National Institute for Health and Care Excellence

Final

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

[C] Accessing health and social care services

NICE guideline NG206

Evidence reviews underpinning recommendations and research recommendations in the NICE guideline

October 2021

Final

These evidence reviews were developed by the National Guideline Centre

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Review questions

1. What are the barriers and facilitators to the diagnosis of ME/CFS?
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Introduction

People with ME/CFS are underserved by health and social care services and commonly report difficulties in accessing care. This starts at the beginning of the person's journey with difficulties in obtaining a diagnosis. There is often a protracted process resulting in feelings of disbelief, lack of understanding and frustration on the part of the patient. This has a significant impact on quality of life and delays are likely to alter the trajectory of care and treatment received.

Medical professionals have often been hesitant in giving a diagnosis of ME/CFS; this may relate to lack of knowledge and various misconceptions about the condition within the health and social care professions. Delays in diagnosis has a significant negative impact on people with ME/CFS, with misdiagnoses also presenting as a problem. Some patients have reported having an ME/CFS diagnosis withheld, whilst others claim that the diagnosis is used as a "waste-basket diagnosis" for all patients with unexplained fatigue. Generally, there seems to be a poor understanding of ME/CFS amongst health and social care professionals.

Challenges may also arise with referral to specialist services; due to the disparate nature of ME/CFS services; (dependent on location), the same person could be referred to neurology, psychiatry, immunology, endocrinology, rheumatology and pain services. This lack of unified approach impacts on the person's understanding and ability to manage their condition and will inevitably lead to different approaches to treatment depending on speciality. These difficulties accessing care can continue.

The committee used both reviews to inform their recommendations on accessing a diagnosis and care for people with or suspected ME/CFS. The evidence found for the review questions outlined above is in sections 1.3 and 2.3. The committee discussion of the evidence and interpretation is in section 3.

1 Barriers and facilitators to the process of diagnosing of ME/CFS

1.1 Summary of the protocol

For full details see the review protocol in appendix A.

Table 1: Characteristics of review question

Objective	To identify the barriers and facilitators in the process of diagnosing people with ME/CFS
Population and setting	Adults, children and young people who are diagnosed with ME/CFS, or who are suspected of having ME/CFS by their primary clinician. Clinicians caring for people with ME/CFS, or people suspected to have ME/CFS Stratification: adults, young people and children
Context	The perceptions of patients and clinicians about the barriers and facilitators in the diagnostic process. For example: • What slowed the process down or got in the way? • What aspects of care helped? • Did preconceived attitudes have an impact on the process and what were the preconceived attitudes?
Review strategy	Synthesis of qualitative research, following a thematic analysis approach. Results presented in narrative and in table format with summary statements of main review findings. Quality of the evidence will be assessed by a GRADE CerQual approach for each review finding.

1.2 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual.

Methods specific to this review question are described in the review protocol in appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.3 Qualitative evidence

1.1.1 Included studies

Fourteen qualitative studies (reported across 16 papers) were included in the review[18, 21, 29, 36-39, 44, 46, 60, 66, 76, 93-95, 143] which are summarised in Table 2 below. Key findings from these studies are summarised in Section 1.4.5 below. See also the study selection flow chart in appendix C, study evidence tables in appendix D, and excluded studies lists in appendix E.

Two studies were relevant to the stratum of children and young people with ME/CFS. One of these studies explored the experiences of adolescents with ME/CFS and their mothers. Relevant results from this study were only reported by the mothers and are included here. The other study explored the experiences of ME/CFS specialist and non-specialist

practitioners working with children and adolescents. Key findings from these studies are summarised separately in Table 5 and Table 6 below.

A large number of papers were identified for this review. Studies were included until saturation of themes was reached. Data saturation is the point at which no new themes, or data contributing to themes emerged from the studies. Studies not included due to saturation being reached are listed in Appendix F.

Where 'CFS/ME' has been used in the evidence review, it is in order to reflect the terminology used in the included studies.

1.1.2 Excluded studies

See the excluded studies list in Appendix F.

1.1.3 Summary of qualitative studies included in the evidence review

Table 2: Summary of studies included in the review

Study	Design	Population	Research aim	Comments
Study of ME/CFS diagnosis in black minority ethnic people in the UK (Bayliss 2014[18]; De Silva 2013[44])	Face-to-face semi-structured interviews and open-explorative thematic coding in line with modified grounded theory. And Secondary analysis of semi-structured interviews using a new analytic framework.	Key stakeholders in NW England: black-minority ethnic group (BME) patients with 'CFS/ME' (n=11, mean age 45.6; SD: 14.05), carers (n=2), BME community leaders (n=5), GPs qualified for 6 to 24 years (n=9), practice nurses (n=5) and 'CFS/ME' specialists (n=4). UK Stratum: adults/mixed population	Primary analysis: To explore the possible reasons for the lower levels of diagnosis of 'CFS/ME' in the BME population and the implications for management. Secondary analysis: To explore making the diagnosis and managing 'CFS/ME' in the UK form the perspectives of patients, carers, community leaders and primary care practitioners, to understand why 'CFS/ME' may not be commonly diagnosed is South Asia (SA)	The secondary analysis did not include interviews with practice nurses (n=5) The secondary researcher was naïve to original research findings. Primary analysis reports on the patients' illness severity: mild/moderate n=9; moderate/severe n=1; severe n=1.
Beasant 2014[21]	In-depth semi-structured face-to-face interviews and thematic analysis.	Mothers (n=13) and adolescents (n=12) diagnosed with 'CFS/ME' by paediatric 'CFS/ME' specialist service (aged 12-18 years, mean age: 13.9 SD 1.6), mildly or moderately affected by	To understand the experiences of adolescents and families in accessing and using a specialist service and explore whether or not they value referral to a specialist service for	Specialist Medical Intervention and Lightning Evaluation (SMILE) study designed to test the feasibility and acceptability of recruiting adolescents to a randomised controlled trial (RCT) comparing specialist medical care with specialist

Study	Design	Population	Research aim	Comments
		'CFS/ME', participating in the SMILE study UK Stratum: children and young people	young people with 'CFS/ME'.	medical care and the Lightning Process.
Broughton 2017[29]	Semi-structured interviews (six face-to-face, 10 via telephone) and thematic analysis. Cross-sectional design using opportunity sampling.	Adults (n=16) concluding treatment at one of three outpatient NHS specialist 'CFS/ME' services (median age 43, range 24-62 years; median self-reported illness duration 7.5 years, range 1-17). UK Stratum: adults/mixed population	To explore the experiences of 'CFS/ME' patients who were completing programmes of treatment at three NHS specialist 'CFS/ME' services in England.	NHS specialist 'CFS/ME' services followed NICE guidelines for diagnosis and management of 'CFS/ME', offering patient centred programmes aiming to increase patients' physical, emotional and cognitive capabilities whilst managing the impact of symptoms. CBT and GET are the two main evidence-based therapies which (or components of which) are used in conjunction with techniques aimed at managing activity, sleep hygiene and relaxation. Patients also receive practical support around employment and the benefits system. Services shared a philosophy of rehabilitation aimed at 'recovery' or 'significant improvement', whilst

Study	Design	Population	Research aim	Comments
				acknowledging that this would not be attained by all patients.
Chew-Graham 2008[37]	Semi-structured interviews and thematic analysis	Family physicians (n=14; mean age: 48, SD: 12 years) and patients (n=24; mean age: 48, SD: 12 years) participating in a RCT of 2 nurse-led interventions in primary care (FINE trial) UK Stratum: adults/mixed population	To explore how patients with 'CFS/ME' and family physicians conceptualise this condition and understand it and how their understanding might affect the primary care consultation.	FINE trial was a primary-care-based RCT examining self-help treatment and pragmatic rehabilitation for patients with ME/CFS.
Chew-Graham 2010[36]	Semi-structured interviews and thematic analysis (using an iterative approach).	GPs working in practices participating in the FINE trial (n=22). UK Stratum: adults/mixed population	To explore GPs' beliefs about the value of the label of 'CFS/ME', implications of the diagnosis and attitudes towards patients suffering with this condition.	FINE trial was a primary-care RCT examining self-help treatment and pragmatic rehabilitation for patients with ME/CFS.
Clarke 1999[38] Clarke 2000[39]	Open-ended focused (telephone) interviews using qualitative analysis (study 1: constant comparative method for analysis; study 2: cross-case analysis).	Patients with 'CFS/ME' (n=59; mean age: 45 years, range: 18 to 80) representing all occupational arenas; 62.5% had symptoms from 1 to 5 years. Canada	Study 1: To compare the experience of men and women with CFS; both their self-perceived illness experiences and their relationships with medical practitioners, in order to investigate the two major explanations for the gender difference in	

Study	Design	Population	Research aim	Comments
		Stratum: adults/mixed population	morbidity rates and the anomalous findings regarding the difference between the genders with respect to morbidity as compared to mortality. Study 2: To examine the process and some of the consequences of diagnosis-seeking in the experiences of people with chronic fatigue syndrome	
Devendorf 2019[46]	Semi-structured telephone interviews (one via email) and deductive thematic analysis	Physicians specialising in ME/CFS (n=10) as well as non- ME/CFS specialists (n=3), of diverse medical specialties (mean age 60 years) USA Stratum: adults/mixed population	To explore physicians' views on the challenges to studying and approaching recovery, to examine these challenges in-depth and provide recommendations that will improve how researchers and practitioners approach the study and quantification of ME and CFS recovery.	
Gilje 2008[60]	Qualitative case study with data drawn from a focus group, written answers to a questionnaire and a follow-up meeting; analysed using thematic analysis.	Patients diagnosed from CFS for at least 1 year (n=12), mean age (range): 41 (22-54) years. Diagnosis had been	To explore obstructions for quality care from experiences by patients suffering from CFS	

Study	Design	Population	Research aim	Comments
		confirmed by various doctors. UK Stratum: adults/mixed population		
Hannon 2012[66]	Semi-structured interviews and grounded theory approach.	Health practitioners (GPs n=9, practice nurses n=5, 'CFS/ME' specialists n=4), Carers (n=10), patients (n=16), aged 28-71 UK Stratum: adults/mixed population	To develop an education and training intervention to support practitioners in making an early diagnosis of 'CFS/ME' and supporting patients in the management of their symptoms.	
Horton 2010[76]	Semi-structured interviews and thematic analysis.	Specialist (n=3) and non-specialist (n=3) health care practitioners working with people with ME/CFS, nominated by 'CFS/ME' patients as having provided them with particularly helpful or effective care. UK Stratum: adults/mixed population	To describe from the perspective of health care practitioners (HCPs) judged by people with ME/CFS as having been particularly helpful and effective, practices that: enable participants to establish the legitimacy of their condition; impact positively on the process of diagnosis and care; and enable patients to overcome experiences of social isolation and other negative effects.	Participants were nominated by people with 'CFS/ME' who had taken part in an associated England-wide study of their support needs (Social inequalities in the impact of living with 'CFS/ME': 'CFS/ME' Observatory project), based on their perceptions of the quality of care they had received.

Study	Design	Population	Research aim	Comments
Lovell 1999[93]	Open-ended one-to-one interviews and grounded theory analysis.	Overseas workers (n=12) fulfilling the Oxford criteria for 'CFS' (mean age 40.33 years, range 27 to 61) UK Stratum: adults/mixed population	To study the perceptions of overseas workers who had developed 'CFS'	
Marks 2016[94]	Semi-structured interviews and grounded theory analysis	Health-care professionals working with children and adolescents (n=10) from two NHS organisations in the UK. UK Stratum: children and young people	To explore HCPs experiences of working with children and adolescents with 'CFS/ME' so as to develop an understanding of the process relating to how they understand the condition	HCPs were paediatricians, physiotherapists and clinical psychologists working with children and adolescents; 5 were ME/CFS specialists
McCue 2004[95]	Semi-structured individual interviews and grounded theory analysis.	Female participants (n=14) who regarded themselves as recovered from CFS (mean age 42 years, range 21 to 70). UK Stratum: adults/mixed population	To explore the illness experience of a group of people who had achieved substantial recovery from CFS	Illness duration range: 2 to 17 years Time recovered range: 6 months to 10 years All but one participant had been previously diagnosed by a GP or specialist consultant.
Taylor 2005[143]	Focus group interviews followed by end-of group reflections for, analysed based on the grounded	Adults meeting the Fukuda criteria for CFS (n=47, mean age 46.9 years, SD 10.4)	To determine what aspects of the disability experience of persons with 'CFS' are explained	Data for this study emerged from a federally funded research project that developed and evaluated a

Study	Design	Population	Research aim	Comments
	theory approach, following a qualitative comparative method.	USA Stratum: adults/mixed population	by the social model of disability, and what aspects of disability fall outside or contradict central tenets of the social model.	participants-driven program for individuals with 'CFS', implemented at a centre of independent living. One aspect of the project was an attempt to integrate persons with 'CFS' into the disability culture represented by the centre of independent living and educate staff in the centre about 'CFS', which is not widely understood within the disability culture.

See Appendix D for full evidence tables.

1.1.4 Summary of the qualitative evidence

Fifteen themes were identified from the 14 included studies (see 2.3.1).

