://doi.org/10.1002/jnr.25048

563. Themelis K, Amato M, Thompson B, Stocks R, Pound A, Cipinova ZC, *et al*. Baseline autonomic function: relevance to fibromyalgia. *Psychosom Med* 2020;**82**:A1–A225. https://doi.org/10.1097/psy.0000000000000835

564. Themelis K, Harrison NA, Davies K, Eccles J. Classification, diagnosis, epidemiology and the evolving concept of fibromyalgia a preliminary investigation into diagnostic and clinical differences and similarities between fibromyalgia and ME/CFS. *Clin Exp Rheumatol* 2019;**37**:S135–S6.

565. Thomas M, Christopher G. Fatigue in developmental coordination disorder: an exploratory study in adults. *Fatigue: Biomed Health Behav* 2017;**6**:41–51. https://doi.org/10.1080/21641846.2018.1419564

566. Thompson DP, Antcliff D, Woby SR. Symptoms of chronic fatigue syndrome/myalgic encephalopathy are not determined by activity pacing when measured by the chronic pain coping inventory. *Physiotherapy* 2018;**104**:129–35. https://doi.org/10.1016/j.physio.2017.07.005

567. Timbol CR, Baraniuk JN. Chronic fatigue syndrome in the emergency department. *Open Access Emerg Med* 2019;**11**:15–28. https://doi.org/10.2147/OAEM.S176843

568. Tingting MA, Jie WU, Lijie Y, Fen F, Huilin Y, Jinhua Z, *et al*. Ginger-indirect moxibustion plus acupuncture versus acupuncture alone for chronic fatigue syndrome: a randomized controlled trial. *J Tradit Chin Med* 2022;**42**:242–9. https://doi.org/10.19852/j.cnki.jtcm.20211214.003

569. Tirelli U, Franzini M, Valdenassi L, Pandolfi S, Berretta M, Ricevuti G, Chirumbolo S. Patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) greatly improved fatigue symptoms when treated with oxygen-ozone autohemotherapy. *J Clin Med* 2021;**11**:29. https://doi.org/10.3390/jcm11010029

570. Tjell C, Iglebekk W, Borenstein P. Can a chronic BPPV with a history of trauma be the trigger of symptoms in vestibular migraine, myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), and whiplash associated disorders (WAD)? A retrospective cohort study. *Otol Neurotol* 2019;**40**:96–102. https://doi.org/10.1097/MAO.0000000000002020

571. Tokumasu K, Honda H, Sunada N, Sakurada Y, Matsuda Y, Yamamoto K, *et al*. Clinical characteristics of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) diagnosed in patients with long COVID. *Medicina (Kaunas)* 2022;**58**:850. https://doi.org/10.3390/medicina58070850

572. Tollit M, Politis J, Knight S. Measuring school functioning in students with chronic fatigue syndrome: a systematic review. *J Sch Health* 2018;**88**:74–89. https://doi.org/10.1111/josh.12580

573. Tomas C, Elson JL, Strassheim V, Newton JL, Walker M. The effect of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) severity on cellular bioenergetic function. *PLOS ONE* 2020;**15**:e0231136. https://doi.org/10.1371/journal.pone.0231136

574. Traianos E, Dibnah B, Lendrem D, Clark Y, Macrae V, Slater V, *et al*. Ab0051 The effects of non-invasive vagus nerve stimulation on immunological responses and patient reported outcome measures of fatigue in patients with chronic fatigue syndrome, fibromyalgia, and rheumatoid arthritis. *Ann Rheum Dis* 2021;**80**:1057.3–1058. https://doi.org/10.1136/annrheumdis-2021-eular.1999

575. Trivedi MS, Oltra E, Sarria L, Rose N, Beljanski V, Fletcher MA, *et al*. Identification of myalgic encephalomyelitis/chronic fatigue syndrome-associated DNA methylation patterns. *PLOS ONE* 2018;**13**:e0201066. https://doi.org/10.1371/journal.pone.0201066

576. Tsai SY, Chen HJ, Chen C, Lio CF, Kuo CF, Leong KH, *et al*. Increased risk of chronic fatigue syndrome following psoriasis: a nationwide population-based cohort study. *J Transl Med* 2019;**17**:154. https://doi.org/10.1186/s12967-019-1888-1

577. Tsai SY, Chen HJ, Lio CF, Kuo CF, Kao AC, Wang WS, *et al*. Increased risk of chronic fatigue syndrome in patients with inflammatory bowel disease: a population-based retrospective cohort study. *J Transl Med* 2019;**17**:55. https://doi.org/10.1186/s12967-019-1797-3

578. Tsai SY, Lin CL, Shih SC, Hsu CW, Leong KH, Kuo CF, *et al*. Increased risk of chronic fatigue syndrome following burn injuries. *J Transl Med* 2018;**16**:342. https://doi.org/10.1186/s12967-018-1713-2

579. Tschopp R, Konig RS, Rejmer P, Paris DH. Health system support among patients with ME/CFS in Switzerland. *J Taibah Univ Med Sci* 2023;**18**:876–85. https://doi.org/10.1016/j.jtumed.2022.12.019

580. Tschudi-Madsen H, Rodevand LN, Boymo K, Granan LP. Chronic Widespread pain in a tertiary pain clinic: classification overlap and use of a patient generated quality of life instrument. *Scand J Pain* 2019;**19**:245–55. https://doi.org/10.1515/sjpain-2018-0097

581. Tsilioni I, Natelson B, Theoharides TC. Exosome-associated mitochondrial DNA from patients with myalgic encephalomyelitis/chronic fatigue syndrome stimulates human microglia to release IL-1beta. *Eur J Neurosci* 2022;**56**:5784–94. https://doi.org/10.1111/ejn.15828

582. Tuuminen T, Jaaskelainen T, Vaali K, Polo O. Dampness and mold hypersensitivity syndrome and vaccination as risk factors for chronic fatigue syndrome. *Autoimmun Rev* 2019;**18**:107–8. https://doi.org/10.1016/j.autrev.2018.08.004

583. Tziastoudi M, Cholevas C, Stefanidis I, Theoharides TC. Genetics of COVID-19 and myalgic encephalomyelitis/chronic fatigue syndrome: a systematic review. *Ann Clin Transl Neurol* 2022;**9**:1838–57. https://doi.org/10.1002/acn3.51631

584. Ueland M, Hajdarevic R, Mella O, Strand EB, Sosa DD, Saugstad OD, *et al*. No replication of previously reported association with genetic variants in the T cell receptor alpha (TRA) locus for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Transl Psychiatry* 2022;**12**:277. https://doi.org/10.1038/s41398-022-02046-1

585. Uhde M, Indart A, Fallon BA, Wormser GP, Marques AR, Vernon SD, Alaedini A. C-reactive protein response in patients with post-treatment lyme disease symptoms versus those with myalgic encephalomyelitis/chronic fatigue syndrome. *Clin Infect Dis* 2018;**67**:1309–10. https://doi.org/10.1093/cid/ciy299

586. Uhde M, Indart AC, Green PHR, Yolken RH, Cook DB, Shukla SK, *et al*. Suppressed immune and metabolic responses to intestinal damage-associated microbial translocation in myalgic encephalomyelitis/chronic fatigue syndrome. *Brain Behav Immun Health* 2023;**30**:100627. https://doi.org/10.1016/j.bbih.2023.100627

587. Uhde M, Indart AC, Yu XB, Jang SS, De Giorgio R, Green PHR, *et al*. Markers of non-coeliac wheat sensitivity in patients with myalgic encephalomyelitis/chronic fatigue syndrome. *Gut* 2019;**68**:377–8. https://doi.org/10.1136/gutjnl-2018-316133

588. Vaes AW, Van Herck M, Deng Q, Delbressine JM, Jason LA, Spruit MA. Symptom-based clusters in people with ME/CFS: an illustration of clinical variety in a cross-sectional cohort. *J Transl Med* 2023;**21**:112. https://doi.org/10.1186/s12967-023-03946-6

589. Valdez AR, Hancock EE, Adebayo S, Kiernicki DJ, Proskauer D, Attewell JR, *et al*. Estimating prevalence, demographics, and costs of ME/CFS using large scale medical claims data and machine learning. *Front Pediatr* 2018;**6**:412. https://doi.org/10.3389/fped.2018.00412

590. Van Booven DJ, Gamer J, Joseph A, Perez M, Zarnowski O, Pandya M, *et al*. Stress-Induced transcriptomic changes in females with myalgic encephalomyelitis/chronic fatigue syndrome reveal disrupted immune signatures. *Int J Mol Sci* 2023;**24**:2698. https://doi.org/10.3390/ijms24032698

591. van Campen C, Rowe PC, Verheugt FWA, Visser FC. Cognitive function declines following orthostatic stress in adults with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Front Neurosci* 2020;**14**:688. https://doi.org/10.3389/fnins.2020.00688

592. van Campen C, Rowe PC, Verheugt FWA, Visser FC. Numeric rating scales show prolonged post-exertional symptoms after orthostatic testing of adults with myalgic encephalomyelitis/chronic fatigue syndrome. *Front Med (Lausanne)* 2020;**7**:602894. https://doi.org/10.3389/fmed.2020.602894

593. van Campen C, Rowe PC, Verheugt FWA, Visser FC. Orthostatic stress testing in myalgic encephalomyelitis/chronic fatigue syndrome patients with or without concomitant fibromyalgia: effects on pressure pain thresholds and temporal summation. *Clin Exp Rheumatol* 2021;**39**:39–47. https://doi.org/10.55563/clinexprheumatol/1qj9zu

594. van Campen C, Rowe PC, Visser FC. Cerebral blood flow remains reduced after tilt testing in myalgic encephalomyelitis/chronic fatigue syndrome patients. *Clin Neurophysiol Pract* 2021;**6**:245–55. https://doi.org/10.1016/j.cnp.2021.09.001

595. van Campen C, Rowe PC, Visser FC. Compression stockings improve cardiac output and cerebral blood flow during tilt testing in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) patients: a randomized crossover trial. *Medicina (Kaunas)* 2021;**58**:51. https://doi.org/10.3390/medicina58010051

596. van Campen C, Rowe PC, Visser FC. Deconditioning does not explain orthostatic intolerance in ME/CFS (myalgic encephalomyelitis/chronic fatigue syndrome). *J Transl Med* 2021;**19**:193. https://doi.org/10.1186/s12967-021-02819-0

597. van Campen C, Verheugt FWA, Rowe PC, Visser FC. Cerebral blood flow is reduced in ME/CFS during head-up tilt testing even in the absence of hypotension or tachycardia: a quantitative, controlled study using Doppler echography. *Clin Neurophysiol Pract* 2020;**5**:50–8. https://doi.org/10.1016/j.cnp.2020.01.003

598. van Campen C, Visser FC. Orthostatic intolerance in long-haul COVID after SARS-CoV-2: a case-control comparison with post-EBV and insidious-onset myalgic encephalomyelitis/chronic fatigue syndrome patients. *Healthcare (Basel)* 2022;**10**:N.PAG–N.PAG. https://doi.org/10.3390/healthcare10102058