Table 3: Review findings for Adults

Main findings	Statement of finding
Lack of health professional knowledge & medical legitimacy[18, 29, 37, 39, 60, 66, 76, 95, 143]	Lack of medical legitimacy, limited health professional knowledge and understanding of ME/CFS and insufficient medical training were reported both from a patient's and clinician's perspective; and meant that health professionals struggled or were unwilling to make a diagnosis, while patients and carers had to seek a diagnosis from multiple doctors or adopt a proactive role.
Nature of diagnosis/ diagnostic procedures[18, 29, 39, 46, 60, 66, 76]	The lack of a diagnostic test or sufficient diagnostic criteria causes doubt among health care professionals and complicates the diagnosis of ME/CFS which is essentially done by exclusion of different conditions through multiple medical tests and medical appointments, as reported by both patients and health care professionals.
Focus on physical symptoms[18]	Both HPs and BME patients were reported to focus on physical symptoms during medical consultations by each other, with the HPs reporting that patients tend not to seek medical advice for symptoms other than physical and patients feeling discouraged to discuss non-specific symptoms.
Referral to specialist services[29, 36, 60, 76]	ME/CFS patients, GPs and ME/CFS specialists reported that referral to specialist services or secondary care facilitates the diagnosis, providing access to experts that can confirm the diagnosis and support GPs and HPs who may lack the confidence to do so alone.
Complicated journey to specialist services[29, 36, 76, 143]	The journey to specialist services, which are likely to facilitate the diagnosis, is complicated by long waiting times, misdiagnoses, numerous tests and medical appointments as well as the limited availability of those services or GPs lack of awareness of them.
Diagnostic overlap (co-morbidities & misdiagnoses)[29, 39, 46, 93, 95]	Conditions with symptomatic overlap and co-morbid conditions were reported to complicate the diagnosis, often leading to unnecessary referrals and misdiagnosis, with ME/CFS patients and health professionals mentioning multiple sclerosis and psychiatric disorders including depression.
Lack of definitive treatment[36, 66]	GPs and practice nurses described how the lack of a clear management pathway and cure for ME/CFS caused reluctance to make a diagnosis, with it even being viewed as harmful.
Heterogeneity of ME/CFS[39, 46, 76]	There is great variability with ME/CFS both on an individual level with symptoms fluctuating from time to time but also from patient to patient and

Main findings	Statement of finding
	within one's lifespan with developmental differences in the illness experience, as reported by ME/CFS patients and health care professionals.
Invisibility of ME/CFS[37]	Physicians and patients raised the invisibility of ME/CFS which could not be demonstrated within the context of medical consultations or diagnostic tests, hindering the diagnosis.
Language barriers[18]	Not speaking English acts as a barrier to the diagnosis and management of ME/CFS, with patients not being able to adequately describe their symptoms or understand their GP during consultations.
BME cultural beliefs[18]	BME people may sometimes turn to religion or spiritual healers rather than primary care when experiencing fatigue, relying on religion and prayer to manage their symptoms and not seeking medical advice, which can result in a delay or lack of diagnosis.
BME community attitudes towards some health issues[18]	The expectation to fulfil certain roles within the family or community as well as the lack of acknowledgment of tiredness and fatigue as symptoms requiring medical assistance may lead people to ignore symptoms of ME/CFS and can be a barrier to the diagnosis and management of ME/CFS in BME communities,
Racism and stereotyping by health-care professionals[18]	The stereotypical beliefs of some health professionals towards people from BME groups may act as a barrier to the diagnosis while BME peoples' awareness of those beliefs and fears of being given stigmatising labels by their community can act as a motivator to avoid the diagnosis of ME/CFS.
Inconsistencies between health-professionals[39, 46]	Lack of consensus in the case definitions used by health care professionals, as well as in what they regarded as the cause of the symptoms patients presented with, could impact the diagnosis given to patients as reported by patients and physicians.
Consultation duration[66]	Health professionals emphasised how challenging it can be to establish an understanding of symptoms within10 minute consultation appointments.
Continuity of care[18, 37]	Establishing an ongoing relationship with their physician was seen as important for the diagnosis of ME/CFS by patients, while lack of continuity of care was considered to impede the diagnosis.
Good health professional practice[76]	Attention to symptom presentation and rigorous history-taking were viewed as vital elements of practice by health care professionals.
Exposure to presentations of ME/CFS[76]	Sufficient exposure to various presentations of ME/CFS was reported to enable practitioners to

Main findings	Statement of finding
	identify the condition and build confidence in their diagnostic skills.

1.1.5 Narrative summary of review findings

1.3.1.1.1 Barriers and facilitators to the diagnosis of ME/CFS in adults

Review finding 1: Lack of health professional knowledge & medical legitimacy

Health professionals including GPs, practice nurses and family physicians described their struggle to make sense of ME/CFS symptoms, admitted their limited clinical knowledge and understanding of ME/CFS, and their doubt towards its existence as a legitimate medical condition. This was reported to result in failure to identify the condition leading to an inappropriate diagnosis, or to cause reluctance or unwillingness to make such a diagnosis. Patients, carers and ME/CFS specialists also emphasised health professionals' limited clinical knowledge and understanding of ME/CFS, which was often attributed to a lack of exposure to patients with the condition and to insufficient medical training and education relative to the diagnosis of ME/CFS. The resulting uncertainty or ignorance and disbelief towards the legitimacy of ME/CFS in the medical community led to a diagnostic dilemma for many GPs who were often reported to have the tendency to overemphasise psychological variables as the causes of patients' symptoms. The lack of health professional knowledge and doubt also led patients and carers to become proactive, turning to other sources and providing their GPs with additional information and asking for diagnostic tests.

Explanation of quality assessment: Very minor concerns over methodological limitations with minor concerns in three studies (due to the role of the researcher not being discussed and concerns over data analysis/data richness with some findings supported by limited quotes) but very minor concerns in four studies (due to the potential influence of the researcher on the findings not being discussed) and no concerns in two studies with nothing to lower the confidence rating; no concerns about coherence with a clear theme emerging across studies; no concerns about relevance with the theme being reported by adult patients some of which were completing treatment, represented various occupational arenas, had suffered with ME/CFS over the long-term or who had recovered and various health care professionals including GPs and professionals caring for black-minority ethnic group patients, family physicians, practice nurses, physiotherapists, clinical psychologists and ME/CFS specialist and non-specialist health care practitioners; no concerns about adequacy, the theme being supported by a large volume of data across contributing studies. Overall assessment of confidence was high.

Review finding 2: Nature of diagnosis/ diagnostic procedures

ME/CFS was described as a diagnosis of exclusion, a difficult diagnosis to make by both patients and health care professionals. Patients reported that diagnostic procedures required ruling out other medical conditions, which involved numerous medical tests and appointments with multiple clinicians thought to be responsible for the organs or systems affected by the sufferer. They emphasised that this made the diagnosis a lengthy process that could take years, even with doctors who were supportive and believed in the patients' symptoms. Health care practitioners, including specialists, described how the diagnosis of ME/CFS was made by exclusion of other diagnoses when no other cause was discovered, due to the lack of positive diagnostic criteria and of a diagnostic test. Absence of the latter in particular was considered to impact both practitioners and patients, causing uncertainty among medical professionals and impacting the diagnosis.

Explanation of quality assessment: Minor concerns over methodological limitations with very minor limitations in three studies (due to the potential influence of the researcher on the

findings not being discussed), minor limitations in three studies (due to concerns over the role of the researcher and data analysis with some findings supported by limited quotes) and no limitations in one study; no concerns about coherence; no concerns about relevance, the theme being reported both by ME/CFS patients and health care professionals including specialist and non-specialist physicians with many years of experience and of different medical specialties; no concerns about adequacy with sufficient information from seven studies supporting the theme. Overall assessment of confidence was high as concerns over methodological limitations were minor and the theme was supported by a wealth of information.

Review finding 3: Focus on physical symptoms

Health professionals (HPs) and black minority ethnic-group (BME) community leaders perceived BME patients as having a biomedical model of illness that leads them to focus on presenting physical symptoms such as headaches and muscle pain when consulting with their GP and refrain from seeking medical advice about non-specific symptoms such as fatigue, loss of concentration and sleep problems, which were often viewed as part of the expected aging process. BME patients and community leaders also suggested that HPs focus on physical symptoms and that this meant that patients might not be encouraged to discuss nonspecific symptoms.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the potential influence of the researcher on the findings not being discussed) that were too minor to lower the confidence rating; no concerns about coherence; moderate concerns about relevance due to the population of the contributing study being black minority ethnic groups and of potentially limited applicability to ME/CFS patients of other ethnic groups; no concerns about adequacy with rich information emerging from one study. Overall assessment of confidence was moderate due to concerns about relevance.

Review finding 4: Referral to specialist services

Patients reported they had their ME/CFS diagnosis confirmed when they were assessed by the specialist services and felt they had benefited from accessing the specialist service. The majority recalled having had hopes and expectations of referral and treatment including confirmation of diagnosis and better management of symptoms. Patients that had been seen by neurologists at a hospital department with a special interest in ME/CFS reported that this was usually the place where the diagnosis had been concluded. Those GPs who felt that making the diagnosis or labelling the patient's condition was helpful suggested that referring the patient to secondary care could potentially assist in achieving a diagnosis and would provide support to GPs who lack confidence in making the diagnosis alone. Specialists were reported to have both experience and expertise to be able to support GPs and other HCPs in reaching or confirming a diagnosis.

Explanation of quality assessment: very minor concerns over methodological limitations with no limitations identified in two contributing studies, very minor limitations in one study (due to the potential influence of the researcher on the findings not being discussed) and minor limitations in one study (due to the potential influence of the researcher and concerns over data richness with findings mostly supported by single quotes); no concerns about coherence; no concerns about relevance with the theme reported by different groups of people including adults with ME/CFS, GPs and ME/CFS specialists; no concerns about adequacy. Overall assessment of confidence was high.

Review finding 5: Complicated journey to (specialist) services

Adults with ME/CFS described a long, difficult and frustrating journey to specialists or the necessary services, involving numerous interactions with healthcare professionals and long waiting times. These were often a result of misdiagnoses and of the diagnostic procedures

involved which required numerous tests and clinical appointments to rule out other medical conditions. GPs reported the limited availability of potentially helpful places/services to support the diagnosis and management of patients, while specialists highlighted that only a minority of GPs make referrals to specialist services (attributed to a lack of understanding of the condition) and emphasised the need for specialist services to be more visible.

Explanation of quality assessment: very minor concerns over methodological limitations due to minor limitations in only one contributing study (due to the potential influence of the researcher on the findings not being discussed and concerns over data analysis with findings mostly supported by single quotes) but no limitations in the other three contributing studies;; no concerns about coherence; no concerns about relevance with the theme reported by different groups of people including, adults with ME/CFS, GPs and ME/CFS specialists; no concerns about adequacy. Overall assessment of confidence was high as concerns over methodological limitations were too minor to lower the confidence rating.

Review finding 6: Diagnostic overlap (co-morbidities & misdiagnosis)

Patients reported initially being misdiagnosed, for example with depression, multiple sclerosis or glandular fever, with many being referred to psychiatrists when they first presented their doctors with their symptoms, being given anti-depressants either at the outset or at some point during the course of their illness. Patients also expressed the opinion that their doctors ignored their physical symptoms and focussed more on the depressive symptoms, reporting that their more physical symptoms were disregarded in favour of any that could be described as pertaining to depression or to mental health issues. Participants themselves sometimes initially believed they had a psychological disorder rather than a physical one as a result of the numerous indefinable symptoms they were experiencing. Health professionals acknowledged that the patients they see often exhibit depressive symptoms and mentioned that misdiagnosis occurs on both ends.

Explanation of quality assessment: minor concerns over methodological limitations with serious limitations in one study (due to the potential influence of the researcher on the findings not being discussed, concerns over a lack of detail on the data collection method and over data richness with limited information to support the findings) but very minor limitations in two studies (due to the potential influence of the researcher on the findings not being discussed), minor limitations in one study (due to the potential influence of the researcher on the findings not being discussed and concerns over data richness with findings mostly supported by single quotes) and no limitations in one study; no concerns about coherence despite the conflicting evidence about the type of symptoms doctors focus on emerging from BME patients included in earlier review finding, as these may be due to population differences and can be explained by reports that BME patients in particular hold a biomedical model of illness which leads them to focus on physical symptoms when consulting with doctors; no concerns about relevance with the theme reported by different groups of people including, adults with ME/CFS and health professionals; minor concerns about adequacy due to concerns about data richness associated with two contributing studies. Overall assessment of confidence was moderate due to the concerns about methodology and adequacy.

Review finding 7: Lack of definitive treatment

GPs and practice nurses reported that they used the ME/CFS label as a last resort and with reluctance because making the diagnosis did not lead to obvious treatment and they believed that there was no cure for it. It was also reported by GPs that the ME/CFS diagnostic label could be harmful because it did not offer a clear management pathway for either the GP or the patient.

Explanation of quality assessment: very minor concerns over methodological limitations with minor limitations in one contributing study (due to the potential influence of the researcher on

the findings not being discussed and concerns over data analysis with findings mostly supported by single quotes) and nothing to lower the confidence rating in the other contributing study; no concerns about coherence; no concerns about relevance, the finding being reported by GPs and practice nurses working with ME/CFS patents; moderate concerns about adequacy due to the finding emerging from relatively limited information from two studies. Overall assessment of confidence was moderate due to concerns about adequacy and very minor concerns over methodological limitations.

Review finding 8: Heterogeneity of ME/CFS

ME/CFS patients reported that their symptoms varied from day to day, week to week, month to month, and even at times from hour to hour. HCPs emphasised the variability between patients presenting with symptoms apart from the fatigue and where other symptoms such as headaches, gut symptoms or muscle pain may predominate for some individuals. Furthermore, physicians noted that ME/CFS may present differently in children than adults but there is little if any research that demarcates these differences. Cognitive abilities and self-awareness also develop with age. Young children may lack awareness that they are sick, or the ability to articulate their experience and symptoms such as fatigue, orthostatic intolerance, and memory issues may be difficult to detect in paediatric populations.

Explanation of quality assessment: minor concerns over methodological limitations with very minor limitations in one study (due to the potential influence of the researcher on the findings not being discussed) and minor limitations in two studies (due to the influence of the researcher not being discussed and concerns over data analysis/data richness with findings mostly supported by single quotes); no concerns about coherence; minor concerns about relevance with the reported between and within patient variability not being explicitly linked to the diagnosis but deduced to be complicating the diagnosis within the context of the present review; minor concerns about adequacy due to concerns about data richness at the individual study level associated with two studies. Overall assessment of confidence was moderate due to concerns over methodological limitations, relevance and adequacy being minor.

Review finding 9: Invisibility of ME/CFS

Family physicians expressed frustrations that they could not measure how the patient was affected by their condition. It was so-called 'invisible' and the symptoms seemed out of proportion to the signs leading some to doubt the condition and the genuineness of its presentation. The inability to demonstrate the extent of their condition beyond the snapshot view revealed in the consultation meant that patients were unable to establish that symptoms come and go and that the condition is invisible on good days. Family physicians described how they ran a battery of tests, which invariably returned negative results. With no manifest sign of patients' symptoms and no confirmation of a diagnosis, the physicians would often reach clinical impasse. Patients were aware their condition was invisible from a biomedical perspective.

Explanation of quality assessment: minor concerns over methodological limitations in the contributing study (due to concerns over data richness with some findings supported by limited quotes) no concerns about coherence; very minor concerns about relevance due to population of the contributing study consisting of people that had been previously recruited in a RCT; minor concerns about adequacy with minor concerns about the richness of the information supporting the theme in the contributing study. Overall assessment of confidence was moderate due to concerns about methodological limitations and adequacy.

Review finding 10: Language barriers

Health professionals, patients, carers and community leaders of BME groups agreed that not speaking English acts as a barrier to the diagnosis and management of ME/CFS, with some BME patients not being able to adequately describe their symptoms or understand their GP during consultations.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the potential influence of the researcher on the findings not being discussed) that were too minor to lower the confidence rating; no concerns about coherence; serious concerns about relevance, the finding being of limited applicability to ME/CFS patients outside black minority ethnic groups; minor concerns about adequacy with information emerging from one study. Overall assessment of confidence was low due to concerns about relevance and adequacy.

Review finding 11: BME cultural beliefs

Patients and community leaders described how some BME people would turn to religion or spiritual healers rather than primary care when experiencing fatigue, believing that spirits or black magic may be causing the condition. Religion and prayer were also cited as motivators for patients to attempt to manage their symptoms and not seek medical advice.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the potential influence of the researcher on the findings not being discussed) that were too minor to lower the confidence rating; no concerns about coherence; serious concerns about relevance, the finding being of limited applicability to ME/CFS patients outside black minority ethnic groups; minor concerns about adequacy with information emerging from one study. Overall assessment of confidence was low due to concerns about relevance and adequacy.

Review finding 12: BME community attitudes towards some health issues and symptoms

The expectation to fulfil certain roles within the family or community was described as a barrier to the diagnosis and management of ME/CFS in BME communities, with some patients commenting on pressures from the family for high academic achievement and the perceived stigma attached to low achievement which pushed them to ignore symptoms of ME/CFS until they reached a crisis point. GPs suggested that patients of BME origin present with vague physical complaints, with somatisation being more common as culturally BME communities do not consider tiredness or fatigue a symptom that requires medical assistance, thus other physical symptoms are usually reported.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the potential influence of the researcher on the findings not being discussed) that were too minor to lower the confidence rating; no concerns about coherence; serious concerns about relevance, the finding being of limited applicability to ME/CFS patients outside black minority ethnic groups; minor concerns about adequacy with information emerging from one study. Overall assessment of confidence was low due to concerns about relevance and adequacy.

Review finding 13: Racism and stereotyping by health-care professionals

BME community leaders described how people with ME/CFS could be given stigmatising labels, such as being ‘liars’ or ‘crazy’ by their community and may therefore want to avoid

this potentially stigmatising diagnosis. Patients, carers and community leaders described how they believed some GPs may hold stereotypical views of people from certain cultures, such as being 'lazy', that might prevent the diagnosis of ME/CFS. Health professionals also recognised the possible influence of racism and stereotypes in preventing the diagnosis of ME/CFS.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the potential influence of the researcher on the findings not being discussed) that were too minor to lower the confidence rating; no concerns about coherence; serious concerns about relevance, the finding being of limited applicability to ME/CFS patients outside black minority ethnic groups; minor concerns about adequacy with information emerging from one study. Overall assessment of confidence was low due to concerns about relevance and adequacy.

Review finding 14: Inconsistencies between health professionals

Physicians reported that case definitions affect whether a patient is diagnosed with ME or CFS and may select more or less severe cases. They felt that compared to other chronic illnesses, there is more variability with ME/CFS patients (e.g. with the Fukuda et al criteria it is possible for two patients to have a diagnosis of CFS without having any of the same symptoms (except for fatigue). This issue confused physicians to the point where a few questioned their patient's symptoms and depending on the case definition used by the physician, patients may be diagnosed differently between providers. Patients observed differences of opinion and even disputes and contradictions between different doctors, with different specialists focussing on the possible problems associated with different organ symptoms and offering different sorts of potential explanations.

Explanation of quality assessment: minor concerns over methodological limitations with minor limitations in one study (due to the potential influence of the researcher on the findings not being discussed and concerns over data analysis with themes mostly supported by single quotes) and very minor limitations in the other study (due to the influence of the researcher not being discussed); no concerns about coherence; no concerns about relevance with the theme emerging from both health professionals and ME/CFS patients; minor concerns about adequacy, the finding being supported by relatively sufficient data within two studies. Overall assessment of confidence was moderate due to concerns about methodological limitations and adequacy.

Review finding 15: Consultation duration

Health professionals reported that a ten-minute consultation with a patient with ME/CFS can be challenging due to the variety and complexity of symptoms. A ten-minute consultation was seen as a potential barrier to diagnosis particularly by ME/CFS specialists reporting that GPs may not be able to gain a complete understanding of the variety of symptoms patients can experience and the impact of those on their life.

Explanation of quality assessment: minor concerns over methodological limitations in the contributing study (due to the role of the researcher on the findings not being discussed and concerns over data analysis with some findings supported by single quotes); no concerns about coherence; no concerns about relevance with information for this finding emerging from health professionals, including ME/CFS specialists; serious concerns about adequacy, the finding being supported by two quotes in one study. Overall assessment of quality was low due to concerns about methodological limitations and adequacy.

Review finding 16: Continuity of care

Patients reported it was important in both the diagnosis and management of their condition to have an established relationship with their family physician. Not having such an ongoing relationship was reported to make it difficult to achieve agreement about the symptoms and the diagnosis, because the primary physician had no prior knowledge of them. High turnover of GPs in the inner-city practices that may provide care for people in BME communities was cited as a reason why some people may not receive a diagnosis of ME/CFS. Patients believed that a lack of continuity meant that they were unable to build a long-term relationship with their health professional, and GPs were unable to take the holistic approach considered necessary for the diagnosis of ME/CFS to be made.

Explanation of quality assessment: minor concerns over methodological limitations with very minor concerns in one study (due to the potential influence of the researcher on the findings not being discussed) and minor concerns in the other study (due to concerns over data richness with some findings supported by limited quotes); no concerns about coherence; minor concerns about relevance, the sample of one study contributing to this finding being limited to black minority ethnic group patients and the sample of the other study consisting of people that had been previously recruited in a RCT; moderate concerns about adequacy with relatively limited data from two studies illustrating the finding. Overall assessment of confidence was moderate due to minor concerns about methodological limitations, relevance and adequacy.

Review finding 17: Good health professional practice

ME/CFS specialist and non-specialist health care professionals that were nominated by patients as having been particularly helpful considered very careful history taking, listening carefully and patiently to presentation of symptoms, with appropriate investigation as vital elements of practice.

Explanation of quality assessment: minor concerns over methodological limitations in the contributing study (due to the role of the researcher not being discussed and concerns over data analysis with some themes supported by single quotes); no concerns about coherence; no concerns about relevance, the finding being reported by ME/CFS specialist and non-specialist HCPs; serious concerns about adequacy due to the finding being supported by limited information from one study. Overall assessment of quality was low due to concerns about methodological limitations and adequacy.

Review finding 18: Exposure to presentations of ME/CFS

Variability between ME/CFS patients as well as the limited cases from lower socio-economic or ethnic minority groups they encounter was emphasised by health care practitioners. Exposure to new presentations of ME/CFS was considered important for improving primary care practice. It enabled practitioners to recognise the condition and develop confidence in their diagnostic skills. Specialist practitioners develop awareness of the wide range of symptoms, whether physical or psychological that can be associated with the condition, and their significance through extensive exposure to ME/CFS.

Explanation of quality assessment: minor concerns over methodological limitations in the contributing study (due to the role of the researcher not being discussed and concerns over data analysis with some themes supported by single quotes); no concerns about coherence; no concerns about relevance, the finding being reported by ME/CFS specialist and non-specialist HCPs; serious concerns about adequacy due to the finding being supported by limited information from one study. Overall assessment of quality was low due to concerns about methodological limitations and adequacy.

1.4 Barriers and facilitators to the diagnosis of ME/CFS in young people

Six themes were identified from the two included studies in children and young people (see table 4).

Table 4: Review findings for children and young people

Main findings	Statement of finding
Lack of health professional knowledge and understanding[21, 94]	Mothers of adolescents with ME/CFS reported the lack of knowledge of both GPs and paediatricians about the condition, while a lack of an empirical understanding of the condition was acknowledged by health care professionals.
Nature of diagnosis[21, 94]	Mothers of adolescent patients reported how the non-specificity of symptoms and repeated tests conducted to rule out other illnesses complicated and delayed the diagnosis, while HCPs emphasised how the absence of a diagnostic test complicates the diagnosis.
Referral to specialist services[21]	Referral to specialist services gave adolescents with ME/CFS and their families access to a team of experts that enabled the diagnosis which had previously been uncertain.
Complicated journey to specialist service[21]	Mothers of adolescents with ME/CFS described a long journey to specialist services involving numerous tests and interactions with multiple professionals, that was complicated by co-morbid conditions and the time needed for the funding required to access services.
Co-morbidities[21]	Mothers of adolescents with ME/CFS reported that co-morbid conditions introduced complexity to the process of diagnosis or masked ME/CFS.
Inconsistencies between health-professionals[94]	There were differences in the conceptualisation of the illness and the terminology used between health-care professionals working with children and adolescents. The aetiological beliefs of HCPs were reported to influence the label HCPs chose to give to patients.

1.1.6 Narrative summary of review findings

Review finding 1CYP: Lack of health professional knowledge & understanding

Mothers of adolescents with ME/CFS felt they had to be proactive and persistent, using additional knowledge sources to bypass potential gatekeepers who acted as barriers because of lack of knowledge about the condition, potential treatment or availability of specialist services. This was felt to be the case for both GPs and paediatricians. Health care professionals working with children and young people acknowledged the lack of health professional understanding of ME/CFS compared to other health conditions and reported that its unknown aetiology, limited evidence and research contradictions contributed to the ambiguity surrounding it.

Explanation of quality assessment: minor concerns over methodological limitations in both contributing studies (due to the potential influence of the researcher not being discussed and concerns over data richness with findings mostly supported by single quotes in one study and due to concerns over recruitment skewing towards HCPs with positive attitudes towards ME/CFS in one study, as participants were recruited on the basis of how they informed and validate emerging theory); no concerns about coherence with mothers of patients focusing on professionals' lack of knowledge and professionals focusing on their lack of an empirically grounded understanding of the condition; minor concerns about relevance since the theme was reported mainly as a barrier to accessing ME/CFS specialist services in one of the studies but is inferred to inevitably impact the diagnosis which was also reported to be uncertain prior to accessing the specialist service; minor concerns about adequacy with the theme supported by two studies and issues with data richness in one study. Overall assessment of quality was moderate due to minor concerns about methodological limitations, relevance and adequacy.

Review finding 2CYP: Nature of diagnosis

Mothers of adolescent patients reported how various tests such as blood tests and brain scans were initially conducted to rule out different conditions, which required a lot of time. They also reported how symptoms such as extreme tiredness could be associated with various different illnesses. Health care professionals described that the absence of a definitive diagnostic test for ME/CFS causes uncertainty in appropriately identifying and labelling the condition making the diagnostic process challenging.

Explanation of quality assessment: minor concerns over methodological limitations in both contributing studies (due to the potential influence of the researcher on the findings not being discussed and concerns over data richness with findings mostly supported by single quotes in one study and due to concerns over recruitment skewing towards HCPs with positive attitudes towards ME/CFS in one study, as participants were recruited on the basis of how they informed and validate emerging theory), no concerns about coherence; minor concerns about relevance, the findings from one study being reported mainly as factors delaying referral to specialist services and inferred to delay diagnosis; minor concerns about adequacy with the theme supported by two studies and issues with data richness in one study. Overall assessment of quality was moderate due to minor concerns about methodological limitations, relevance and adequacy.