599. van Campen C, Visser FC. Psychogenic pseudosyncope: real or imaginary? Results from a case-control study in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) patients. *Medicina (Kaunas)* 2022;**58**:09. https://doi.org/10.3390/medicina58010098

600. van Campen CLM, Riepma K, Visser FC. Open trial of vitamin B12 nasal drops in adults with myalgic encephalomyelitis/chronic fatigue syndrome: comparison of responders and non-responders. *Front Pharmacol* 2019;**10**:1102. https://doi.org/10.3389/fphar.2019.01102

601. van Campen CMC, Rowe PC, Verheugt FWA, Visser FC. Physical activity measures in patients with myalgic encephalomyelitis/chronic fatigue syndrome: correlations between peak oxygen consumption, the physical functioning scale of the SF-36 questionnaire, and the number of steps from an activity meter. *J Transl Med* 2020;**18**:228. https://doi.org/10.1186/s12967-020-02397-7

602. van der Schaaf ME, Geerligs L, Toni I, Knoop H, Oosterman JM. Disentangling pain and fatigue in chronic fatigue syndrome: a resting state connectivity study before and after cognitive behavioral therapy. *Brain Behav Immun* 2021;**98**:51. https://doi.org/10.1016/j.bbi.2021.08.190

603. van der Schaaf ME, Roelofs K, de Lange FP, Geurts DEM, van der Meer JWM, Knoop H, Toni I. Fatigue is associated with altered monitoring and preparation of physical effort in patients with chronic fatigue syndrome. *Biol Psychiatry Cogn Neurosci Neuroimaging* 2018;**3**:392–404. https://doi.org/10.1016/j.bpsc.2018.01.015

604. van Deuren S, van Dulmen-den Broeder E, Boonstra A, Gielissen M, Blijlevens N, Loonen J, Knoop H. Fatigue-related cognitive-behavioral factors in survivors of childhood cancer: comparison with chronic fatigue syndrome and survivors of adult-onset cancer. *J Adolesc Young Adult Oncol* 2021;**10**:92–9. https://doi.org/10.1089/jayao.2020.0094

605. Van Oosterwijck J, Marusic U, De Wandele I, Meeus M, Paul L, Lambrecht L, *et al*. Reduced parasympathetic reactivation during recovery from exercise in myalgic encephalomyelitis/chronic fatigue syndrome. *J Clin Med* 2021;**10**:4527. https://doi.org/10.3390/jcm10194527

606. Vangeel EB, Kempke S, Bakusic J, Godderis L, Luyten P, Van Heddegem L, *et al*. Glucocorticoid receptor DNA methylation and childhood trauma in chronic fatigue syndrome patients. *J Psychosom Res* 2018;**104**:55–60. https://doi.org/10.1016/j.jpsychores.2017.11.011

607. Vasiliu O. Therapeutic approaches in chronic fatigue syndrome. *Eur Psychiatry* 2021;**64**:S436–S436. https://doi.org/10.1192/j.eurpsy.2021.1163

608. Vasudevan A, Bailey H, Slavin M, Ledingham A, Kang M, Hickey E, Kazis L. Myalgic encephalomyelitis/chronic fatigue syndrome: a vocabulary. *Arch Phys Med Rehabil* 2022;**103**:e79. https://doi.org/10.1016/j.apmr.2022.08.635

609. Venter M, Tomas C, Pienaar IS, Strassheim V, Erasmus E, Ng WF, *et al*. MtDNA population variation in myalgic encephalomyelitis/chronic fatigue syndrome in two populations: a study of mildly deleterious variants. *Sci Rep* 2019;**9**:2914. https://doi.org/10.1038/s41598-019-39060-1

610. Vera-Nunez M. Using a learning health system to optimize the clinical care of patients with chronic illness treated with a functional medicine approach. *Glob Adv Health Med* 2022;**11**:130–1. https://doi.org/10.1177/2164957x221096590

611. Verdam M, Ller FM, Oort F, Riper H, Straten AV, Leeuw IVD, *et al*. Response shift induced by cognitive behavioral therapy targeting fatigue: results of three randomized controlled trials. *Qual Life Res* 2020;**29**:1–196. https://doi.org/10.1007/s11136-020-02626-y

612. Vergauwen K, Huijnen IPJ, Smeets R, Kos D, van Eupen I, Nijs J, *et al*. An exploratory study of discrepancies between objective and subjective measurement of the physical activity level in female patients with chronic fatigue syndrome. *J Psychosom*

Res 2021;**144**:110417. https://doi.org/10.1016/j.jpsychores.2021.110417

613. Vernon SD, Funk S, Bateman L, Stoddard GJ, Hammer S, Sullivan K, *et al*. Orthostatic challenge causes distinctive symptomatic, hemodynamic and cognitive responses in long COVID and myalgic encephalomyelitis/chronic fatigue syndrome. *Front Med (Lausanne)* 2022;**9**:917019. https://doi.org/10.3389/fmed.2022.917019
614. Vernon SD, Hartle M, Sullivan K, Bell J, Abbaszadeh S, Unutmaz D, Bateman L. Post-exertional malaise among people with long COVID compared to myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Work* 2023;**74**:1179–86. https://doi.org/10.3233/WOR-220581
615. Vigener-Buxel CB, Langer HE, Werner SG, Chatelain R. Fatigue in psoriatic arthritis-prevalence and impact in daily rheumatologic outpatient care. *Ann Rheum Dis* 2020;**79**:1732.2–1732.
616. Vink M, Vink-Niese F. Work rehabilitation and medical retirement for myalgic encephalomyelitis/chronic fatigue syndrome patients: a review and appraisal of diagnostic strategies. *Diagnostics (Basel)* 2019;**9**:124. https://doi.org/10.3390/diagnostics9040124
617. Vogel SK, Primavera IR, Marden CL, Jasion SE, Cranston EM, Flaherty MAK, *et al*. The presentation of myalgic encephalomyelitis/chronic fatigue syndrome is not influenced by the presence or absence of joint hypermobility. *J Pediatr* 2022;**240**:186–91.e2. https://doi.org/10.1016/j.jpeds.2021.09.014
618. Vogl T, Kalka IN, Klompus S, Leviatan S, Weinberger A, Segal E. Systemic antibody responses against human microbiota flagellins are overrepresented in chronic fatigue syndrome patients. *Sci Adv* 2022;**8**:eabq2422. https://doi.org/10.1126/sciadv.abq2422
619. Vreijling SR, Troudart Y, Brosschot JF. Reduced heart rate variability in patients with medically unexplained physical symptoms: a meta-analysis of HF-HRV and RMSSD. *Psychosom Med* 2021;**83**:2–15. https://doi.org/10.1097/PSY.0000000000000874
620. Vuong QC, Allison JR, Finkelmeyer A, Newton J, Durham J. Brain responses in CFS and TMD to autonomic challenges: an exploratory fMRI study. *JDR Clin Trans Res* 2020;**5**:224–32. https://doi.org/10.1177/2380084419872135
621. Vyas J, Muirhead N, Singh R, Ephgrave R, Finlay AY. Impact of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) on the quality of life of people with ME/CFS and their partners and family members: an online cross-sectional survey. *BMJ Open* 2022;**12**:e058128. https://doi.org/10.1136/bmjopen-2021-058128
622. Wallis A, Ball M, Butt H, Lewis DP, McKechnie S, Paull P, *et al*. Open-label pilot for treatment targeting gut dysbiosis in myalgic encephalomyelitis/chronic fatigue syndrome: neuropsychological symptoms and sex comparisons. *J Transl Med* 2018;**16**:24. https://doi.org/10.1186/s12967-018-1392-z
623. Walsh RS, Denovan A, Drinkwater K, Reddington S, Dagnall N. Predicting GP visits: a multinomial logistic regression investigating GP visits amongst a cohort of UK patients living with myalgic encephalomyelitis. *BMC Fam Pract* 2020;**21**:105. https://doi.org/10.1186/s12875-020-01160-7
624. Wang R, Huang X, Wu Y, Sun D. Efficacy of Qigong exercise for treatment of fatigue: a systematic review and meta-analysis. *Front Med (Lausanne)* 2021;**8**:684058. https://doi.org/10.3389/fmed.2021.684058
625. Wang T, Yu L, Xu C, Pan K, Mo M, Duan M, *et al*. Chronic fatigue syndrome patients have alterations in their oral microbiome composition and function. *Int J Prosthodont* 2018;**31**:586.
626. Wang Z, Waldman MF, Basavanhally TJ, Jacobs AR, Lopez G, Perichon RY, *et al*. Autoimmune gene expression profiling of fingerstick whole blood in chronic fatigue syndrome. *J Transl Med* 2022;**20**:486. https://doi.org/10.1186/s12967-022-03682-3
627. Washington SD, Rayhan RU, Garner R, Provenzano D, Zajur K, Addiego FM, *et al*. Exercise alters brain activation in gulf war illness and myalgic encephalomyelitis/chronic fatigue syndrome. *Brain Commun* 2020;**2**:fcaa070.629. https://doi.org/10.1093/braincomms/fcaa070
628. Weigel B, Eaton-Fitch N, Passmore R, Cabanas H, Staines D, Marshall-Gradisnik S. A preliminary investigation of nutritional intake and supplement use in Australians with myalgic encephalomyelitis/chronic fatigue syndrome and the implications on health-related quality of life. *Food Nutr Res* 2021;**65**:1–17. https://doi.org/10.29219/fnr.v65.5730
629. Weigel B, Eaton-Fitch N, Passmore R, Cabanas H, Staines D, Marshall-Gradisnik S. Dietary supplements, daily nutrient intake, and health-related quality of life among people with myalgic encephalomyelitis/chronic fatigue syndrome. *Proc Nutr Soc* 2022;**81**:E80. https://doi.org/10.1017/s0029665122001057
630. White PD, Etherington J. Adverse outcomes in trials of graded exercise therapy for adult patients with chronic fatigue syndrome. *J Psychosom Res* 2021;**147**:110533. https://doi.org/10.1016/j.jpsychores.2021.110533
631. Wilde L, Quincey K, Williamson I. 'The real me shining through M.E.': visualizing masculinity and identity threat in men with myalgic encephalomyelitis/chronic

fatigue syndrome using photovoice and IPA. *Psychol Men Masc* 2020;**21**:309–20. https://doi.org/10.1037/men0000220

632. Williams AM, Christopher G, Jenkinson E. The psychological impact of dependency in adults with chronic fatigue syndrome/myalgic encephalomyelitis: a qualitative exploration. *J Health Psychol* 2019;**24**:264–75. https://doi.org/10.1177/1359105316643376

633. Wilshire CE, Kindlon T, Courtney R, Matthees A, Tuller D, Geraghty K, Levin B. Rethinking the treatment of chronic fatigue syndrome – a reanalysis and evaluation of findings from a recent major trial of graded exercise and CBT. *BMC Psychol* 2018;**6**:6. https://doi.org/10.1186/s40359-018-0218-3