Review finding 3CYP: Referral to specialist service

Mothers of adolescents with ME/CFS reported that referral to the specialist service gave families access to an informative team of experts, for some a formal diagnosis and for all, a tailored, patient-centred specialist medical intervention that had not been available earlier. Before accessing the specialist service the diagnosis was reported to be uncertain or to be given with a lack of conviction.

Explanation of quality assessment: minor concerns over methodological limitations in the contributing study (due to the potential influence of the researcher on the findings not being discussed and concerns over data richness with findings mostly supported by single quotes); no concerns about coherence; no concerns about relevance; minor concerns about adequacy due to the finding emerging from one study. Overall assessment of quality was moderate due to minor concerns about methodological limitations and adequacy.

Review finding 4CYP: Complicated journey to specialist services

Most mothers described a long and difficult journey to specialist services that involved numerous interactions with healthcare professionals at various locations, and long periods of waiting that were often a result of the diagnostic procedures involved requiring numerous tests to rule out other medical conditions. The journey as reported by the mothers was further complicated by the waiting time associated with the approval for the funding needed to

access the services, as well as by co-morbid conditions masking ME/CFS and introducing complexity to the process of diagnosis.

Explanation of quality assessment: minor concerns over methodological limitations in the contributing study (due to the potential influence of the researcher on the findings not being discussed and concerns over data richness with findings mostly supported by single quotes); no concerns about coherence; minor concerns about relevance related to the applicability of the evidence to the phenomenon of interest, with most factors cited to complicate access to specialist services being extrapolated as barriers to diagnosis since the diagnosis was reported to result from referral to specialist services and to be uncertain prior to that; minor concerns about adequacy with the reported finding being supported by a limited number of quotes. Overall assessment of quality was moderate due to minor concerns over methodological limitations, relevance and adequacy.

Review finding 5CYP: Co-morbidities

Mothers of adolescents with ME/CFS reported that co-morbid conditions introduced complexity to the process of diagnosis or masked ME/CFS and suggested that other conditions, such as behavioural issues or depression, had developed because of prolonged illness with ME/CFS.

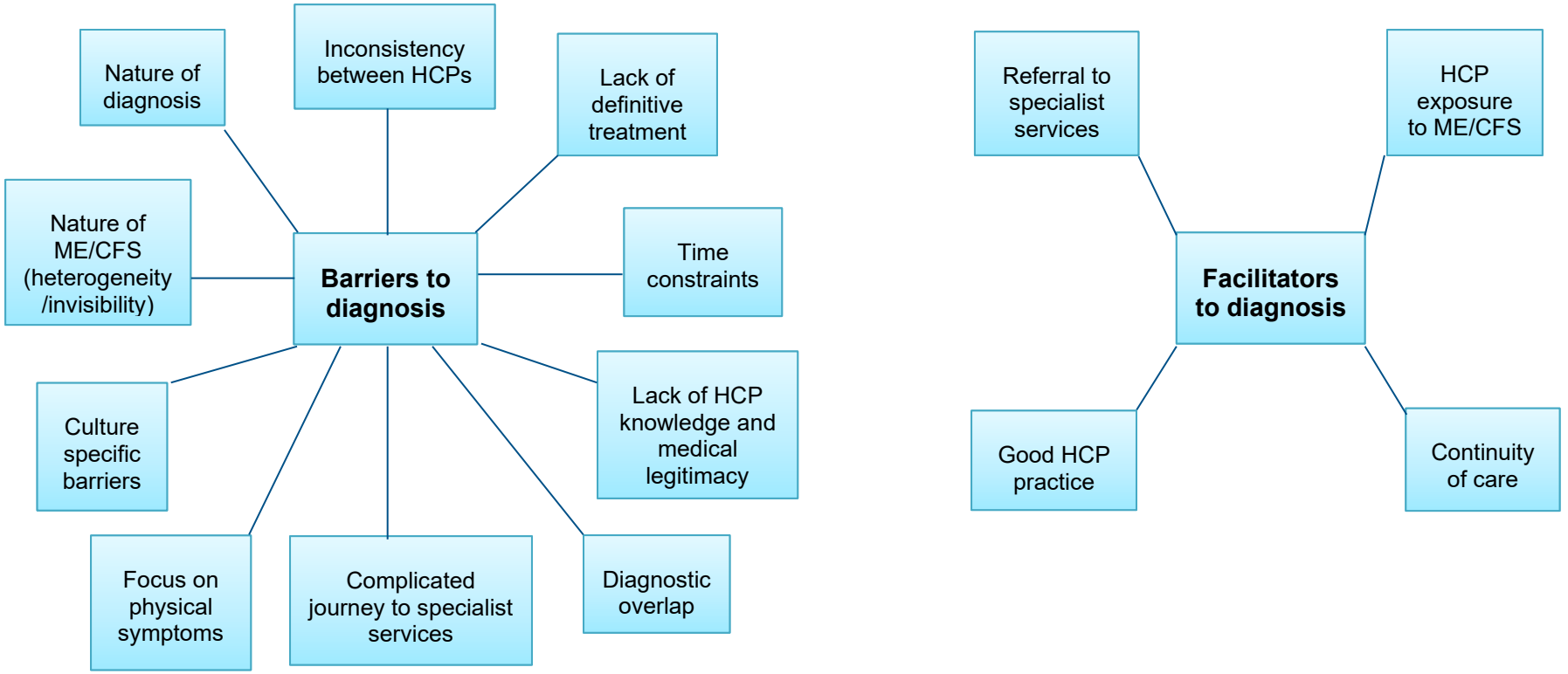
Explanation of quality assessment: minor concerns over methodological limitations in the contributing study; no concerns about coherence; no concerns about relevance with nothing to lower the confidence rating over the relevance of the sample or the emerging finding to the population of the current review; serious concerns about adequacy, the finding being supported by very limited information from one study. Overall assessment of quality was low due to the concerns about methodological limitations and adequacy.

Review finding 6CYP: Inconsistencies between health professionals

Among health-care professionals, there was inconsistency in the use of the terms 'Chronic fatigue' and 'CFS'. For some these were synonymous, but others felt the latter conveyed increased symptom severity or that terms differentiated between fatigue rooted in psychological factors and fatigue stemming from psychosocial issues. Young people presenting to the services with medically unexplained fatigue could receive one of a range of labels, including ‘CFS/ME’, CFS, Chronic fatigue, Chronic Pain and MUPS; difficulties could also be conceptualised and labelled as depression and anxiety. Within the context of working with uncertainty participants described 'finding a label that fits' with how they conceptualised the young person's difficulties. Aetiological beliefs also appeared to vary between HCPs. While all recognised the contribution of physiological and psychological factors, differences appeared in the emphasis given to these. Some HCPs described feeling more comfortable giving a diagnosis of medically unexplained physical symptoms (MUPS) rather than ‘CFS/ME’, because of not being able to provide a clear aetiology.

Explanation of quality assessment: minor concerns over methodological limitations in the contributing study (due to concerns over participant recruitment skewing towards HCPs with positive attitudes towards ME/CFS in one study, as participants were recruited on the basis of how they informed and validated emerging theory); no concerns about coherence; no concerns about relevance the finding emerging from NHS health professionals working with children and young people; minor concerns about adequacy due to the finding supported by one study but with a wealth of information. Overall assessment of quality was moderate due to minor concerns about methodological limitations and adequacy.

Figure 1: Theme map of review findings



Source/Note: No additional (different) themes were identified in children/young people.

Source/Note: Some themes may be classified as a barrier or a facilitator to diagnosis depending on presence/absence, e.g. HCP exposure to ME/CFS would be a facilitator, whereas lack of exposure would be a barrier.

1.1.7 Economic evidence

The committee agreed that health economic studies would not be relevant to this review question, and so were not sought.

2 Barriers and facilitators to the care of people with ME/CFS

2.1 Summary of the protocol

For full details see the review protocol in Appendix A.

Table 3: Characteristics of review question

Objective	To identify the barriers and facilitators to the care of people with ME/CFS
Population and setting	• Adults, children and young people who are diagnosed with ME/CFS, or who are suspected of having ME/CFS by their primary clinician and their families/carers. • Health and social care professionals caring for people with ME/CFS, or people suspected to have ME/CFS.
Context	Any barriers and facilitators to care described by people with or suspected to have ME/CFS, and by health and social care professionals caring for people with ME/CFS.
Review strategy	Thematic synthesis of qualitative research. Results presented in narrative and table format. Quality of the evidence will be assessed by a GRADE CerQual approach for each review finding.

2.2 Methods and process

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

Declarations of interest were recorded according to NICE's conflicts of interest policy.

2.3 Qualitative evidence

2.3.1 Included studies

Twenty-six qualitative studies were included in the review; [8, 17, 18, 21, 26, 29, 34-37, 43-45, 48, 49, 65, 66, 76, 89, 94, 109, 112, 149, 151, 155-157, 159] these correspond to twenty-eight papers and are summarised in Table 4 below. Key findings from these studies are summarised in the clinical evidence summary below (Table 5). See also the study selection flow chart in Appendix C, study evidence tables in Appendix D, and excluded studies lists in Appendix F.

There were seven studies that were relevant to children and young people, three of which included health-care professionals working with children or adolescents with ME/CFS and three of which included the parents of children and young people with ME/CFS. One study included the perspectives of children, parents, teachers and health-care professionals.

As a large number of papers were identified for this review, inclusion was halted once data saturation was reached. Data saturation is the point at which no new themes emerged from studies, or data contributing to themes emerged from studies that were found to match the review protocol.

2.3.2 Excluded studies

See excluded studies list in Appendix F.

2.4 Summary of studies included in the qualitative evidence

Table 4: Summary of studies included in the evidence review

Study	Design	Population	Research aim	Comments
Arrol 2008[8]	Semi-structured interviews and Interpretative Phenomenological Analysis (IPA)	Patients with ME/CFS (n=10); mean age (SD): 55.5 (9.4) UK Stratum: adults/mixed population	To investigate the process by which individuals conceptualise their bodily signs and sensations as consistent with the label ME/CFS	
Bayliss 2014[18, 44]	Face-to-face semi-structured interviews and open-explorative thematic coding in line with modified grounded theory. And Secondary analysis of semi-structured interviews using a new analytic framework.	Key stakeholders in NW England: black-minority ethnic group (BME) patients with 'CFS/ME' (n=11, mean age 45.6; SD: 14.05), carers (n=2), BME community leaders (n=5), GPs qualified for 6 to 24 years (n=9), practice nurses (n=5) and 'CFS/ME' specialists (n=4). UK Stratum: adults/mixed population	Primary analysis: To explore the possible reasons for the lower levels of diagnosis of 'CFS/ME' in the BME population and the implications for management. Secondary analysis: To explore making the diagnosis and managing 'CFS/ME' in the UK form the perspectives of patients, carers, community leaders and primary care practitioners, to understand why 'CFS/ME' may not be commonly diagnosed is South Asia (SA)	The secondary analysis did not include interviews with practice nurses (n=5) The secondary researcher was naïve to original research findings. Primary analysis reports on the patients' illness severity: mild/moderate n=9; moderate/severe n=1; severe n=1.
Bayliss 2016[17]	Semi-structured interviews and thematic analysis followed by theory-driven analysis.	Patients (n=11), mean age (range): 46 (27 to 71) years; GPs (n=8) Patients were recruited from participating GP practices where GPs had been given access to an online	To explore the extent to which 'CFS/ME' training and resources can be implemented in routine primary care, leading to a better understanding of the barriers and facilitators to the adoption and	Not all interviewed GPs had fully engaged in the training or research: 6/8 GPs interviewed had participated in the training, although not all had completed the online test and downloaded their completion certificate.

Study	Design	Population	Research aim	Comments
		'CFS/ME' training module; that involved patient resource packs for use in consultation with new and existing CFS/ME patients. UK Stratum: adults/mixed population	integration of new practices associated with medically unexplained conditions.	ME/CFS diagnosis: Searches of GP practice databases were conducted by the research team to identify individuals with an existing diagnosis of CFS/ME. GPs were asked to review these lists and to exclude patients with other conditions, or other factors that may account for their fatigue.
Beasant 2014[21]	In-depth semi-structured face-to-face interviews and thematic analysis.	Mothers (n=13) and adolescents (n=12) diagnosed with 'CFS/ME' by paediatric 'CFS/ME' specialist service (aged 12-18 years, mean age: 13.9 SD 1.6), mildly or moderately affected by 'CFS/ME', participating in the SMILE study UK Stratum: children and young people	To understand the experiences of adolescents and families in accessing and using a specialist service and explore whether or not they value referral to a specialist service for young people with 'CFS/ME'.	Specialist Medical Intervention and Lightning Evaluation (SMILE) study designed to test the feasibility and acceptability of recruiting adolescents to a randomised controlled trial (RCT) comparing specialist medical care with specialist medical care and the Lightning Process.
Brigden 2020[26]	Semi-structured interviews and thematic and comparative analysis	Families (n=22: 14 parents, 8 children; mean age 8.5, range 5-11 years), teachers (n=11; 7 class teachers, 3 head of year/lead teachers, 1 Specialist Educational Needs Coordinator (SENCO), 1 deputy head, 1 intervention officer (safeguarding and pastoral care)) and healthcare	To examine the extent to which the care of children (aged 5-11 years) with 'CFS/ME' is integrated across settings (home, education and health settings),in order to understand barriers and generate recommendations for integrating care.	Participants were sampled from two studies taking place at a large specialist Paediatric 'CFS/ME' service: EXPLORER (a mixed-methods study investigating the epidemiology and qualitative experiences of 'CFS/ME' in younger children) and MAGENTA (an RCT evaluating two behavioural treatments for paediatric 'CFS/ME'.