634. Wilson RL, Paterson KB, McGowan V, Hutchinson CV. Visual aspects of reading performance in myalgic encephalomyelitis (ME). *Front Psychol* 2018;**9**:1468. https://doi.org/10.3389/fpsyg.2018.01468

635. Winchester RL, Themelis K, Cipinova ZC, Shah-Goodwin L, Davies K, Eccles J. Mechanisms of chronic pain and fatigue in fibromyalgia and ME/CFS: contribution of autonomic arousal. *Psychosom Med* 2019;**81**:A1–A213. https://doi.org/10.1097/psy.0000000000000699

636. Wood E, Hall KH, Tate W. Role of mitochondria, oxidative stress and the response to antioxidants in myalgic encephalomyelitis/chronic fatigue syndrome: a possible approach to SARS-CoV-2 'long-haulers?'. *Chronic Dis Transl Med* 2021;**7**:14–26. https://doi.org/10.1016/j.cdtm.2020.11.002

637. Worm-Smeitink M, Monden R, Groen RN, van Gils A, Bekhuis E, Rosmalen J, Knoop H. Towards personalized assessment of fatigue perpetuating factors in patients with chronic fatigue syndrome using ecological momentary assessment: a pilot study. *J Psychosom Res* 2021;**140**:110296. https://doi.org/10.1016/j.jpsychores.2020.110296

638. Worm-Smeitink M, van Dam A, van Es S, van der Vaart R, Evers A, Wensing M, Knoop H. Internet-based cognitive behavioral therapy for chronic fatigue syndrome integrated in routine clinical care: implementation study. *J Med Internet Res* 2019;**21**:e14037. https://doi.org/10.2196/14037

639. Wormgoor MEA, Rodenburg SC. The evidence base for physiotherapy in myalgic encephalomyelitis/chronic fatigue syndrome when considering post-exertional malaise: a systematic review and narrative synthesis. *J Transl Med* 2021;**19**:1. https://doi.org/10.1186/s12967-020-02683-4

640. Wortman MSH, Lokkerbol J, van der Wouden JC, Visser B, van der Horst HE, Olde Hartman TC. Cost-effectiveness of interventions for medically unexplained symptoms: a systematic review. *PLOS ONE* 2018;**13**:e0205278. https://doi.org/10.1371/journal.pone.0205278

641. Wright A, Fisher PL, Baker N, O'Rourke L, Cherry MG. Perfectionism, depression and anxiety in chronic fatigue syndrome: a systematic review. *J Psychosom Res* 2021;**140**:110322. https://doi.org/10.1016/j.jpsychores.2020.110322

642. Wu K, Li Y, Zou Y, Ren Y, Wang Y, Hu X, *et al*. Tai Chi increases functional connectivity and decreases chronic fatigue syndrome: a pilot intervention study with machine learning and fMRI analysis. *PLOS ONE* 2022;**17**:e0278415. https://doi.org/10.1371/journal.pone.0278415

643. Wu TY, Khorramshahi T, Taylor LA, Bansal NS, Rodriguez B, Rey IR. Prevalence of aspergillus-derived mycotoxins (ochratoxin, aflatoxin, and gliotoxin) and their distribution in the urinalysis of ME/CFS patients. *Int J Environ Res Public Health* 2022;**19**:2052. https://doi.org/10.3390/ijerph19042052

644. Xie F, Dong W, Guan C, Yao F. Effects of Yijinjing Qigongin alleviating fatigue, sleep quality, and health status on patients with chronic fatigue syndrome: a randomized, controlled, and parallel group clinical study. *Complement Med Res* 2023;**30**:204–12. https://doi.org/10.1159/000528827

645. Xie F, You Y, Guan C, Xu J, Yao F. The Qigong of prolong life with nine turn method relieve fatigue, sleep, anxiety and depression in patients with chronic fatigue syndrome: a randomized controlled clinical study. *Front Med (Lausanne)* 2022;**9**:828414. https://doi.org/10.3389/fmed.2022.828414

646. Xiong R, Gunter C, Fleming E, Vernon SD, Bateman L, Unutmaz D, Oh J. Multi-'omics of gut microbiome-host interactions in short- and long-term myalgic encephalomyelitis/chronic fatigue syndrome patients. *Cell Host Microbe* 2023;**31**:273–87.e5. https://doi.org/10.1016/j.chom.2023.01.001

647. Xu H. Scientific physical training on the clinical recovery of chronic fatigue injury. *Revista Brasileira de Medicina do Esporte* 2021;**27**:793–5. https://doi.org/10.1590/1517-8692202127082021_0376

648. Yang CA, Bauer S, Ho YC, Sotzny F, Chang JG, Scheibenbogen C. The expression signature of very long non-coding RNA in myalgic encephalomyelitis/chronic fatigue syndrome. *J Transl Med* 2018;**16**:231. https://doi.org/10.1186/s12967-018-1600-x

649. Yang G, Gu R, Kubo J, Kakuda W. Is the efficacy of repetitive transcranial magnetic stimulation influenced by baseline severity of fatigue symptom in patients with myalgic encephalomyelitis. *Int J Neurosci* 2020;**130**:64–70. https://doi.org/10.1080/00207454.2019.1663189

650. Yang J, Shin KM, Abu Dabrh, AM, Bierle DM, Zhou X, Bauer BA, Mohabbat AB. Ginseng for the treatment of chronic fatigue syndrome: a systematic review of clinical studies. *Glob Adv Health Med* 2022;**11**:1–8. https://doi.org/10.1177/2164957X221079790

651. Yang M, Keller S, Lin JS. Assessing sleep and pain among adults with myalgic encephalomyelitis/chronic fatigue syndrome: psychometric evaluation of the PROMIS(R) sleep and pain short forms. *Qual Life Res* 2022;**31**:3483–99. https://doi.org/10.1007/s11136-022-03199-8

652. Yang T, Yang Y, Wang D, Li C, Qu Y, Guo J, *et al*. The clinical value of cytokines in chronic fatigue syndrome. *J Transl Med* 2019;**17**:213. https://doi.org/10.1186/s12967-019-1948-6

653. Yang TY, Lin CL, Yao WC, Lio CF, Chiang WP, Lin K, *et al*. How mycobacterium tuberculosis infection could lead to the increasing risks of chronic fatigue syndrome and the potential immunological effects: a population-based retrospective cohort study. *J Transl Med* 2022;**20**:99. https://doi.org/10.1186/s12967-022-03301-1

654. Yin ZH, Wang LJ, Cheng Y, Chen J, Hong XJ, Zhao L, Liang FR. Acupuncture for chronic fatigue syndrome: an overview of systematic reviews. *Chin J Integr Med* 2021;**27**:940–6. https://doi.org/10.1007/s11655-020-3195-3

655. You J, Ye J, Li H, Ye W, Hong E. Moxibustion for chronic fatigue syndrome: a systematic review and meta-analysis. *Evid Based Complement Alternat Med* 2021;**2021**:6418217. https://doi.org/10.1155/2021/6418217

656. Yu X. The therapeutic effect of sports on relieving chronic fatigue. *Revista Brasileira de Medicina do Esporte* 2021;**27**:338–41. https://doi.org/10.1590/1517-8692202127032021_0085

657. Zalewski P, Finkelmeyer A, Frith J, Maclachlan L, Blamire A, Newton Julia L. Liver volume is lower and associates with resting and dynamic blood pressure variability in chronic fatigue syndrome. *Fatigue: Biomed Health Behav* 2018;**6**:141–52. https://doi.org/10.1080/21641846.2018.1488525

658. Zambolin F, Duro-Ocana P, Faisal A, Bagley L, Gregory WJ, Jones AW, McPhee JS. Fibromyalgia and chronic fatigue syndromes: a systematic review and meta-analysis of cardiorespiratory fitness and neuromuscular function compared with healthy individuals. *PLOS ONE* 2022;**17**:e0276009. https://doi.org/10.1371/journal.pone.0276009

659. Zhang F, Wu C, Jia C, Gao K, Wang J, Zhao H, *et al*. Artificial intelligence based discovery of the association between depression and chronic fatigue syndrome. *J Affect Disord* 2019;**250**:380–90. https://doi.org/10.1016/j.jad.2019.03.011

660. Zhang Q, Gong J, Dong H, Xu S, Wang W, Huang G. Acupuncture for chronic fatigue syndrome: a systematic review and meta-analysis. *Acupunct Med* 2019;**37**:211–22. https://doi.org/10.1136/acupmed-2017-011582

661. Zhang X, Wang M, Zhou S. Advances in clinical research on traditional chinese medicine treatment of chronic fatigue syndrome. *Evid Based Complement Alternat Med* 2020;**2020**:4715679. https://doi.org/10.1155/2020/4715679

662. Zhang Y, Jin F, Wei X, Jin Q, Xie J, Pan Y, Shen W. Chinese herbal medicine for the treatment of chronic fatigue syndrome: a systematic review and meta-analysis. *Front Pharmacol* 2022;**13**:958005. https://doi.org/10.3389/fphar.2022.958005

663. Zhao S, Chi A, Wan B, Liang J. Differential metabolites and metabolic pathways involved in aerobic exercise improvement of chronic fatigue symptoms in adolescents based on gas chromatography-mass spectrometry. *Int J Environ Res Public Health* 2022;**19**:2377. https://doi.org/10.3390/ijerph19042377

664. Zhu Z, Zhao X, OuYang Q, Wang Y, Xiong Y, Cong S, *et al*. Waterfall forest environment regulates chronic stress via the NOX4/ROS/NF-kappaB signaling pathway. *Front Neurol* 2021;**12**:619728. https://doi.org/10.3389/fneur.2021.619728

665. Zinn MA, Jason LA. Cortical autonomic network connectivity predicts symptoms in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Int J Psychophysiol* 2021;**170**:89–101. https://doi.org/10.1016/j.ijpsycho.2021.10.004

666. Zinn MA, Zinn ML, Valencia I, Jason LA, Montoya JG. Cortical hypoactivation during resting EEG suggests central nervous system pathology in patients with chronic fatigue syndrome. *Biol Psychol* 2018;**136**:87–99. https://doi.org/10.1016/j.biopsycho.2018.05.016

667. NIH. *Report of the ME/CFS Research Roadmap Working Group of Council (May 15, 2024)*. USA; 2024. URL: www.ninds.nih.gov/sites/default/files/2024-07/Report%20of%20the%20MECFS%20Research%20Roadmap%20Working%20Group%20of%20Council_07_09_2024_508C.pdf (accessed 15 October 2024).

Appendix 1 MEDLINE search strategy

1 exp Fatigue Syndrome, Chronic/
2 Asthenia/
3 Neurasthenia/
4 akureyri disease.ti,ab.
5 Akuteyri disease.ti,ab.
6 atypical poliomyelitis.ti,ab.
7 benign myalgic encephalomyelitis.ti,ab.
8 CFIDS.ti,ab.
9 chronic fatigue*.ti,ab.
10 (chronic adj5 mononucleos*).ti,ab.
11 epidemic neuromyasthenia.ti,ab.
12 fatigue syndrom*.ti,ab.
13 myalgic encephalomyelit*.ti,ab.
14 neurasthenic neuroses.ti,ab.
15 neurasthenic syndrome*.ti,ab.
16 neurataxia.ti,ab.
17 neuroasthenia.ti,ab.
18 (neuromuscular adj6 fatigue).ti,ab.
19 (perspective adj5 asthenia).ti,ab.
20 post infectious encephalomyelitis.ti,ab.
21 postviral fatigue syndrome*.ti,ab.
22 PVFS.ti,ab.
23 royal free disease*.ti,ab.
24 "Neuro Inflammatory and Oxidative fatigue".ti,ab.
25 NIOF.ti,ab.
26 Post exertion.ti,ab.
27 Post exertional.ti,ab.
28 PEM.ti,ab.
29 Systemic Exertion Intolerance Disease.ti,ab.
30 ME CFS.ti,ab.
31 or/1-30
32 exp animals/ not humans.sh.
33 31 not 32
34 limit 33 to english language
35 (2018* or 2019* or 2020* or 2021* or 2022* or 2023*).ed.
36 34 and 35

Note: Search strategy lines 2–7, 9–11 and 14–19 are terms commonly associated with outdated views of ME/CFS. These terms have been included in order to ensure that a comprehensive map of evidence in this field is produced. The protocol for this evidence map recognises the importance of using up-to-date, accepted, diagnostic criteria for ME/CFS, and the diagnostic criteria used in studies will be central to the evidence maps produced. The primary output is an evidence map which is limited to studies in which PEM was a key component of the diagnostic criteria adopted during the study (i.e. CCC, ICC, IOM or NICE 2021 criteria). The identification of studies of populations which authors describe as people with ME/CFS, but which use outdated diagnostic criteria, could play an important role in highlighting gaps/limitations in the current evidence base. This comprehensive search strategy was designed to ensure that we identified these studies.

Appendix 2 Final topics and subtopics

Topic	Subtopic	Description (as used in evidence map)	Link to JLA top 10+ questions[10,11]	Link to NICE (2021)[6] recommendations for research
Diagnosis and assessment	Diagnosis of ME/CFS	Studies focused on the development or testing of a diagnostic test for ME/CFS. Includes studies developing, investigating or evaluating diagnosis assessment criteria/tools/questionnaires. Includes studies comparing different diagnostic criteria	P3 Priority 3: How can an accurate and reliable diagnostic test be developed for ME/CFS?	1. Diagnostic tests. What diagnostic tests are clinically effective and cost-effective in people with suspected ME (or encephalopathy)/CFS (ME/CFS)? 3. Diagnostic criteria. In people with suspected ME/CFS, how effective is the NICE 2021 consensus-based diagnostic criteria in identifying people with ME/CFS?
	Biomarkers for diagnosis	Studies which *specifically test* whether a biomarker can predict a ME/CFS diagnosis (NOT studies that are exploring potential biomarkers, but do not specifically test use as a diagnostic tool). Includes studies which have explored sensitivity and/or specificity of biomarkers as diagnostic tests		
	Distinguishing different kinds of ME/CFS	Studies developing and exploring criteria to distinguish different kinds, variants or severities, of ME/CFS For example, studies which explore possible symptoms or biomarkers to identify and/or group together people with similar presentations of ME/CFS, or similar triggers to ME/CFS. Includes studies investigating different types of PEM response	P5a Priority 5: Are there different types of ME/CFS linked to different causes and how severe it becomes? • P5b: Do different types of ME/CFS need different treatments or • P5c have different chances of recovery?	
	Diagnosis of PEM	Studies specifically focused on the diagnosis and testing of PEM. For example, this may include studies exploring the use of CPET as a diagnostic tool		
	Assessment of ME/CFS symptom	Studies focused on development, evaluation or testing of a test or tool to assess a specific ME/CFS symptom and/or severity of a symptom Includes studies focused on selection of assessment tools; for example, development of a core outcome set for clinical practice or research. Includes studies exploring methods of assessment of impact of living with ME/CFS		2. A core outcome set. What core set of relevant health outcome measures should be used for trials of treatments for ME/CFS and managing symptoms of ME/CFS?
	Other (diagnosis)	Other studies with a focus on diagnosis which do not fit into the above subtopics		
What is the problem? (Descriptive epidemiology: what, who, where, when)	Signs and symptoms	Studies reporting signs and symptoms of ME/CFS or prevalence of symptoms (without any treatment/intervention). These may include (but not be limited to) symptoms relating to: • exertion intolerance/PEM • fatigue (physical and cognitive) • sleep • pain • circulatory system/cardiovascular system/respiratory system • digestive system • brain/central nervous system function (including neuro-psychology, emotion, etc.) • musculoskeletal system		

continued

This article should be referenced as follows:
Todhunter-Brown A, Campbell P, Broderick C, Cowie J, Davis B, Fenton C, *et al.* Recent research in myalgic encephalomyelitis/chronic fatigue syndrome: an evidence map [published online ahead of print March 26 2025]. *Health Technol Assess* 2025. https://doi.org/10.3310/BTBD8846

DOI: 10.3310/BTBD8846

DOI: 10.3310/BTBD8846

Topic	Subtopic	Description (as used in evidence map)	Link to JLA top 10+ questions[10,11]	Link to NICE (2021)[6] recommendations for research
	Course of ME/CFS over time	Studies specifically reporting changes in signs and symptoms over time (e.g. patterns of recovery or disease progression)	• P5c: Do different types of ME/CFS have different chances of recovery?	
	Comparison with symptoms (and diagnosis) of other conditions	Studies comparing the diagnosis, signs and symptoms of ME/CFS with the diagnosis, signs and symptoms of people with other health conditions		
	Prevalence	Prevalence and/or incidence in a defined population.		
What is the cause? What contributes to severity? (Analytic epidemiology: risk factors and disease mechanisms)	General/multiple risk factors	A risk factor is a characteristic, condition or behaviour that increases the likelihood of getting a disease or injury. Risk factors are often presented individually, however, in practice, they do not occur alone. They often coexist and interact with one another Included here are studies which look at more than one risk factor (note: studies included here are not also coded into the individual risk factors)	• P5a Priority 5: Are there different types of ME/CFS linked to different causes and how severe it becomes? • P9 Priority 9: What causes ME/CFS to become severe?	
	Biological mechanisms of PEM	Studies specifically focused on cause of PEM (i.e. the single component of PEM and not wider components of ME/CFS). Includes studies exploring pathological mechanisms of and biomarkers for PEM	• P1a Priority 1: What is the biological mechanism that causes PEM (symptoms caused or made worse by physical, mental or emotional effort, which can be delayed) in people with ME/CFS?	
	Behavioural/lifestyle risk factors	Behavioural and lifestyle risk factors usually relate to actions or habits that the individual incorporates into their day-to-day life. For example, diet, smoking, drinking, physical activity or hobbies. Studies exploring risks relating to psychosocial factors are included here		
	Physiological risk factors (general/other)	Physiological risk factors are those relating to an individual's body or biology 'Wet' biomarkers include biomarkers identified from physical specimens (e.g. blood, urine, cerebrospinal fluid, saliva and muscle biopsy) 'Dry' biomarkers include physiological assessments and measures such as imaging and physiological measurements (e.g. heart rate, blood pressure and respiratory rate) (Excludes studies focusing on inflammatory/immune response, mitochondrial dysfunction, oxygen use and nervous system function – see subtopics below)	(Also links to: P3 Priority 3: How can an accurate and reliable diagnostic test be developed for ME/CFS?)	
	Physiological risk factors: immune system	As above, but with a focus on biomarkers relating to inflammatory/immune responses For example, this includes investigations focused on glucocorticoid receptor function, cytokines, T-cell metabolism, lymphocyte cell surface markers, NK, growth-differentiation factor 15 (GDF-15). Also includes indicators of inflammation of the gut (e.g. gut eukaryotes, bacterial microbiome). Studies investigating vaccination as a risk factor are included here	• P4a Priority 4: Is ME/CFS caused by a faulty immune system? • P4b: Is ME/CFS an autoimmune condition? • P6a Priority 6: Why do some people develop ME/CFS following an infection? • P6b: Is there a link with long COVID?	

DOI: 10.3310/BTBD8846

Topic	Subtopic	Description (as used in evidence map)	Link to JLA top 10+ questions[10,11]	Link to NICE (2021)[6] recommendations for research
	Physiological risk factors: mito-chondrial dysfunction/oxygen	As above, but with a focus on biomarkers relating to mitochondrial function or processes involved in the delivery and/or use of oxygen within the body	• P10a Priority 10: How are mitochondria, responsible for the body's energy produc-tion, affected in ME/CFS? • P10b: Could this understanding lead to new treatments? • P10 + a Priority 10+: Does poor delivery or use of oxygen within the body cause ME/CFS symptoms? • P10 + b: If so, how is this best treated?	
	Physiological risk factors – nervous system function	As above, but with a focus on risk factors relating to peripheral, central and autonomic nervous system functions	• P7a Priority 7: What causes the central and peripheral nervous systems (brain, spinal cord and nerves in the body) to malfunction in people with ME/CFS? • P7b: Could this understanding lead to new treatments?	
	Demographic risk factors	Demographic risk factors are those that relate to the overall population. These include individual/personal factors. Examples include; age, gender and population subgroups, such as occupation, religion or income. Personal factors such as the experience of adverse events (e.g. childhood trauma) are included here		
	Environmental risk factors	Environmental risk factors cover a wide range of topics such as social, economic, cultural and political factors as well as physical, chemical and biological factors. Includes studies focused on social risk factors, such as family relationships		
	Genetic risk factors	Genetic risk factors are based on an individual's genes	• P8a Priority 8: Is there a genetic link to ME/CFS? • P8b: If yes, how does this affect the risk of ME/CFS in families? • P8c: Could this lead to new treatments?	
	Comorbidities	Studies investigating potential shared risk factors or mecha-nisms between ME/CFS and comorbid health conditions	(Also possibly: • P6a Priority 6: Why do some people develop ME/CFS following an infection? • P6b: Is there a link with long COVID?)	
What can we do about it? (Experimental)	Treatment/management (general/mixed)	Any treatment/management or combination of different treatment/management strategies (excluding those which fall into other subtopics below)	• P5b: Do different types of ME/CFS need different treatments?	

continued

This article should be referenced as follows:
Todhunter-Brown A, Campbell P, Broderick C, Cowie J, Davis B, Fenton C, *et al.* Recent research in myalgic encephalomyelitis/chronic fatigue syndrome: an evidence map [published online ahead of print March 26 2025]. *Health Technol Assess* 2025. https://doi.org/10.3310/BTBD8846