Study	Design	Population	Research aim	Comments
		providers (n=9; 5 psychologists, 2 doctors, 2 physiotherapists) UK Stratum: children and young people		
Broughton 2017[29]	Semi-structured interviews (six face-to-face, 10 via telephone) and thematic analysis. Cross-sectional design using opportunity sampling.	Adults (n=16) concluding treatment at one of three outpatient NHS specialist 'CFS/ME' services (median age 43, range 24-62 years; median self-reported illness duration 7.5 years, range 1-17). UK Stratum: adults/mixed population	To explore the experiences of 'CFS/ME' patients who were completing programmes of treatment at three NHS specialist 'CFS/ME' services in England.	NHS specialist 'CFS/ME' services followed NICE guidelines for diagnosis and management of 'CFS/ME', offering patient centred programmes aiming to increase patients' physical, emotional and cognitive capabilities whilst managing the impact of symptoms. CBT and GET are the two main evidence-based therapies which (or components of which) are used in conjunction with techniques aimed at managing activity, sleep hygiene and relaxation. Patients also receive practical support around employment and the benefits system. Services shared a philosophy of rehabilitation aimed at 'recovery' or 'significant improvement', whilst acknowledging that this would not be attained by all patients.
Cheshire 2020[34]	Semi structured interviews with thematic analysis	Adults (n=19); mean age (range): 40.89 (21-66) years. UK	To explore patient experiences of Guided Graded Exercise Self-help (GES) delivered as part of a randomised controlled trial	Severely affected patients were not included in the trial

Study	Design	Population	Research aim	Comments
		Stratum: adults/mixed population	(GETSET) for people with ME/CFS to answer the research question: 'What are the differences and similarities in treatment perceptions and experiences of GES among 'CFS/ME' participants reporting an improvement compared with those reporting a deterioration in their condition?'	
Chew-Graham 2008[37]	Semi-structured interviews and thematic analysis	Family physicians (n=14; mean age: 48, SD: 12 years) and patients (n=24; mean age: 48, SD: 12 years) participating in a RCT of 2 nurse-led interventions in primary care (FINE trial) UK Stratum: adults/mixed population	To explore how patients with 'CFS/ME' and family physicians conceptualise this condition and understand it and how their understanding might affect the primary care consultation.	FINE trial was a primary-care-based RCT examining self-help treatment and pragmatic rehabilitation for patients with ME/CFS. To be included in the trial, registered patients with 'CFS/ME' referred by physicians in 44 primary care trusts in North West England, had to fulfil the Oxford inclusion criteria for 'CFS/ME', score 70% or less on the SF-36 physical functioning scale and 4 or more on the 11-item Chalder fatigue scale. In line with the review protocol, themes emerging from the information provided by the patient population have only been extracted.
Chew-Graham 2010[36]	Semi-structured interviews and thematic analysis.	GPs working in practices participating in the FINE trial (n=22).	To explore GPs' beliefs about the value of the label of 'CFS/ME',	FINE trial was a primary-care RCT examining self-help treatment and

Study	Design	Population	Research aim	Comments
		UK Stratum: adults/mixed population	implications of the diagnosis and attitudes towards patients suffering with this condition.	pragmatic rehabilitation for patients with ME/CFS.
Chew-Graham 2011[35]	Semi-structured interviews and thematic analysis	Patients receiving pragmatic rehabilitation (n=19); recruited via a RCT of two nurse led interventions for 'CFS/ME' in primary care (FINE trial) UK Stratum: adults/mixed population	To establish what factors are important for patients to engage in a new intervention for 'CFS/ME' and make recommendations to general practitioners GPs on preparing a patient for referral/ the referral process to such a service.	Registered patients with 'CFS/ME' referred by GPs from 44 primary care trusts in the North West of England, also fulfilling the Oxford criteria.
De Carvalho Leite 2011[43]	Focus groups (n=6) and semi-structured interviews (n=35) and (data-led) thematic analysis.	Adults with 'CFS/ME' (n=35), purposively selected to include a diverse range of illness severity, duration, social variation (age, gender, ethnic background and socio-economic conditions) and year of diagnosis. UK Stratum: adults/mixed population	To investigate the impact of CFS/ME on people from varied social background, including those from ethnic minorities, and what challenges may be posed to health care practitioners in providing appropriate and equitable care for this condition.	Six of the 35 participants were purposively selected to include a diverse range of illness severity, for both an initial focus group discussion and a later one-to-one interview. The study was part of the National Observatory of people with 'CFS/ME' in England, which aims to produce and to facilitate epidemiological and social research, in response to the needs of these people so as to fill a major gap in the evidence of the occurrence and the impact of this disease.
Devendorf 2018[48]	Mixed-methods design; qualitative analysis of participants' open-ended survey	Patients who self-identify as having ME/CFS and endorsed suicidal ideation (SI) but	To investigate factors, other than depression that explain suicidal ideation, including	The study was hosted online using Research Electronic Data Capture.

Study	Design	Population	Research aim	Comments
	responses from a previous project that examined illness severity, stigma, physician interactions and depression.	did not meet depression criteria (N=29); mean age: 51.48 years; Mean BDI-PC score (range): 2.38 (1-3); one participant endorsed active SI (i.e. score of 3, 'I would kill myself if I had the chance'), 28 participants endorsed passive SI (i.e. score of 1, 'I have thoughts of killing myself, but I would not carry them out'). USA Stratum: adults/mixed population	quality of life, loss of functioning, isolation, and hopelessness about prognosis.	
Dennison 2010[45]	Semi structured interviews with thematic analysis	Young people (n=16), mean age (range): 19.9 (16-24; 13-18 at the time of starting therapy) years. The parents of parents of young people (n=16). UK Stratum: children and young people	To explore in detail adolescent patients' and their parents' experience of both family-focused CBT and psychoeducation for CFS. The study aimed to elicit participants' experiences in their own terms in order to better understand participants' expectations, therapy experiences and views regarding the effectiveness of their treatment.	Participants had participated in a randomised controlled trial comparing family focused CBT with psychoeducation. Mixed sample consisting of people involved in CBT or psychoeducation.
Donalek 2009[49]	Semi-structured interviews and thematic analysis	Family members (n=21) of adults with 'CFS' from eight families USA	To describe the impact of a chronic illness (i.e. CFS) on the ill parent and to embed the experience of the	Families in which one biological parent or parent figure (stepparent or parental partner) had been diagnosed with 'CFS' by a

Study	Design	Population	Research aim	Comments
		Stratum: adults/mixed population	ill parent within the wider family system responses to this chronic parental illness.	healthcare professional and met the Fukuda et al (1994) criteria were recruited.
Hannon 2012[66]	Semi-structured interviews and grounded theory approach.	Health practitioners (GPs n=9, practice nurses n=5, 'CFS/ME' specialists n=4), Carers (n=10), patients (n=16), aged 28-71 UK Stratum: adults/mixed population	To develop an education and training intervention to support practitioners in making an early diagnosis of 'CFS/ME' and supporting patients in the management of their symptoms.	
Haig-Ferguson 2019[65]	Semi-structured interviews (young people and parents) and one focus-group (health-care professionals) and thematic analysis.	Young people (n=12), aged 9-18 years, who were actively attending video-conferencing (n=6), had been previously attending video-conferencing (n=3) or had declined video-conferencing (n=3). Mothers of children with ME/CFS (n=6). Health-care professionals from a specialist paediatric 'CFS/ME' service. UK Stratum: children and young people	To explore the views of children and young people, their parents, and healthcare professionals of treatment delivered by videoconferencing in a specialist paediatric 'CFS/ME' team	Eligible young people were receiving treatment of any sort within the specialist 'CFS/ME 'team.
Horton 2010[76]	Semi-structured interviews and thematic analysis.	Specialist (n=3) and non-specialist (n=3) health care practitioners working with people with ME/CFS,	To describe from the perspective of health care practitioners (HCPs) judged by people with	Participants were nominated by people with 'CFS/ME' who had taken part in an associated England-wide study of their

Study	Design	Population	Research aim	Comments
		nominated by 'CFS/ME' patients as having provided them with particularly helpful or effective care. UK Stratum: adults/mixed population	ME/CFS as having been particularly helpful and effective, practices that: enable participants to establish the legitimacy of their condition; impact positively on the process of diagnosis and care; and enable patients to overcome experiences of social isolation and other negative effects.	support needs (Social inequalities in the impact of living with 'CFS/ME': 'CFS/ME' Observatory project), based on their perceptions of the quality of care they had received.
Lin 2009[89]	Health-care utilisation questionnaires with responses recorded as open-ended text, analysed qualitatively with SPSS text analysis.	Random population sample (n=780, 112 with CFS) USA Stratum: adults/mixed population	To investigate the prevalence of barriers to healthcare utilisation in persons with fatiguing illness	Data derived from a cross-sectional population-based study of CFS and chronic unwellness in Georgia, investigating the prevalence of CFS. CFS diagnosed as specified in the 1994 international research case definition using validated instruments as specified in the 1994 international research case definition (Fukuda 1994).
Marks 2016[94]	Semi-structured interviews and grounded theory analysis	Health-care professionals working with children and adolescents (n=10) from two NHS organisations in the UK. UK Stratum: children and young people	To explore HCPs experiences of working with children and adolescents with 'CFS/ME' so as to develop an understanding of the process relating to how they understand the condition	HCPs were paediatricians, physiotherapists and clinical psychologists working with children and adolescents; 5 were ME/CFS specialists
Parslow 2017[109]	Focus groups and semi-structured	Health professionals working in a	To explore the views of health professionals who	

Study	Design	Population	Research aim	Comments
	interviews with thematic analysis	multidisciplinary team of NHS ME/CFS paediatric specialist services Stratum: children and young people	work in specialist paediatric 'CFS/ME' services in England and have regular contact with children with 'CFS/ME' and identify outcomes that are clinically important.	
Picariello 2017[112]	Semi-structured interviews with thematic analysis	Adults (n=13); age range 18-46, majority being between 25-34 years. UK Stratum: adults/mixed population	To explore the experiences of patients with CFS who undertook CBT at a specialist service for CFS.	Participants had completed CBT or were in the follow-up stage.
van der Vaart[149]	Semi-structured interviews with thematic analysis	Therapists (n=14), mean age (SD): 41.9 (9) and team managers (n=4), mean age (SD): 51.8 (11.2) from mental health clinics. Netherlands Stratum: adults/mixed population	To identify factors experienced by mental health care practitioners and managers influencing the implementation process of Internet-based cognitive behavioural therapy (ICBT) for chronic pain and CFS in mental health care	Study evaluates the implementation of two specific ICBT programs, one for chronic pain ('Master you Pain') and one for chronic fatigue syndrome ('Master your Fatigue'), implemented in various mental health care clinics in the Netherlands. Programs are translated from evidence-based regular CBT protocols specific for these conditions.
Ward 2008[151]	Unstructured interviews with thematic analysis	Adults (n=25) who had received a formal diagnosis of ME from a medical practitioner and who had experienced any type of counselling intervention; mean age (SD, range): 44 (11, 23-65) years UK	To explore users' views and perceptions of their experiences of counselling, in particular what they found useful and what they found unhelpful or negative	Participants had been recruited through advertisements in the newsletters of the ME Association and the Action for ME user group

Study	Design	Population	Research aim	Comments
		Stratum: adults/mixed population		
Webb 2011[155]	Mixed methods study involving semi-structured interviews with thematic analysis	Parents of children with 'CFS/ME' (n=9; mean age (SD): 11.9 (4.3) Illness severity: mild/moderate (n=4) or severe (n=3) UK Stratum: children and young people	Study aim: To examine factors associated with time taken to access specialist services and explore the issues experience by parents prior to assessment in a specialist service. Interview aim: To explore the barriers to accessing healthcare experienced by parents of children with CFS/ME.	Parents had children under 16 years with a confirmed diagnosis of 'CFS/ME', attending assessment or follow-up at the Bath Specialist paediatric 'CFS/ME' service.
Whitehead 2006[156, 157]	Longitudinal qualitative study involving up to three in-depth interviews and analysis using narrative topologies	People aged 13 to 63 years (n=17) UK Stratum: mixed population of children and young people and adults	Study 1: To explore how people with 'CFS/ME' describe and interpret their illness experience. Study 2: To further illuminate the reconstruction of identity in 'CFS/ME' with an emphasis on the experiences that facilitate this and to explore a possible trajectory.	
Williams 2016[159]	Semi-structured interviews with thematic analysis.	Adults with ME/CFS who are physically dependent on others for help in daily life (n=10); mean age (range): 45.5 (25-60) years. UK	To explore the impact of physical dependency on well-being for adults with ME/CFS.	

Study	Design	Population	Research aim	Comments
		Stratum: adults/mixed population		

See Appendix D for full evidence tables.

2.5 Summary of the qualitative evidence

Eighteen themes were identified from the nineteen included studies in adults (see table 5).