Topic	Subtopic	Description (as used in evidence map)	Link to JLA top 10+ questions[10,11]	Link to NICE (2021)[6] recommendations for research
	Energy management	Studies focused on self-monitoring strategies and techniques in guiding energy management. Covers management of: • PEM • all types of activity (cognitive, physical, emotional and social) • rest, relaxation and sleep • environmental factors (including sensory stimulation) Includes adjustments to activity during and after flare-ups and relapse NB. Studies focused specifically on GET are included as a separate subtopic below	• P1b: How is this (PEM) best treated and managed?	Self-monitoring management strategies. What is the clinical and cost-effectiveness of self-monitoring strategies and techniques in guiding energy management? Sleep management strategies What is the clinical and cost-effectiveness of sleep management strategies in managing ME/CFS?
	Physical function management	Pharmacological and non-pharmacological strategies to maintain and prevent deterioration of physical functioning and mobility. Covers strategies to maintain/prevent deterioration of: • joint mobility • muscle flexibility • balance • postural and positional support • muscle function • bone health • cardiovascular health NB. Studies focused specifically on GET are included as a separate subtopic below. Includes studies investigating activity programmes such as Tai-Chi and yoga		
	GET (*NB: NICE 2021 states that people with ME/CFS should not be offered 'any programme that does not follow the approach in recommendation 1.11.13 or that uses fixed incremental increases in physical activity or exercise,* e.g. GET')	GET is defined [according to NICE (2021) guidelines] as first establishing an individual's baseline of achievable exercise or physical activity, then making fixed incremental increases in the time spent being physically active		
	OI management	Pharmacological and non-pharmacological strategies for the management of OI, including POTS	P2 Priority 2: Which existing drugs used to treat other conditions might be useful for treating ME/CFS, such as low dose naltrexone, or drugs used to treat POTS?	
	Pain management	Pharmacological and non-pharmacological management of pain, including management and treatment of neuropathic pain and headaches		

DOI: 10.3310/BTBD8846

DOI: 10.3310/BTBD8846

Topic	Subtopic	Description (as used in evidence map)	Link to JLA top 10+ questions[10,11]	Link to NICE (2021)[6] recommendations for research
	Diet and supplements	Dietary management, supplements and related strategies, including: • fluid intake • diet • vitamins and supplements • probiotics • nutraceuticals • strategies to minimise complications caused by gastrointestinal symptoms Includes lifestyle advice and strategies relating to diet and eating. Includes studies investigating Ginseng and Wasabi		Dietary strategies. What is the clinical and cost-effectiveness of dietary strategies in managing ME/CFS?
	Psychological management	Psychological therapies, including CBT, psychotherapy and other psychological therapies to support people who live with ME/CFS to manage their symptoms, improve their functioning and reduce the distress associated with having a chronic illness. Includes psychological therapies provided with an aim of treating ME/CFS NB. Studies focused specifically on the ‘Lightning Process’ are included as a separate subtopic below		
	Lightning Process (*NB:* NICE *2021 recommendations state ‘Do not offer the Lightning Process, or therapies based on it, to people with* ME/CFS’)	NICE (2021) describes the Lightning Process as one which ‘encourages people with ME/CFS to ignore and “push through” their symptoms and this could potentially cause harm’. NICE makes the recommendation: ‘Do not offer the Lightning Process, or therapies based on it, to people with ME/CFS’		
	Pharmacological treatments (general/other)	Studies focused on any pharmacological treatments not covered by the symptom management subtopics above (i.e. excluding those for physical function management, pain or OI) Any studies focused on oxygen as a treatment (including hyperbaric oxygen) are included here	P2 Priority 2: Which existing drugs used to treat other conditions might be useful for treating ME/CFS, such as low dose naltrexone, or drugs used to treat POTS?	
	Non-pharmacological treatments (general/other)	Studies focused on any non-pharmacological treatment or management strategy not covered by the symptom management subtopics. Includes studies focused on management of multiple symptoms. Studies investigating faecal transplants are included here		
	Complementary/alternative therapies	Complementary and alternative therapies are defined by the NHS as ‘treatment that falls outside of mainstream healthcare’. These include treatments such as acupuncture, homeopathy and TCMs		

continued

This article should be referenced as follows:
Todhunter-Brown A, Campbell P, Broderick C, Cowie J, Davis B, Fenton C, *et al.* Recent research in myalgic encephalomyelitis/chronic fatigue syndrome: an evidence map [published online ahead of print March 26 2025]. *Health Technol Assess* 2025. https://doi.org/10.3310/BTBD8846

Topic	Subtopic	Description (as used in evidence map)	Link to JLA top 10+ questions[10,11]	Link to NICE (2021)[6] recommendations for research
	Organisation of care and support	Any service-related management, such as: • organisation of health and social care services • access to specialist assessment, care and support • hospital care for people with severe or very severe ME/CFS • support within schools and educational establishments Plus provision of informal support services, such as: • peer-support groups • online/virtual support		
Other	Living with ME/CFS	Includes studies reporting qualitative experience of living with ME/CFS, including those focused on health-related quality of life or burden of disease		
	Economics/cost	Includes studies reporting economic factors or costs relating to ME/CFS, including treatments for ME/CFS (cost-effectiveness or cost-of-illness studies)		
	Other	Any other topic not covered elsewhere		

NK, natural killer cells; TCM, traditional Chinese medicine.

DOI: 10.3310/BTBD8846

Appendix 3 Rating of confidence in results of systematic reviews

Following completion of all agreed AMSTAR judgements we rated our confidence in the results of each review, as high, moderate, low or critically low confidence, using the approach recommended by Shea (2017).[22] This was not pre-stated in our protocol, but it was introduced in order to provide a mechanism to enable reporting of our confidence in the included SRs. This approach defined confidence as follows:

- High confidence. No or one non-critical weakness within AMSTAR domains. An accurate and comprehensive summary of the results of studies that address the research question is provided.
- Moderate confidence. More than one non-critical weakness, but no critical flaws, within the AMSTAR domains. An accurate and comprehensive summary of the results of included studies may be provided. A judgement that the presence of multiple non-critical weaknesses reduces confidence can support a further downgrading to low confidence.
- Low confidence. One critical flaw, with or without non-critical weaknesses, within the AMSTAR domains. The review may not provide an accurate and comprehensive summary of the results of studies that address the research question.
- Very low confidence. More than one critical flaw within the AMSTAR domains. The review cannot be assumed to provide an accurate and comprehensive summary of relevant studies.

Again, following recommendations of Shea (2017),[22] critical domains were defined as a judgement of high ROB on the following items: item 2 (registered protocol), item 4 (search strategy), item 7 (justification for study exclusions), item 9 (study ROB assessment), item 11 [meta-analysis (MA)], item 13 (interpretation of results, with consideration of ROB) and item 15 (publication bias). High ROB on any other domain was considered as a non-critical weakness. One reviewer considered the agreed AMSTAR judgements and assigned a confidence level; this was checked by a second reviewer.

Appendix 4 Study designs and definitions used within the evidence map

Study type	Study design	Definition
Evidence studies (*studies that bring together the findings from research studies which have included people with ME/CFS as participants*)	SRs	A research process involving searching for and identification of studies which meet a pre-specified set of eligibility criteria. Information (data) from studies which are relevant to the research question are brought together. This can involve combining data from different studies statistically (known as MA) or a narrative (textual) description to bring the findings together. There are a number of different types of SRs (e.g. scoping reviews, reviews of quantitative studies and reviews of qualitative studies)
Experimental studies (*studies that test a treatment, intervention or management strategy*)	Randomised studies	A study in which there have been two, or more, groups of participants. Each person has been randomly assigned to one of two (or more) different treatment groups (one might be a treatment, and another a placebo, control or 'no treatment' group)
	Non-randomised studies	Studies which have tested a treatment or intervention, but without random allocation of participants to treatment groups. These studies may or may not have a control group
Observational studies (*studies that collect data from people, but do not give a treatment or intervention as part of the study*)	Observational studies with a focus on physical specimens	Physical specimens, sometimes referred to as biospecimens, include human tissue, blood, urine or other biologically derived material
		These studies primarily investigate features relating to biospecimens collected from people with ME/CFS
		This includes studies in which biospecimens from people with ME/CFS are compared to biospecimens of people without ME/CFS (either 'healthy' people or people with other diseases)

continued

Study type	Study design	Definition
	Case-control studies	Studies in which information from a group of people with ME/CFS is compared with information from a group of 'healthy' controls (This includes studies in which there is careful matching of individual 'cases' and 'controls' and studies where there is simply one group of cases and another of controls)
	Cohort studies	Studies in which a group of people with ME/CFS are followed over a period of time. This means that data are collected at two or more different time-points These studies can be prospective (recruiting participants and following them into the future) or retrospective (looking into the past, e.g. by using medical records). These studies may be described as longitudinal studies
	Cross-sectional studies	Studies in which data are collected at one specific time (only) Data could be collected by asking people to complete a survey or questionnaire, or by taking measurements or collecting data at a one-off appointment
	Case-series (descriptive studies)	Reports in which information about a number of patients is brought together and reported. A case report can report information about a single patient, or a number of patients with similar conditions. When bringing together information about a number of patients, this can be described as a case-series In this map, we have only included case-series in which information about at least 10 patients with ME/CFS has been reported
Other	Mixed-method studies	Mixed-method studies combine qualitative (non-numerical) and quantitative (numerical) data
	Qualitative studies	Qualitative studies collect and analyse non-numerical data to explore and provide greater understanding of peoples' lived experiences
	Other	Where we have found research studies that do not fit any of the above categories, they will be placed here For example, this includes studies which have carried out new, or additional, analyses of data that have been collected elsewhere (maybe bringing together data from a number of different studies, or from other registries of data)

Appendix 5 Overview of included systematic reviews

Study ID	Aim of SR	Number of included studies (addressing ME/CFS)	Number of participants with ME/CFS within included studies	Overall confidence in the results of the review (based on AMSTAR2 judgement of ROB)
Diagnosis and assessment				
Diagnosis of ME/CFS				
Almutairi 2020[39]	To evaluate the use of sMRI and fMRI to investigate CFS/ME	35	884	Low
Franklin 2022[210]	To synthesise studies in which the test-to-retest (24 hours) changes in VO_2 and work rate have been compared between people with ME/CFS and controls	6	116	Critically low
Lim 2021[348]	To provide comprehensive data on CFS/ME prevalence from multiple aspects	46	5370	Critically low
Wormgoor 2021[639]	Effects of physiotherapy on symptoms and functioning in ME/CFS patients	18	2320	Low
Biomarkers for diagnosis				
0 reviews				