Table 5: Review findings: Adults (severity: mixed/ unclear)

Main findings	Statement of finding
Lack of health professional knowledge and medical legitimacy[8, 18, 29, 35, 37, 43, 48, 49, 66, 76, 112, 156, 157]	The general lack of health professional knowledge, disbelief and unsupportive attitudes patients encountered constitute a barrier to care, leading to diagnostic delay, limited, incorrect or no management advice, can hinder access to specialist services and treatments and lead patients to disengage from health services.
Lack of diagnosis[8, 43, 76, 112, 156, 157]	The negative implications of a lack of a ME/CFS diagnosis on patients' access to appropriate treatment and support, their relationship with health care providers, improvement and 'recovery' were acknowledged by both patients and health-care professionals.
Referral to specialist services [17, 29, 36, 66, 76, 89, 156, 157]	Specialist services can benefit patients in terms of diagnosis, advice and symptom management but the genera lack of or delayed referral due to a lack of medical knowledge, fragmented healthcare services or the lengthy diagnostic procedures associated with ME/CFS presents a barrier to care, often leading to self-diagnosis and the use of alternative or complementary therapies.
Time constraints in primary care [17, 43, 66, 76]	Time limited consultations in the health-care system present a barrier to the provision of appropriate care, impeding health professionals' understanding of patients' symptoms and preventing patients from benefiting from consultations, often leading them to seek support outside the NHS.
The nature of ME/CFS[8, 36, 159]	The nature of ME/CFS in terms of its uncertain aetiology, its complicated diagnostic process, its non-specific symptoms and the absence of cure made the role of health professionals in managing patients difficult, while the invisibility of the illness often meant patients' need for help remained unrecognised and made them reluctant to ask for help
Lack of cure and clear management pathway[36, 66]	Lack of cure and clear management pathway for ME/CFS caused health-professionals' reluctance to make a diagnosis and impeded their management of patients
Accessibility of treatment options in primary care [8, 43, 76]	Patients lack access to helpful treatment options for managing ME/CFS due to the unavailability of those in primary care or due to their strict acceptance criteria often involved.

Main findings	Statement of finding
Unworkable treatment models [35]	Patients may experience difficulty implementing certain treatment models into their life.
Realistic goal setting [29]	Realistic goal setting towards management rather than cure was seen as vital for treatment success.
Patients' acceptance of ME/CFS [29, 35, 76, 112]	The importance of acceptance of the diagnosis of ME/CFS and its implications for one's life, although challenging, was reported to be crucial in engaging with treatment and health services and obtaining the most benefit from them by both patients and ME/CFS specialists.
Patient's personal circumstances & availability[29, 34, 112]	Attending medical appointments and benefiting from treatment can depend on being able to invest time and effort in the treatment which is influenced by patients' personal circumstances at the time including their work commitments and symptom severity.
Symptom or illness severity[29, 76, 149, 151, 159]	Symptom and illness severity can influence patients' ability to articulate their problems and ask for help, their physical capacity to attend medical appointments or keep up with the length of intervention sessions and can limit the extent to which health professionals can provide helpful suggestions; while the experience of co-morbidities and symptoms including cognitive difficulties may limit the effectiveness of interventions for some patients.
Practical accessibility of care[29, 48, 89]	The geographical location of healthcare providers, transportation links as well as the availability of appointments can implicate patients' ability to attend health care services and have access to healthcare.
Flexibility in medical appointments[29, 66, 76]	Flexibility in the frequency and mode of medical appointments can help overcome barriers of practical accessibility and symptom severity that implicate treatment attendance.
Relationship with health-care professionals[17, 18, 37, 112]	Absence of an established and on-going relationship with a health care professional (GP, family physician or therapist delivering care) influenced the management of patients, implicating their ability to demonstrate their symptoms, communicate their experiences and their engagement to primary care.
Patients' beliefs & attitudes towards ME/CFS and treatment[18, 34, 35, 89, 112, 149]	Pre-existing beliefs about the illness and the treatment offered can influence patients' decision to seek medical advice for their symptoms and treatment acceptance or engagement.
Personal attributes & motivation[29, 34, 37, 112]	Patient attributes such as being proactive, determined and positive can facilitate treatment access and their motivation to engage in and benefit from treatment even in the face of challenges.
Individual characteristics of the therapist[149]	Individual characteristic of the therapists such as their attitude towards treatment, the ability to flexibly tailor the intervention to the needs of the individual and to effectively communicate with them were seen as important factors influencing the implementation of interventions.

See Appendix E for full GRADE-CERQual tables.

2.5.1 Narrative summary of review findings for adults (severity mixed or unclear)

Review finding 1: Lack of health professional knowledge and medical legitimacy

Although some patients reported having positive experiences with their GPs who had been very supportive and had played a key role in the care they received, the majority of patients reported encountering disdain, disbelief and a lack of knowledge from their healthcare providers. Health professionals were reported to often have given incorrect advice recommending exercise or prescribing antidepressants or to have given very limited or no advice at all on symptom management or support. Patients reiterated experiences of not being listened to or not being taken seriously by practitioners who often dismissed their symptoms attributing them to a virus or a common cold. Some patients reported to encounter unsupportive attitudes by health-care professionals even when bedbound which greatly undermined their chances of wider belief and support.

Many GPs attributed their uncertainty and unwillingness to make a diagnosis to their lack of knowledge about the condition and its management. GPs, practice nurses and family physicians reflected on their limited clinical understanding of ME/CFS and their lack of awareness of its evidence base. They questioned its legitimacy and attributed symptoms to psychological problems or secondary gains (motivators patients may have to use their illness or exaggerate symptoms to gain an advantage of some sort, such as attention from others or financial benefit; these may be unconscious). Those who did recognise ME/CFS as a legitimate illness were aware that some of their colleagues fail to identify this condition.

Specialists also recognised this knowledge gap reporting that most GPs' lack an understanding of ME/CFS, view it as a psychological rather than physical condition, with even whole practices having decided it does not exist and highlighted a need for training in primary care.

Problematic encounters with health professionals both delayed and reduced patients' access to support including their ability to obtain work modifications or unemployment compensations and profoundly impacted their life. The dismissive attitudes and general lack of medical legitimacy were reported to alienate patients from treatment, to cause self-doubt and often presented a barrier to accessing specialist services. Patients often felt they needed to take a proactive role in their care by doing their own research to persuade health-professionals to meet their needs, by asking for diagnostic tests, seeking treatment elsewhere, turning to private or alternative health services, and in some cases withdrawing from services and managing symptoms themselves.

Explanation of quality assessment: minor concerns regarding methodological limitations due to minor concerns in the majority of the contributing studies (due to the role of the researcher not being explored in 7 studies, one study being a follow-up of a previous study involving open-ended questionnaire responses implicating our ability to assess risk of bias in the data collection method, potential selection bias due to the recruitment strategy of one study with only patients who had completed treatment being selected and 2/8 interviews being discarded in one study, issues with data richness in two studies); very minor concerns about coherence associated with only one study in which some participants reported positive experiences with healthcare professionals; very minor concerns over relevance associated with two of the contributing studies (due to patients in one study being self-identified as having ME/CFS and GPs in another study largely caring for black-minority ethnic group people); no concerns over adequacy with a wealth of information from 12 studies supporting the theme. Overall judgment of confidence was high due to the wealth of information supporting the finding and the considerations over methodological limitations, coherence and relevance being too minor to lower the confidence rating.

Review finding 2: Lack of diagnosis

Achieving a diagnosis was seen as a crucial milestone for patients as this led to advice from doctors and other health care professionals with particular knowledge of ME/CFS. However, patients most often encountered resistance and a reluctance to diagnose ME/CFS. As a result, patients had to consult multiple GPs to be referred to a specialist who provided them with a diagnosis or they decided to use a private or alternative health services as a way of getting a diagnosis or help. This route often resulted in stress, uncertainty and financial pressures.

This prolonged period between initial symptom occurrence, the search for a diagnosis and then treatment was a lengthy ordeal with numerous unfruitful meetings which often led to difficult relationships between participants and their care providers. It was also reported that until a diagnosis was gained, social services could not assess patients' needs in order for them to gain access to social care support.

Disagreements over diagnoses and over-attention to psychological symptoms could lead to inappropriate treatments and these were reported to contribute to deterioration in emotional well-being. The lengthy process of diagnosis was particularly reported to act as a barrier to CBT uptake by some patients.

The negative impact of a lack of a diagnosis, a delayed diagnosis or a misdiagnosis were acknowledged by health-care professionals. They saw the lack of a diagnostic test giving conclusive proof of the condition as impacting on practitioners and patients alike. The negative consequences of a delayed diagnosis on improvement and recovery were considered significant, acknowledging this left patients in a state of uncertainty.

Explanation of quality assessment: Minor concerns regarding methodological limitations with moderate limitations in one study (due to the role of the researcher not being explored and potential selection bias as only participants who had completed treatment were selected), no limitations identified to lower the confidence rating in one study, very minor limitations in one study (due to the role of the researcher not being explored) and minor limitations in two studies (due to the role of the researcher not being explored in both studies, potential selection bias with 2/8 interviews being discarded in one study and data richness with some data supported by single quotes in one study); no concerns about coherence; very minor concerns about relevance linked with only one study (due to the population not being limited to the adult age stratum); no concerns over adequacy with sufficient information across studies supporting the theme. Overall judgment of confidence was moderate due to the minor concerns over methodological limitations and relevance.

Review finding 3: Referral to specialist services

Most GPs highlighted the complexity of the condition and believed that it would be more appropriate for 'CFS/ME' to be managed by a specialist service. Patients wanted more access to specialist services recognising that GPs didn't have time to manage their condition. Those who had accessed specialist services felt they had benefited with diagnosis being confirmed and better management of their symptoms.

Referral to the specialist service was reported by patients to have been a lengthy process, mainly because of the diagnostic processes to rule out other medical conditions, this involved numerous medical tests and appointments with multiple clinicians. It was also suggested that improved communication between primary care and the specialist service may enable the GP to manage the patient's symptoms better during the long waiting-time to getting a diagnosis from specialist services. The lack of a referral system and access to specialist care meant that some patients self-diagnosed their symptoms or illness. Their symptoms were interpreted as the consequences of a lack of exercise, being overweight, aging or depression. Patients reported often using over-the-counter medications for pain or alternative/complementary therapies, including diets.

Health professionals also described difficulties with referral to secondary care due to fragmented services and a lack of collaboration. A number of GPs and practice nurses were unaware of specialist ME/CFS services. Specialist HCPs identified a minority group of GPs in their region who made referrals to their service and reported that many GPs never made referrals to a specialist service due to their lack of belief in ME/CFS as a medical condition. The specialists acknowledged how much pressure some people had to exert just to get a referral to their service and emphasised that there is a need for specialist services to be more visible and to provide education for other HCPs.

Specialists had both experience and expertise to be able to support GPs and other HCPs in reaching or confirming a diagnosis, giving advice on appropriate medication, or providing services such as specialist Occupational Therapy. GPs reported experiences of limited availability of specialist centres to support them in either making a diagnosis or managing the patient's symptoms. Limited referral options to secondary care were seen by GPs as a barrier to successfully working with patients to manage 'CFS/ME'.

Explanation of quality assessment: moderate concerns regarding methodological limitations due to serious concerns over one study (due to risk of selection bias as the sample was originally recruited for a different study and selection criteria were unclear, the role of the researcher not being explored, lack of transparency in data analysis not allowing us to assess data richness and whether findings are well grounded in the data) and minor concerns in two studies (due to the role of the researcher not being explored and data richness with some data supported by single quotes) but no or very minor concerns in the majority of studies: very minor in one study (due to the role of the researcher not being explored) and no concerns to lower confidence over three studies; no concerns about coherence; very minor concerns about relevance associated with two studies (due to the population of one study not being limited to the adult age stratum and the sample of one study consisting of people previously recruited in a RCT); no concerns over adequacy with sufficient information across studies supporting the theme. Overall judgment of confidence was low due to the moderate methodological limitations lowering the confidence rating and very minor concerns over relevance associated with two studies.

Review finding 4: Time constraints in primary care

Patients highlighted the limited time for consultation as a barrier to appropriate care provision and another reason for seeking support outside the NHS. Health professionals recognised that a 10-minute consultation can be challenging due to the variety and complexity of ME/CFS symptoms. Within the limited consultation time, patients reported feeling unable to explain the complexity of their condition to their GP. Without the opportunity to relay fully this information, patients struggled to work with their GP to manage their symptoms. Specialists reported that in the limited time available GPs may not be able to gain a complete understanding of the variety of symptoms patients can experience and the impact of those on their life.

Health professionals also emphasised the importance of having the time to listen and the therapeutic value of patient feeling heard but the time limits for consultations prevented this and patients from recounting their full story.

Explanation of quality assessment: minor concerns regarding methodological limitations due to very minor concerns in two studies (due to the role of the researcher not being discussed) and minor concerns in two studies (due to lack of exploration of the role of the researcher on the findings and some data supported by single quotes); no concerns about coherence; no concerns about relevance; minor concerns about adequacy with limited information to support the theme in two studies but sufficient information in the remaining two studies. Overall judgment of confidence was moderate due to minor concerns over both methodological limitations and adequacy.