Study ID	Aim of SR	Number of included studies (addressing ME/CFS)	Number of participants with ME/CFS within included studies	Overall confidence in the results of the review (based on AMSTAR2 judgement of ROB)
Distinguishing different 'types' of ME/CFS				
0 reviews				
Diagnosis of PEM				
Brown 2020[102]	To assess PEM in ME/CFS samples (as contrasted to controls) in a comparable MA	31	2878	Critically low
Lim 2020[346]	This study aimed to estimate the potential of CPET	5	98	Critically low
Wormgoor 2021[639]	Effects of physiotherapy on symptoms and functioning in ME/CFS patients	18	2320	Low
Assessment of ME/CFS symptom				
0 reviews				
Other (diagnosis)				
0 reviews				
What is the problem?				
Signs and symptoms				
Aoun Sebaiti 2022[45]	To delineate the cognitive profile of ME/CFS	40	1086	Critically low
Davenport 2019[172]	To (1) define CI and discuss its applications to clinical populations; (2) summarize existing data regarding heart rate responses to exercise obtained during maximal CPET in people with ME/CFS and (3) discuss how trends related to CI in ME/CFS should influence future patho-etiological research designs and clinical practice	36	2270	Critically low
Deumer 2021[178]	How immune dysfunction, hormonal imbalance, genetics/epigenetics and cognitive alterations affect ME/CFS patients	19	1468	Critically low
Mohamed 2023[399]	To analyse the existing literature on objective sleep measurements in ME/CFS based on the parameters outlined in the National Sleep Foundation's sleep quality recommendation	24	668	Low
Natelson 2021[417]	To describe cardiac abnormalities that occur in ME/CFS patients and whether these cardiovascular factors contribute to this syndrome	87	NR	Critically low
Nelson 2019[420]	To report markers of cardiac autonomic regulation in patients with ME/CFS to determine whether there were differences in heart rate parameters between patients and controls	64	2286	Low
Shan 2020[512]	To facilitate a better-informed hypothesis of ME/CFS aetiology based on consistent findings, to reconcile some inconsistent findings, and to identify a future research focus	63	NR	Moderate
Wright 2021[641]	The association between perfectionism and both depression and anxiety in people living with CFS/ME	7	702	Low
Course of ME/CFS over time				
Moore 2021[405]	To describe definitions of recovery in paediatric CFS/ME, what proportion recover, time to recovery and whether recovery rate differs between younger (< 12 years) and older children	10	826	Critically low

continued

Study ID	Aim of SR	Number of included studies (addressing ME/CFS)	Number of participants with ME/CFS within included studies	Overall confidence in the results of the review (based on AMSTAR2 judgement of ROB)
Prevalence				
Estevez-Lopez 2020[199]	To determine the prevalence and incidence of ME/CFS in Europe	3	341	Moderate
Lim 2020[345]	To provide comprehensive data on CFS/ME prevalence from multiple aspects	46	5370	Critically low
Lim 2021[348]	To estimate and compare the prevalence of ME/CFS in Korea and Japan	8	445	Critically low
Comparison with symptoms (and diagnosis) of other conditions				
Hulens 2023[269]	To explore the similarities in clinical characteristics between primary empty sella and FM/CFS	29	NR	Critically low
Ramirez-Morales 2022[463]	To estimate the clinical overlap between FM and ME based on the published research on this area	21	2586	Critically low
Teodoro 2018[556]	To define the key neuropsychological characteristics of FM/CFS patients	95 with CFS out of 186	4181	Critically low
Tziastoudi 2022[583]	The genetic association involving COVID-19 and/or ME/CFS	26 with CFS out of 97	7481	Critically low
Zambolin 2022[658]	To determine physical performance of people living with CFS and FMS compared with healthy controls	33	1692	Critically low
What is the cause?				
General risk factors				
Deumer 2021[178]	How immune dysfunction, hormonal imbalance, genetics/ epigenetics and cognitive alterations affect ME/CFS patients	19	1468	Critically low
Muller 2020[412]	To examine predisposing, triggering and maintaining factors to CFS/ME	1161	NR	Critically low
Natelson 2021[417]	To describe cardiac abnormalities that occur in ME/CFS patients and whether these cardiovascular factors contribute to this syndrome	87	NR	Critically low
Nelson 2019[420]	To report markers of cardiac autonomic regulation in patients with ME/CFS to determine whether there were differences in heart rate parameters between patients and controls	64	2286	Low
Biological mechanisms of PEM				
Davenport 2019[172]	To (1) define CI and discuss its applications to clinical populations; (2) summarize existing data regarding heart rate responses to exercise obtained during maximal CPET in people with ME/CFS; and (3) discuss how trends related to CI in ME/CFS should influence future patho-etiological research designs and clinical practice	36	2270	Critically low
Lim 2020[346]	This study aimed to estimate the potential of CPET	5	98	Critically low
Behavioural/lifestyle risk factors				
Ko 2022[320]	Explore the differences between FSS patients and patients with explained conditions concerning stigma	2	248	Critically low
Raanes 2021[458]	An overview of the empirical state of the field concerning associations between specific psychological constructs (e.g. executive function) and specific immunological parameters	14	807	Critically low

Study ID	Aim of SR	Number of included studies (addressing ME/CFS)	Number of participants with ME/CFS within included studies	Overall confidence in the results of the review (based on AMSTAR2 judgement of ROB)
Sarter 2021[497]	To summarize results of research on patient-related variables predicting therapy outcome in CBT across different syndromes of MUS	12 with CFS out of 37	2227	Moderate
Wright 2021[641]	The association between perfectionism and both depression and anxiety in people living with CFS/ME	7	702	Low
Physiological risk factors (general/other)				
Barhorst 2020[62]	To quantify RPE responses to acute aerobic exercise involving people with ME/CFS or FM	37	665	Critically low
Christensen 2020[136]	To compare CPET performance between individuals with ME/CFS and matched control subjects	18	975	Critically low
Hulens 2023[269]	To explore the similarities in clinical characteristics between primary empty sella and FM/CFS	29	NR	Critically low
Huth 2020[270]	To evaluate if there is any evidence of metabolomics contributing to the pathogenesis of CFS/ME/SEID	11	487	Critically low
Monzon-Nomdedeu 2021[403]	To identify metabolic signatures in FM and/or ME/CFS supporting the existence of disease-associated plasma factors to be sensed by induced pluripotent stem cells	12	391	Critically low
Vreijling 2021[619]	HF-HRV and root mean square of successive differences in fibromyalgia, irritable bowel syndrome and CFS	12	271	Critically low
Zambolin 2022[658]	To determine physical performance of people living with CFS and FMS compared with healthy controls	33	1692	Critically low
Physiological risk factors: immune system				
Chaves-Filho 2019[128]	To review microglia physiological and pathological mechanisms, microglial disturbances in depression and microglial alterations underlying fatigue and CFS	15	495	Critically low
Corbitt 2019[160]	Cytokines in CFS/ME/SEID to determine whether alterations exist when compared with healthy individuals	15	783	Critically low
Preez 2018[187]	To assess the existing literature for evidence of gut dysbiosis and whether changes to microbial ecology contributes to the pathomechanism CFS/ME	7	296	Low
Eaton-Fitch 2019[190]	NK cell phenotype, receptor expression, cytokine production and cytotoxicity in ME/CFS patients	17	817	Low
Eriksen 2018[196]	To determine whether differences in EBV serology between ME/CFS patients and controls vary with the case definition that is used	27	2684	Critically low
Mozhgani 2022[410]	To explore the relationships between the HHV-6 infection and development of CFS	17	959	Critically low
Newberry 2018[425]	To provide a comprehensive review of the current evidence supporting microbiome alterations in ME/CFS patients	11	1711	Critically low
Raanes 2021[458]	An overview of the empirical state of the field concerning associations between specific psychological constructs (e.g. executive function) and specific immunological parameters	14	807	Critically low

continued

Study ID	Aim of SR	Number of included studies (addressing ME/CFS)	Number of participants with ME/CFS within included studies	Overall confidence in the results of the review (based on AMSTAR2 judgement of ROB)
Safadi 2022[493]	To (1) summarize the evidence on differences in proxy markers of gut dysbiosis in severe mental illnesses and CF vs. controls and (2) investigate the association between these peripheral biomarkers and the severity of sickness behaviour symptoms across diagnostic boundaries	5	240	Critically low
Strawbridge 2019[540]	To examine naturally circulating inflammatory protein levels in CFS in comparison with a non-affected control group	42	2515	Critically low
Tziastoudi 2022[583]	The genetic association involving COVID-19 and/or ME/CFS	26 with CFS out of 97	7481	Critically low
Yang 2019[652]	To examine the potential clinical value of using cytokines for the monitoring of CFS and as targets for the treatment of CFS	46	1575	Critically low
Physiological risk factors: mitochondrial dysfunction/oxygen				
Franklin 2019[209]	To provide a MA of the cross-sectional studies on VO_2 peak (peak oxygen uptake) in patients with CFS/ME compared to apparently healthy controls	32	1025	Low
Franklin 2022[210]	To synthesise studies in which the test-to-retest (24 hours) changes in VO_2 and work rate have been compared between people with ME/CFS and controls	6	116	Critically low
Holden 2020[262]	To compare ME/CFS/SEID participants to healthy controls and the role mitochondria may have in pathology	19	1145	Critically low
Huth 2020[270]	To evaluate if there is any evidence of metabolomics contributing to the pathogenesis of CFS/ME/SEID	11	487	Critically low
Wood 2021[636]	The links between mitochondrial dysfunction and oxidative stress – and the possible therapeutic effects of antioxidants levels upon these pathways in ME/CFS	19	NR	Critically low
Zambolin 2022[658]	To determine physical performance of people living with CFS and FMS compared with healthy controls	33	1692	Critically low
Physiological risk factors – nervous system function				
Almutairi 2020[39]	To evaluate the use of sMRI and fMRI to investigate CFS/ME	35	884	Low
Chaves-Filho 2019[128]	To review microglia physiological and pathological mechanisms, microglial disturbances in depression and microglial alterations underlying fatigue and CFS	15	495	Critically low
Hulens 2023[269]	To explore the similarities in clinical characteristics between primary empty sella and FM/CFS	29	NR	Critically low
Maksoud 2020[365]	To collect and appraise the literature related to the structural and functional neurological changes in ME/CFS patients as measured by imaging techniques	55	1828	Low
Nelson 2021[422]	To (1) integrate the relevant MRI findings of the research field and (2) derive a synthesized evaluation of the brainstem role in ME/CFS	11	338	Critically low
Shan 2020[512]	To facilitate a better-informed hypothesis of ME/CFS aetiology based on consistent findings, to reconcile some inconsistent findings, and to identify a future research focus	63	NR	Moderate
Demographic risk factors				
Wright 2021[641]	The association between perfectionism and both depression and anxiety in people living with CFS/ME	7	702	Low

Study ID	Aim of SR	Number of included studies (addressing ME/CFS)	Number of participants with ME/CFS within included studies	Overall confidence in the results of the review (based on AMSTAR2 judgement of ROB)
Environmental risk factors				
Wright 2021[641]	The association between perfectionism and both depression and anxiety in people living with CFS/ME	7	702	Low
Genetic risk factors				
Almenar-Perez 2019[36]	Compares and contrasts the available ME/CFS epigenetic data	14	296	Critically low
Almenar-Perez 2019[37]	Discriminating between drug-effects and true disease-associated differential miRNA expression	3	83	Critically low
Tziastoudi 2022[583]	The genetic association involving COVID-19 and/or ME/CFS	26 with CFS out of 97	7481	Critically low
Comorbidities				
Brown 2020[102]	To assess PEM in ME/CFS samples (as contrasted to controls) in a comparable MA	31	2878	Critically low
Chaves-Filho 2019[128]	To review microglia physiological and pathological mechanisms, microglial disturbances in depression and microglial alterations underlying fatigue and CFS	15	495	Critically low
Clery 2022[145]	To address the treatment options, efficacy and outcomes for depression and anxiety in children with CFS/ME	16	965	Low
Hulens 2023[269]	To explore the similarities in clinical characteristics between primary empty sella and FM/CFS	29	NR	Critically low
Sarter 2021[497]	To summarize results of research on patient-related variables predicting therapy outcome in CBT across different syndromes of MUS	12 with CFS out of 37	2227	Moderate
What can we do about it?				
Treatment/management (general/mixed)				
Ahmed 2020[31]	The effectiveness of CBT and GET for ME/CFS patients	14	NR	Low
Ascough 2020[51]	The efficacy of interventions to treat pain in children with CFS/ME	5	414	Low
Clery 2022[145]	To address the treatment options, efficacy and outcomes for depression and anxiety in children with CFS/ME	16	965	Low
Collard 2020[149]	To investigate management of CFS/ME in a paediatric population within the key areas of nutrition, exercise, psychology and social factors	29	3319	Critically low
Vink 2019[616]	The prognosis of ME/CFS with the impact on work and whether CBT and/or GET restore the ability to work in ME/CFS	97	23,906	Critically low
Wormgoor 2021[639]	Effects of physiotherapy on symptoms and functioning in ME/CFS patients	18	2320	Low
Energy management				
Casson 2022[117]	To investigate whether activity pacing interventions improve fatigue, physical function, psychological distress, depression, and anxiety in people with CFS	14	1764	Critically low
Larun 2019[332]	To determine the effects of exercise therapy for adults with CFS compared with any other intervention or control	8	1518	Low

continued

Study ID	Aim of SR	Number of included studies (addressing ME/CFS)	Number of participants with ME/CFS within included studies	Overall confidence in the results of the review (based on AMSTAR2 judgement of ROB)
Wormgoor 2021[639]	Effects of physiotherapy on symptoms and functioning in ME/CFS patients	18	2320	Low
Physical function management				
De Orleans Casagrande 2023[175]	To investigate the effects of yoga on depressive symptoms, anxiety, sleep quality and mood of patients with rheumatic diseases	4 with CFS out of 27	87	Critically low
Galeoto 2018[218]	To investigate the efficacy of rehabilitation treatments available for CFS in both physical and mental behaviour	4	190	Critically low
Larun 2019[332]	To determine the effects of exercise therapy for adults with CFS compared with any other intervention or control	8	1518	Low
Wormgoor 2021[639]	Effects of physiotherapy on symptoms and functioning in ME/CFS patients	18	2320	Low
OI management				
0 reviews				
Pain management				
0 reviews				
Dietary management				
Corbitt 2018[159]	To explore probiotics as an option for irritable bowel and GI symptoms in CFS/ME	2 with CFS out of 25	63	Critically low
Maksoud 2021[364]	To appraise literature assessing these nutraceuticals as a possible intervention for treating ME/CFS	9	421	Critically low
Roman 2018[481]	To systematically review the reported effect of probiotic treatments in patients diagnosed with FMS or CFS	2	83	Critically low
Yang 2022[650]	To evaluate the safety and effectiveness of ginseng in patients with CFS	2	68	Low
Psychological therapies				
Ahmed 2020[31]	The effectiveness of CBT and GET for ME/CFS patients	14	NR	Low
Ingman 2022[273]	To investigate CBT and GET, compared to active or passive control conditions, to determine the prognosis of CFS in an adult population	15	1990	Moderate
Khanpour 2021[309]	To review MBIs for the treatment of ME/CFS symptoms	12	564	Moderate
Larun 2019[332]	To determine the effects of exercise therapy for adults with CFS compared with any other intervention or control	8	1518	Low
Sarter 2021[497]	To summarize results of research on patient-related variables predicting therapy outcome in CBT across different syndromes of MUS	12 with CFS out of 37	2227	Moderate
Vasiliu 2021[607]	Pharmacological and psychotherapeutic recommendations in CFS	NR	NR	Critically low
Vink 2019[616]	The prognosis of ME/CFS with the impact on work and whether CBT and/or GET restore the ability to work in ME/CFS	97	23,906	Critically low

Study ID	Aim of SR	Number of included studies (addressing ME/CFS)	Number of participants with ME/CFS within included studies	Overall confidence in the results of the review (based on AMSTAR2 judgement of ROB)
Pharmacological treatments (general/other)				
Almenar-Perez 2019[37]	Discriminating between drug-effects and true disease-associated differential miRNA expression	3	83	Critically low
Kim 2020[311]	To identify the assessment tools that help in the clinical study process for CFS/ME, the primary measurements used and changes in use	56	6956	Critically low
Larun 2019[332]	To determine the effects of exercise therapy for adults with CFS compared with any other intervention or control	8	1518	Low
Vasiliu 2021[607]	Pharmacological and psychotherapeutic recommendations in CFS	NR	NR	Critically low
You 2021[655]	To evaluate the efficacy and safety of moxibustion for CFS	15	1030	Low
Zhang 2022[662]	To assess the effectiveness and safety of CHM in treating CFS	84	6944	Moderate
Non-pharmacological treatments (general/other)				
Kim 2020[311]	To identify the assessment tools that help in the clinical study process for CFS/ME, the primary measurements used and changes in use	56	6956	Critically low
Kim 2020[312]	To determine the efficacy of herbal medicines for the treatment of idiopathic chronic fatigue	19 with CFS out of 21	1819	Moderate
Mengshoel 2020[388]	To map the effects of non-pharmacological therapies in patients with ME/CFS and to examine what patients find important in the treatment process.	16	1069	Critically low
Complementary and alternative therapies				
Fang 2022[202]	To evaluate the existing RCTs, compare the efficacy of acupuncture, moxibustion and other TCM treatments	51	3473	Low
Khanpour 2021[309]	To review MBIs for the treatment of ME/CFS symptoms	12	564	Moderate
Wang 2021[624]	To evaluate the therapeutic benefits of Qigong Exercise on fatigue	6	495	Low
Yin 2021[654]	To evaluate the quality of the existing studies and summarize evidence of important outcomes of MAs/SRs (MAs/SRs) of CFS	10 SRs (130 studies)	10,684	Moderate
You 2021[655]	To evaluate the efficacy and safety of moxibustion for CFS	15	1030	Low
Zhang 2019[660]	To evaluate evidence for the efficacy of acupuncture for CFS	16	1346	Low
Zhang 2020[661]	The efficacy of TCM in the treatment of CFS	77	NR	Critically low
Zhang 2022[662]	To assess the effectiveness and safety of CHM in treating CFS	84	6944	Moderate
Lightning process				
0 studies				
GET				
Ahmed 2020[31]	The effectiveness of CBT and GET for ME/CFS patients	14	NR	Low
Ingman 2022[273]	To investigate CBT and GET, compared to active or passive control conditions, to determine the prognosis of CFS in an adult population	15	1990	Moderate

continued

Study ID	Aim of SR	Number of included studies (addressing ME/CFS)	Number of participants with ME/CFS within included studies	Overall confidence in the results of the review (based on AMSTAR2 judgement of ROB)
Larun 2019[332]	To determine the effects of exercise therapy for adults with CFS compared with any other intervention or control	8	1518	Low
Vink 2019[616]	The prognosis of ME/CFS with the impact on work and whether CBT and/or GET restore the ability to work in ME/CFS	97	23,906	Critically low
Organisation of care and support				
Galeoto 2018[218]	To investigate the efficacy of rehabilitation treatments available for CFS in both physical and mental behaviour	4	190	Critically low
Geraghty 2019[221]	To assess the potential negative impact of biopsychosocial practices on patients with ME/CFS	NR	NR	Critically low
Pheby 2020[449]	To assess whether primary care doctors' awareness, under-standing and acceptance of ME/CFS as a disease have changed in the intervening years	12	2595	Critically low
Pilkington 2020[451]	To apply the relational goods framework to investigate the ways people with CFS/ME understand, perceive, experience and prefer their formal and informal support	47	1028	Low
Tollit 2018[572]	To appraise the methods used to assess school functioning in children and adolescents with CFS	36	3701	Critically low
Other				
Living with ME/CFS				
Fatt 2019[204]	To characterise individuals with prolonged or chronic fatigue, compared to those who meet the criteria for ME/CFS	12	736	Critically low
Geraghty 2019[221]	To assess the potential negative impact of biopsychosocial practices on patients with ME/CFS	NR	NR	Critically low
Pheby 2020[449]	To assess whether the primary care doctors' awareness, understanding and acceptance of ME/CFS as a disease have changed in the intervening years	12	2595	Critically low
Pilkington 2020[451]	To apply the –relational goods– framework to investigate the ways people with CFS/ME understand, perceive, experience and prefer their formal and informal support	47	1028	Low
Tollit 2018[572]	To appraise the methods used to assess school functioning in children and adolescents with CFS	36	3701	Critically low
Vink 2019[616]	The prognosis of ME/CFS with the impact on work and whether CBT and/or GET restore the ability to work in ME/CFS	97	23,906	Critically low
Economics/cost				
Cochrane 2021[148]	To assess the cost-effectiveness of interventions for CFS/ME	10	2094	Low
Wortman 2018[640]	To investigate the evidence regarding cost-effectiveness of interventions for patients with MUS and FSS	8	NR	Moderate

CHM, Chinese herbal medicine; CI, chronotropic intolerance; CPET, cardiopulmonary exercise testing; fMRI, functional magnetic resonance imaging; FMS, fibromyalgia syndrome; FSS, functional somatic syndromes; GI, gastrointestinal; HF-HRV, high-frequency heart rate variability; miRNA, microribonucleic acid; MUS, medically unexplained symptoms; NR, not reported; SEID, Systemic Exertion Intolerance Disease; sMRI, structural magnetic resonance imaging; VO_2, volume peak oxygen.

Appendix 6 Summary of volume of data for each topic/subtopic

The interactive evidence map (see *Report Supplementary Material 7*) provides details of the studies that address each topic/subtopic. *Table 3* summarises the type and number of studies addressing each topic. The following sections (and *Tables 4–8*) provide further information about the volume of data for each subtopic.

Diagnosis and assessment

Table 4 summarises the type and number of studies (and participants) addressing each subtopic relating to diagnosis and assessment. There are a total of 99 studies; references to studies are provided in the evidence map. Further details relating to SRs are provided in *Appendix 5*. Around 48% of studies described using diagnostic criteria in which PEM was an essential component.

What is the problem?

Table 5 summarises the type and number of studies (and participants) addressing each subtopic relating to studies describing aspects of ME/CFS. There are a total of 246 studies; references to studies are provided in the evidence map. Further details relating to SRs are provided in *Appendix 5*. Around 36% of studies described using diagnostic criteria in which PEM was an essential component.

What is the cause?

Table 6 summarises the type and number of studies (and participants) addressing each subtopic relating to studies describing aspects of the cause of ME/CFS. There are a total of 339 studies; references to studies are provided in the evidence map. Further details relating to SRs are provided in *Appendix 5*. Around 44% of studies described using diagnostic criteria in which PEM was an essential component.