Review finding 5: The nature of ME/CFS

The nature of the illness can lead patients to believe their symptoms are associated with relatively innocuous and brief pathologies or to attempt to rationalise them as general complaints caused by stress. It is the persistence of symptoms that directed patients towards the evaluative process. The uncertain aetiology of the illness had an impact on the diagnostic process as, it was reported that doctors could not supply patients with a definitive response. ME/CFS was described as an ‘invisible illness’, with sufferers sometimes looking healthy to those around them but feeling incredibly unwell. Participants linked this to difficulty in being recognised as needing help, and not feeling able to ask for help.

GPs reported frustrations with supporting patients with ME/CFS, implying they found ME/CFS difficult to manage as no 'cure' was possible and that the work invested in working with such patients is largely unrecognised by other practitioners in the medical field. They articulated a process of diagnosis that prioritised excluding physical causes for a patient’s symptoms and presentation, which they viewed as treatable.

Explanation of quality assessment: moderate concerns over methodological limitations due minor limitations in two of three studies contributing to the finding (due to potential selection bias in both studies and the role of the researcher not being discussed in one study); no concerns about coherence; very minor concerns about relevance associated with one study (due to the sample consisting of people previously recruited in an RCT); no concerns about adequacy. Overall judgment of confidence was moderate due to the methodological concerns identified as concerns over relevance were only associated with one study and were too minor to further lower the confidence rating.

Review finding 6: Lack of cure and clear management pathway

GPs and practice nurses were reluctant to make a diagnosis of ‘ME/CFS’ and reported using the label as a last resort because making the diagnosis did not lead to obvious treatment and they believed that the illness had no cure. Some believed that as a result, a diagnosis of ME/CFS can even be harmful and reported frustration with supporting patients once a diagnosis was made implying that ‘CFS/ME’ was difficult to manage due to its lack of cure.

Explanation of quality assessment: minor concerns over methodological limitations with very minor limitations in one study (due to the role of the researcher not being explored and lack of data richness with data supported by single quotes); no concerns about coherence; very minor concerns about relevance associated with one study (due to the study sample consisting of people previously recruited in a RCT), being too minor to lower the confidence rating; moderate concerns about adequacy with information supporting the theme emerging from two studies and the concerns over data richness associated with one study. Overall judgment of confidence was low due to the concerns over adequacy and methodological limitations identified.

Review finding 7: Accessibility of treatment options in primary care

Following on from the process of gaining a diagnosis, patients looked to their medical practitioners for treatment options, but there was a deficiency in conventional treatments, apart from anti-depressants, that together with limited guidance led patients to search for self-treatment methods. They appeared to suffer from a lack of control over choices of treatment for managing their illness, which they saw as due to both lack of resources in the National Health and social systems and relative lack of recognition or value given to their own experience with illness. Patients desperate for relief of feelings of pain or illness reported finding treatments such as massage, osteopathy, dietary advice and acupuncture helpful, and it caused ongoing frustration that such interventions were not funded by either the NHS or by a private health insurance for ME/CFS.

Specialist health care professionals said they often used CBT principles in their practice, especially where unhelpful patterns of thought and behaviour, anxiety or stress were evident. However, NHS health care professionals emphasised how difficult it was for adults with

ME/CFS to access formal CBT as they rarely met the strict acceptance criteria set by NHS mental health services for CBT.

Explanation of quality assessment: minor concerns regarding methodological limitations due to very minor to minor limitations in the contributing studies (due to the role of the researcher not being discussed across studies, potential risk of selection bias in one study with 2/8 interviews being discarded, and issues with data richness of one study with some data supported by single quotes); no concerns about coherence; no concerns about relevance; minor concerns about adequacy with the idea of accessibility to certain treatments being implicated by their strict acceptance criteria only emerging from limited information in one study. Overall judgment of confidence was moderate due to the minor methodological limitations and minor concerns about adequacy identified.

Review finding 8: Unworkable treatment models

Some patients receiving a nurse-led intervention (pragmatic rehabilitation) reported that although the treatment model sounded logical they had difficulty applying it. Patients who could not work the management plan into their everyday life felt that it was not a workable model.

Explanation of quality assessment: very minor methodological limitations identified in the contributing study (due to the impact of the researcher on the findings not being explored); minor concerns about coherence, the theme supported only by part of the participants in the study; moderate concerns over relevance due to the finding emerging from one study where the sample consisted of patients previous recruited in a RCT and who had received a 'pragmatic rehabilitation' intervention and may thus not be applicable to other treatment models; serious concerns over adequacy with very limited information to support the theme. Overall judgment of confidence was very low due concerns about coherence, relevance and adequacy.

Review finding 9: Realistic goal setting

Patients recalled that clinicians assisted with and encouraged the development of new goals which had not been held prior to accessing specialist services. Some viewed these as vital to treatment success, representing a shift in focus towards management rather than cure. New goals were described as smaller, a lot more realistic and more sensible, involving breaking down existing goals, lowering expectations and focusing on the day to day rather than the future.

Explanation of quality assessment: no concerns regarding methodological limitations identified in the contributing study; very minor concerns about coherence, the theme being supported by some patients in the study but not all but with no oppositional views reported to lower the confidence rating; minor concerns about relevance due to the finding emerging from one study which excluded severely affected patients; minor concerns about adequacy the theme emerging from one study supported by relatively rich information. Overall judgment of confidence was moderate due to the minor concerns over relevance and adequacy identified.

Review finding 10: Patients' acceptance of ME/CFS

The diagnosis of ME/CFS and its acceptance emerged as a difficult time for patients. Engaging with the therapy was dependent upon the patient accepting what their symptoms represented and the diagnostic that was applied. Accepting their condition and diagnosis was described by patients as being necessary to allow progress with treatment and enable them to believe that the intervention might be appropriate for them. For some people undergoing CBT, acceptance of psychological explanations for their illness experience in particular, was reported to be crucial in the process of engagement with treatment. The importance of acceptance in obtaining the most benefit from treatment was also highlighted

by patients who reflected upon what they had lost or relinquished, including social networks, employment, career and study aspirations and independence.

Specialist health care practitioners reported that some people continue to fight the idea of 'CFS/ME' and its implications, including actively seeking to engage with health professional services and that it may take months before they accept the condition and decide to make positive steps to change their lives by giving up work, reducing working hours, and making significant lifestyle changes.

Explanation of quality assessment: moderate concerns regarding methodological limitations with very minor and minor concerns identified in two studies (due to the role of the researcher not being discussed in both studies, and data supported by single quotes in one study) but moderate limitations in one study (due to the recruitment strategy with selection of participants who had completed treatment and the role of the researcher not being discussed); no concerns about coherence; very minor concerns about relevance due to concerns identified in one study (with the sample consisting of people previously recruited in a RCT) which were too minor to lower the confidence rating; no concerns about adequacy with sufficient information supporting the theme across contributing studies. Overall judgment of confidence was moderate due to the methodological limitations identified.

Review finding 11: Patients' personal circumstances & availability

Patients discussed the importance of being able to attend appointments and accommodate treatment programmes around their commitments. They reported that work commitments could be a barrier to attending appointments and that it was important to have time and space in their lives to follow a treatment programme. Guided graded Exercise Self-help (GES) in particular was reported to work best for participants who had fewer commitments that interfered with the intervention (such as life responsibilities including work and looking after children). If a supportive partner or workplace could relieve the participant of other commitments, then they seemed to be better placed to benefit from GES. Patients receiving CBT also reported that in order to benefit from treatment, they must be ready to invest effort, which may as well depend on illness severity and personal circumstances at the time of therapy. Symptom severity as a potential barrier to attending medical appointments was also highlighted by adults completing treatment at NHS specialist services.

Explanation of quality assessment: minor concerns over methodological limitations with moderate concerns in one study (due to the recruitment strategy with selection of participants who had completed treatment and the role of the researcher not being examined) but no concerns over the remaining two studies contributing to the finding; no concerns about coherence; no concerns about relevance the finding being reported by people receiving different treatment programmes; no concerns about adequacy with evidence of sufficient depth emerging from three studies. Overall judgment of confidence was high due the methodological limitations identified being minor and no further concerns to lower the confidence rating.

Review finding 12: Symptom or illness severity

Patients noted that accessing clinics would have been difficult if experiencing severe symptoms with some discussing the need for assistance to attend appointments, including help from partners or friends, particularly when symptoms were severe. Although they reported the ease of access to clinics improved over time as symptoms improved, it was raised that travel during the early stages could be incredibly hard with patients finding the journey stressful and needing to recover after appointments. They particularly raised concerns about the ability of those severely affected by ME/CFS to access specialist services. Several patients who had received a type of counselling intervention mentioned the physical impact of counselling on someone with severe 'ME' and described the difficulty of making their way to and from the session each week, and the strain of keeping up a session of 50 minutes. Patients who were physically dependent on others for help in daily life

expressed that the task of explaining to someone how, when and why they need help could be exhausting and they often had to weigh up their energy resources in order to determine whether asking for help was the best course of action.

Specialist health-care professionals reported that a very small proportion of the people they were seeing were living with a severe condition and were significantly unwell, confined to home, or bedbound in a darkened room, unable to communicate. This was seen as extremely challenging for professionals who may have very few helpful suggestions. The presence of comorbidity, such PTSD, depression, or personality disorders were highlighted as barriers to the implementation of interventions. Specifically, health-care professionals implementing ICBT reported this intervention would not be enough to help these patients effectively. It was also reported that patients often struggle with a low level of energy and concentration, which was described as a 'low load capacity', which made it difficult for some to read the texts in the programs or to even sit behind a computer.

Explanation of quality assessment: Moderate concerns over methodological limitations due to very minor concerns in one study (due to the role of the researcher not being discussed), minor concerns in two studies (due to the role of the researcher and data supported by single quotes in one study and potential selection bias in the other study as participants were self-selected through their support group coordinator in one study), moderate concerns in one study (due to recruitment of participants from ME/CFS charities that were hence more likely to be patients who did not recover, and data analysis with insufficient data presented to support all findings) and no concerns in one study; very minor concerns about coherence with different aspects of severity reported to influence care between different groups of patients and between patients and health-care professionals but views not contradicting one another; no concerns about relevance as the theme did not only emerge from patients who were reported to be physically dependent on others but mostly from individuals of mixed or unclear disease severity and considering the nature of ME/CFS and how symptoms can greatly fluctuate from time to time the theme is not of limited applicability to severely affected individuals; moderate concerns about adequacy with the information supporting the theme in four out of the five contributing studies being limited. Overall judgment of confidence was low due to the methodological limitations, concerns about coherence and adequacy identified.

Review finding 13: Practical accessibility of care

Patients discussed practical aspects influencing the accessibility of care. Although some patients were pleased with the practical accessibility of clinics, describing journeys as being manageable or easy they acknowledged that accessibility could be a barrier to attendance. They discussed the importance of good public transport links to specialist services and some felt that they would not have been able to attend appointments without the use of a car. Other patients reported there were not enough healthcare providers in their area and highlighted their difficulty in obtaining transportation to the providers' office, obtaining timely appointments to see a provider and inconvenient office hours. Some patients living in rural areas lacked access to healthcare altogether.

Explanation of quality assessment: Serious concerns over methodological limitations with no concerns in one contributing study but moderate concerns in one study (due to the appropriateness of the data collection method, the study being a follow-up to a quantitative study with open-ended online responses which also implicated our ability to assess risk of bias in the data collection method) and serious concerns in the other study (due to selection bias as the sample was originally recruited for a different study and selection criteria were unclear, the role of the researcher not being discussed and lack of transparency over the data collection and analysis method not allowing us to assess data richness and whether findings are well grounded in the data); no concerns about coherence with nothing to lower the confidence rating; moderate concerns about relevance associated with two studies (due to the majority of the sample of one study consisting of people suspected of having ME/CFS

at the time of data collection but who did not actually have ME/CFS and the sample of the other study consisting of people who were self-identified as having ME/CFS and had suicidal ideations); minor concerns about adequacy due to concerns over data richness in two studies but with sufficient information supporting the theme in the other contributing study. Overall judgment of quality was very low due to concerns over methodological limitations, relevance and adequacy lowering the confidence rating of the finding.

Review finding 14: Flexibility in medical care appointments

Flexibility in the frequency and mode of medical appointments was valued by patients, who mentioned their appreciation of being offered later appointments because of travel burden and symptom fluctuation. The option of having some appointments by telephone was highly valued, particularly when symptom severity or travel problems made attendance difficult. Skype was also mentioned as a possibility. Specialist health care professionals reported they would visit people with serious condition at home, or if appropriate maintain contact by phone, especially to offer support for the family.

Explanation of quality assessment: very minor concerns over methodological limitations with minor limitations in two studies (due to the role of the researcher not being discussed and lack of data richness with some findings supported by single quotes in both studies) that did not lower our overall confidence in the finding as there were no concerns over methodological limitations in the study where the most information for this theme emerged from; no concerns about coherence; no concerns about relevance; minor concerns about adequacy with the information supporting the theme in two studies being very limited but with rich information emerging from the third study. Overall judgment of quality was moderate due to the concerns over adequacy.

Review finding 15: Relationship with health-care professional

Patients reported it was important in both the diagnosis and management of their condition to have an established relationship with their family physician. Not having such an ongoing relationship was reported to make it difficult to achieve agreement about the symptoms and the diagnosis, because the primary physician had no prior knowledge of them. Patients recognised a continued lack of commitment to the management of ME/CFS by GPs. They wanted their GP to be accessible and actively involved in the longer-term management of their condition and where support was not received, patients reported disengaging from primary care. Some reported difficulties communicating their experiences to health care professionals; they valued building a relationship with their therapist and reported a preference for face-to-face consultations as these were more personal and enabled them to be more forthcoming.