TABLE 3 Overview of the number of studies identified, the study design and the topics that these address

		Diagnosis and assessment (see *Table 4*)	What is the problem? (see *Table 5*)	What is the cause (see *Table 6*)	What can we do about it? (see *Table 7*)	Other (*Table 8*)	Total *unique* studies[a]
Evidence studies	SRs	6	17	40	33	9	81
Experimental studies	Randomised studies	0	2	2	28	2	29
	Non-randomised studies	0	8	9	42	1	43
Observational studies	Biospecimen studies	41	30	133	2	0	137
	Case-control studies	28	69	76	6	3	116
	Cohort studies	9	33	31	9	8	51
	Cross-sectional studies	34	74	41	19	27	118
	Case-series	0	0	0	1	0	1
Other	Economic studies	0	0	0	1	1	2
	Mixed-method studies	2	5	2	4	7	8
	Qualitative studies	5	7	0	10	22	25
	Other	12	12	7	9	2	28
Total							639

a Each of the 639 included studies only appears in one row (i.e. has been categorised as having one specific study design) but may appear in multiple columns (as one study may address multiple topics relating to ME/CFS).

DOI: 10.3310/BTBD8846

TABLE 4 Volume of evidence relating to diagnosis and assessment of ME/CFS

		Diagnosis of ME/CFS	Biomarkers for diagnosis	Distinguishing different kinds of ME/CFS	Diagnosis of PEM	Assessment of ME/CFS symptom	Other (diagnosis)
Evidence studies	SRs	4 reviews			3 reviews		
Experimental studies	Randomised studies						
	Non-randomised studies						
Observational studies	Biospecimen studies	14 (1064)	10 (636)	18 (1354)		3 (140)	1 (141)
	Case-control studies	7 (376)	4 (114)	6 (271)	4 (159)	11 (1040)	
	Cohort studies	2 (266,564)		2 (2370)	1 (29)	4 (1776)	
	Cross-sectional studies	4 (1451)	1 (272)	8 (3146)	5 (3468)	16 (2604)	3 (394)
	Case-series						
Other	Economic studies						
	Mixed-method studies					1 (198)	1 (20,140)
	Qualitative studies				1 (43)	3 (49)	1 (36)
	Other	7 (5977)		2 (840)		3 (1291)	
TOTAL (primary studies (participants))		38 (275,432)	15 (1022)	36 (7981)	14 (3699)	41 (7098)	6 (20,711)
Total number of primary studies using diagnostic criteria which included PEM[a]		25	8	24	5	14	1

a These studies may also have referred to use of other diagnostic criteria.

TABLE 5 Volume of evidence relating to 'what is the problem?'

		Signs and symptoms	Course of ME/CFS over time	Comparison with symptoms (and diagnosis) of other conditions	Prevalence
Evidence studies	SRs	8 reviews	1 review	5 reviews	3 reviews
Experimental studies	Randomised studies	1 (236)		1 (240)	
	Non-randomised studies	4 (234)		4 (119)	
Observational studies	Biospecimen studies	7 (1745)	3 (141)	21 (4267)	
	Case-control studies	42 (3728)	2 (41)	27 (1584)[a]	3 (20,688)
	Cohort studies	14 (5411)	13 (2447)	7 (267,481)	3 (266,822)
	Cross-sectional studies	46 (13,183)		30 (3843)	8 (1045)
	Case-series				
Other	Economic studies				
	Mixed-method studies	2 (203)	2 (114)		1 (20,140)
	Qualitative studies	4 (116)	3 (46)		
	Other	7 (6772)	1 (511)	3 (33,845)	
Total [primary studies (participants)]		127 (31,628)	24 (3300)	93 (311,379)	16 (338,015)
Total number of primary studies using diagnostic criteria which included PEM[a]		53	8	37	5

a These studies may also have referred to use of other diagnostic criteria.

What can we do about it?

Table 7 summarises the type and number of studies (and participants) addressing each subtopic relating to studies focused on the treatment and/or management of ME/CFS. There are a total of 164 studies; references to studies are provided in the evidence map. Further details relating to SRs are provided in *Appendix 5*. Around 24% of studies described using diagnostic criteria in which PEM was an essential component.

Other

Table 8 summarises the type and number of studies (and participants) which related to 'other' subtopics. There are a total of 83 studies; references to studies are provided in the evidence map. Further details relating to SRs are provided in *Appendix 5*. Around 19% of studies described using diagnostic criteria in which PEM was an essential component.

DOI: 10.3310/BTBD8846

TABLE 6 Volume of evidence relating to 'what is the cause?'

		General/ multiple risk factors	Biological mechanisms of PEM	Behavioural/ lifestyle risk factors	Physiological risk factors (general/ other)	Physiological risk factors: immune system	Physiological risk factors: mitochondrial dysfunction/ oxygen	Physiological risk factors – nervous system function	Demographic risk factors	Environmental risk factors	Genetic risk factors	Comorbidities
Evidence studies	SRs	4 reviews	2 reviews	4 reviews	7 reviews	12 reviews	6 reviews	6 reviews	1 review	1 review	3 reviews	5 reviews
Experimental studies	Randomised studies		1 (11)				1 (46)					
	Non-randomised studies	1 (22)			2 (29)	1 (40)	1 (69)	2 (84)	2 (237)			1 (22)
Observational studies	Biospecimen studies	7 (3175)			30 (4575)	81 (9471)	21 (1251)	8 (426)	1 (35)	1 (236)	39 (11,284)	7 (524)
	Case-control studies	4 (10,241)		5 (4677)	16 (1438)	10 (525)[a]	2 (36)	30 (1007)	4 (952)	1 (41)	2 (4)	10 (27,577)
	Cohort studies	5 (2031)	1 (27)	2 (292)	5 (484)	9 (3170)			5 (1013)	3 (170)	1 (120)	14 (5266)
	Cross-sectional studies	11 (1686)	4 (553)	4 (333)	3 (531)	3 (306)		4 (372)	1 (73)	4 (787)	1 (100)	16 (2384)
	Case-series											
Other	Economic studies											
	Mixed-method studies	1 (617)								1 (39)		
	Qualitative studies											
	Other	1 (150)				1 (1773)			1 (2308)		1 (31,578)	1 (99)
Total [primary studies (participants)]		30 (17,922)	6 (591)	15 (5302)	56 (6526)	105 (15,285)	25 (1402)	44 (1889)	14 (4618)	9 (1273)	44 (43,176)	49 (35,872)
Total number of primary studies using diagnostic criteria which included PEM[b]		9	15	2	38	62	21	17	2	0	26	14

a Includes one study where participant numbers not specified.
b These studies may also have referred to use of other diagnostic criteria.

This article should be referenced as follows:
Todhunter-Brown A, Campbell P, Broderick C, Cowie J, Davis B, Fenton C, *et al.* Recent research in myalgic encephalomyelitis/chronic fatigue syndrome: an evidence map [published online ahead of print March 26 2025]. *Health Technol Assess* 2025. https://doi.org/10.3310/BTBD8846

DOI: 10.3310/BTBD8846

TABLE 7 Volume of evidence relating to 'what can we do about it?'

		Treatment/ management (general/ mixed)	Energy management	Physical function management	GET	OI management	Pain management	Diet and supplements	Psychological management	Lightning Process	Pharmacological treatments (general/other)	Non-pharmacological treatments (general/ other)	Complementary/ alternative therapies	Organisation of care and support
Evidence studies	SRs	6 reviews	3 reviews	4 reviews	4 reviews			4 reviews	7 reviews		6 reviews	3 reviews	8 reviews	5 reviews
Experimental studies	Randomised studies		2 (169)	3 (46)	2 (1118)	1 (16)		4 (243)	7 (867)	1 (100)	4 (387)		8 (809)	2 (189)
	Non-randomised studies		4 (206)	4 (57)	1 (92)			4 (590)	8 (1926)		16 (1020)	3 (1261)		4 (1515)
Observational studies	Biospecimen studies										2 (130)			
	Case-control studies	2 (12,612)		2 (41)							1 (20)	1 (32)		
	Cohort studies	1 (27)		1 (55)					2 (575)		1 (101)			4 (1355)
	Cross-sectional studies	7 (1882)	3 (1903)	1 (441)	1 (954)			1 (24)	3 (2412)					10 (3823)
	Case-series							1 (42)				1 (42)		
Other	Economic studies													1 (NR)
	Mixed-method studies													4 (20,330)
	Qualitative studies	1 (15)	2 (62)						2 (28)					7 (641)
	Other				2 (1920)				6 (1832)		1 (208)			2 (270)
Total [primary studies (participants)]		11 (14,536)	11 (2340)	11 (640)	4 (4084)	1 (16)		16 (899)	22 (7640)	1 (100)	24 (1866)	5 (135,135)	8 (809)	32 (28,123)
Total number of primary studies using diagnostic criteria which included PEM[a]		6	2	4	1	0	0	7	3	0	15	2	1	7

a These studies may also have referred to use of other diagnostic criteria.

TABLE 8 Volume of evidence relating to 'other' topics

		Living with ME/CFS	Economics/cost	Other
Evidence studies	SRs	6 reviews	2 reviews	
Experimental studies	Randomised studies		2 (264)	
	Non-randomised studies	1 (11)		
Observational studies	Biospecimen studies			
	Case-control studies	3 (144)	1 (52)	
	Cohort studies	5 (1512)	1 (266,444)	1 (95)
	Cross-sectional studies	25 (10,451)	3 (337)	
	Case-series			
Other	Economic studies		1 (85)	
	Mixed-method studies	7 (21,150)		
	Qualitative studies	22 (933)		
	Other			2 (2850)
Total [primary studies (participants)]		63 (34,201)	8 (267,182)	3 (2945)
Total number of primary studies using diagnostic criteria which included PEM[a]		13	2	1

a These studies may also have referred to use of other diagnostic criteria.

Appendix 7 Protocol amendments

Reflections on search dates

We planned to reflect on the search period during the course of the review and seek the views of stakeholders relating to whether there would be benefits to extending the search for SRs of specific topics. However, the volume of evidence and time restrictions for completion of this evidence map meant that there was no opportunity to conduct any further searching. Instead, we have reflected on the need for further searching and SRs within our discussion section, providing clear recommendations for future research.

Stakeholder involvement

Planned open events/meetings were not held. A second Review Advisory Group was held. Details of these changes, and reasons for these, are provided in *Report Supplementary Material 3*.

Quality assessment of included studies

As described in *Methods*, we rated our confidence in the results of each included SR, as high, moderate, low or critically low confidence using the approach recommended by Shea (2017).[22] This was not pre-stated in our protocol.

Evidence map

In our protocol we stated that, following Campbell guidance, we would aim to create a map which had a maximum of 25 row and columns (4–6 categories, each with up to 5 subcategories).[18] After receiving feedback on the test/pilot map from our stakeholders, we modified it accordingly. This feedback from stakeholders on the test/pilot map and the topics/subtopics led to a decision to extend the number of subtopics and consequently resulted in 37 columns.