Black-minority ethnic group patients believed that a lack of continuity in care, which they thought to be due to high GP turnover rate, meant that they were unable to build a long-term relationship with their health professional and thus GPs were unable to take the holistic approach considered necessary for the diagnosis of ‘CFS/ME’ to be made.

Explanation of quality assessment: minor methodological limitations with moderate limitations in one study (due to potential selection bias with selection of participants who had completed treatment and the role of the researcher not being discussed), but very minor to minor limitations in the majority of the contributing studies, with minor limitations in one study (due to issues with data richness) and very minor limitations in two studies (due to the role of the researcher not being discussed); no concerns about coherence; very minor concerns about relevance with participants in one study consisting of people previously recruited in a RCT and participants in one study being limited to black-minority ethnic group patients; very minor concerns about adequacy due to concerns over the richness of data supporting the theme in one study but with sufficient information to support the theme overall. Overall judgment of confidence was moderate mainly due to the methodological limitations identified as concerns over relevance and adequacy were very minor.

Review finding 16: Patients' beliefs & attitudes towards ME/CFS and treatment

Patients' prior beliefs and attitudes towards their treatment, including their acceptance of the model of ME/CFS implied by the treatment offered, was an important facilitator of treatment engagement. Adopting the model presented in the intervention was dependent on whether it was perceived as making sense while rejecting the rationale for treatment was often due to patients' pre-existing models of illness that were contradictory to those of the intervention (for example several patients held a model of illness which implied that activity was potentially damaging, so patients were fearful of relapse). Some patients regarded the treatment intervention as unsuitable for them because they perceived their condition as being not amendable to treatment. The ability to be open and receptive towards the treatment received and believing in its usefulness for ME/CFS were key factors for maintaining motivation to engage with therapy. According to mental health care practitioners providing ICBT, patients' attitudes regarding online therapy could be a barrier to implementation as it was reported that some patients did not want to start with ICBT at all or those who did start had problems staying engaged, because they lacked trust, felt hesitance to take responsibility and/or had no interest in computers.

Attitudinal barriers to healthcare utilisation included patients' thinking that their problem was 'no big deal' or would get better on its own' and that individuals needed a better reason to see a healthcare professional. Health professionals also suggested that having a biomedical model of illness could prevent people from seeking medical advice for non-specific symptoms of ME/CFS such as fatigue, loss of concentration or sleep problems.

Explanation of quality assessment: Moderate concerns over methodological limitations with no limitations in one study and very minor limitations in three studies (due to the role of the researcher not being examined), but moderate concerns (due to the role of the researcher not being examined and potential selection bias with selection of participants who had completed treatment) and serious concerns (due to selection bias as the sample was originally recruited for a different study and selection criteria were unclear, the role of the researcher not being discussed and lack of transparency over the data collection and analysis method not allowing us to assess data richness and whether findings are well grounded in the data) in the other two studies contributing to the finding; no concerns about coherence; serious concerns about relevance due to concerns over four out of six contributing studies with minor concerns in two studies (due to the population of one study being limited to black minority ethnic groups and of the other study consisting of people previously recruited for a RCT), moderate concerns in one study (due to the majority of the sample consisting of people who were suspected of having ME/CFS at the time of data collection but did not actually have ME/CFS) and serious concerns over one study (because the study was not limited to the implementation of ICBT treatment for 'CFS' but also for 'Chronic pain' and it was not always possible to distinguish whether reported barriers and facilitators were applicable to ICBT for CFS, chronic pain or both; no concerns about adequacy. Overall judgment of confidence was very low due to the methodological concerns identified and concerns over relevance.

Review finding 17: Personal attributes & motivation

Personal attributes such as being positive, proactive, open, willing to try anything, being determined, stubborn or having perseverance, were reported by patients to be important motivating factors for treatment engagement and for overcoming challenging periods during treatment. It was reported that in order to benefit from CBT in particular, motivation must come from within. Being proactive in seeking and bringing evidence to medical consultations was also reported to facilitate access to treatments and services.

Explanation of quality assessment: Minor concerns over methodological limitations with moderate limitations in one study (due to the role of the researcher not being discussed and potential selection bias with recruitment of participants who had completed treatment) but no significant limitations identified in two studies and minor limitations (due to minor issues with

data richness) in the other contributing study; no concerns about coherence; very minor concerns about relevance due the sample of one study consisting of people recruited in a RCT; very minor concerns about adequacy due to the concerns over data richness in one study. Overall judgment of confidence was moderate due to the minor methodological limitations and very minor concerns over relevance and adequacy slightly lowering the confidence rating.

Review finding 18: Individual characteristics of the therapist

Therapists implementing internet-based cognitive behavioural therapy (ICBT) in mental healthcare clinics and their managers mentioned individual characteristics among therapists as factors that influenced implementation of interventions. The attitude of the therapist was reported to be key, which is often expressed in a feeling of confidence and trust in the intervention, and also confidence in therapist's own skills and working with a strict protocol. Also, the ability to use the intervention (ICBT) in a flexible manner was frequently mentioned. Skills to tailor the intervention to the needs of each individual patient were reported to be a prerequisite in order to use the program beneficially. For example, therapists who mentioned they still saw their patients face-to-face from time to time, or who skipped certain assignments if they did not seem appropriate, valued ICBTs a lot more. This also relates to the self-efficacy that therapists report. Feeling in control of the program and the treatment process was essential. Clear and positive communication about the program towards patients was perceived as very beneficial, also increasing the motivation of patients to work with the program.

Explanation of quality assessment: very minor concerns over methodological limitations with very minor concerns identified in the contributing study (due to the role of the researcher not being explored) that was considered too minor to lower the confidence rating; no concerns about coherence; serious concerns over relevance, the information reported being of potentially limited applicability to ICBT and the research not being limited to the implementation of ICBT for ‘CFS’ but also for ‘Chronic pain’ meaning it was not always possible to distinguish whether reported barriers and facilitators were applicable to ICBT for CFS, chronic pain or both; minor concerns about adequacy with the theme supported by limited quotes in one study. Overall judgment of confidence was very low due to concerns over relevance and adequacy.

See Appendix D for full evidence tables.

2.6 Summary of the qualitative evidence

Fifteen themes were identified from the eight included studies in children and young people (see Table 6).

Table 6: Review findings: Children and young people (severity: mixed/unclear)

Main findings	Statement of finding
Health professionals’ knowledge & attitudes[94, 155-157]	HCP knowledge and attitudes towards ME/CFS can influence the support they provide, with a lack of knowledge and unsupportive attitudes acting as a barrier to the diagnosis or referral to services that can provide care and with professionals with experience in ME/CFS facilitating access to appropriate care.
Referral to specialist services[21, 156, 157]	Specialist services gave young people and their families access to information, treatment and support that enabled symptom management and improvement while a lack of referral to specialist services presented a barrier to the diagnosis and management of ME/CFS and led patients to alternative therapies.

Main findings	Statement of finding
Acceptance and adaptation to ME/CFS[21]	Young people or their families may experience difficulty adapting their everyday life to medical care strategies and to the implications of ME/CFS.
Diagnosis of ME/CFS and its communication across settings[26, 94]	The diagnostic label given to people with ME/CFS will influence the intervention that follows and sharing the diagnosis with the school setting is crucial in receiving support, while the explanation given around it can influence treatment engagement.
Nature of ME/CFS[109]	The great variability and fluctuation of ME/CFS symptoms can greatly complicate management in children while the circularity of low mood characterising the illness can be a barrier to improvement.
Practical accessibility of care[45, 65]	The location of therapy or health services as well as the everyday commitments of young people and their parents can negatively impact patients' health and their ability to fully engage in therapy while videoconferencing could overcome the barriers to care posed by the distance of healthcare services, the family's availability and symptom severity.
Technical problems as a barrier to care[65]	Technical difficulties associated with videoconferencing can impede effective communication with health-care professionals.
Virtual care[65]	Despite the benefits that can be provided by a virtual connection with health professionals, communication can be compromised compared to face-to-face interactions with emotional cues being missed, the content and depth of discussions being limited.
Child-centred care[26, 109]	Children can benefit from treatment that is tailored to their individual functional needs and priorities and the involvement of children with their care to facilitate this is crucial.
Ongoing communication across schools, families and health care professionals[26, 109]	There is often a lack of sufficient or direct communication between schools, families and health-care professionals, implicating the care of children with ME/CFS and the importance of such an ongoing communication across settings is acknowledged by all parties.
Lack of social support[109]	Negative attitudes from the social environment can act as a barrier to improvement implicating the family's ability to follow clinical advice.
Communication barrier[155]	Both children and their parents may have difficulty communicating their experiences with health-care professionals.
Limited capacity to self-manage and need for support[26]	Children cannot manage their condition independently across the home, school and clinical setting and rely on adults for support with management, communication, understanding and self-regulation.
Integrated/Shared care across settings[26]	Clinicians, parents as well as teachers have a distinct role in the diagnosis and care of children with ME/CFS and the involvement and communication of all three is crucial to maximise the quality of the care received.
Accommodations in the school setting[26]	Health professionals, teachers and parents raised the importance of a management plan that involves the school setting, the responsibility of teachers in day-to-day management and of accommodations at school to support the care of children with ME/CFS.

2.6.1 Narrative summary of review findings for Children and young people (severity: mixed/ unclear

Review finding 1 CYP: Health professionals' knowledge and attitudes

Parents of children with ME/CFS felt both GPs and paediatricians lacked knowledge of the condition, were unsure how to make a diagnosis and didn't understand the referral process or how to access practical support. They felt that GPs in particular knew little about the condition or the recommended guidelines when ME/CFS was suspected or diagnosed. This led to a delay in diagnosis and to the parent having to inform the GP about the specialist service and referral criteria. Parents felt they were dismissed by GPs as worrying over normal childhood illnesses and weren't signposted to the practical support they were entitled to. It was reported that GPs and in one case a Child Psychiatrist, delegitimised the child's experience, were patronising, didn't listen and dismissed parents' concerns. They also failed to ask questions and empower their child to talk; nor did they express empathy. Parents reported having to attend the GP surgery on many occasions to convey the seriousness of the problem; they felt they were patronised and made to feel inadequate as parents. Experiences of unsupportive health professionals were reported to often lead to withdrawal from healthcare services.

As reported by health care professionals (HCPs) working with children and adolescents with ME/CFS, their belief in the existence of ME/CFS facilitated engagement and granted access to appropriate care, while past clinical experience biased HCPs towards one perspective (e.g. focussing on psychosocial aspects at the expense of physiological factors).

Explanation of quality assessment: minor concerns over methodological limitations with minor concerns in one study (due to potential selection bias in the recruitment strategy where participants were recruited on the basis of how they informed and validated emerging theory), very minor limitations in one study (due to the role of the researcher not being discussed) and no significant limitations identified in the other contributing study to further lower the confidence rating; minor concerns about coherence the information supporting the theme emerging only from a small number of people in the sample of one study; very minor concerns over relevance with the sample of the study contributing the least information to the theme not being limited to the stratum of children and young people; no concerns about adequacy with sufficient information to support the theme. Overall judgment of quality was moderate due to minor methodological limitations and minor concerns about coherence.

Review finding 2 CYP: Referral to specialist services

Mothers of adolescents with ME/CFS who had accessed specialist services reported that the service recognised and acknowledged the young person's condition, resulting in a sense of relief and reassurance. They felt symptoms were now being understood and they would receive help. Referral to a specialist service gave families access to an informative team of experts, for some a formal diagnosis, and for all a tailored, patient centred specialist medical intervention that had not been available earlier. This enabled positive change and steps towards a managed recovery. Some mothers felt that the 'CFS/ME' service reinforced symptom management strategies that they had been trying to get their child to follow, and that they felt their child would be more likely to listen if techniques were legitimised by a health-care professional. Adolescents reported that specialist medical care was positive, as it enabled them to talk about their illness and gave guidance on how to manage their condition, which brought structure and a sense of normality back into their lives.

Several patients reported they had not been referred to secondary care when visiting the GP in the first 6 months of onset of symptoms. These participants remained without a diagnosis, despite further investigation and repeat visits to the GP. They reported using books, media publicity and complementary/alternative medicine instead to help interpret their symptoms

and support the diagnostic label. The use of alternative therapies and most commonly diets was widespread and was linked to a lack of access to specialist care.

Explanation of quality assessment: minor concerns over methodological limitations with minor concerns over one study (due to the role of the researcher not being discussed and richness of data supporting themes) and no concerns over the other contributing study; no concerns about coherence; minor concerns over relevance associated with both contributing studies (due to the population of one study not being limited to the children and young people stratum and that of one study consisting of people recruited in a feasibility RCT); no concerns over adequacy with rich information supporting the theme. Overall judgment of confidence was moderate due to the methodological limitations and concerns over relevance.

Review finding 3 CYP: Acceptance and adaptation to ME/CFS

Adolescents with ME/CFS reported that, although specialist medical care resulted in better symptom management, accepting that for a time they must reduce activity levels and adopt a routine was challenging. A few mothers noted that specialist medical care strategies had an impact on the whole family and could be difficult to integrate with their lifestyle.

Explanation of quality assessment: minor concerns over methodological limitations in the contributing study (due to the role of the researcher not being discussed and issues with data richness with findings supported by single quotes); no concerns about coherence; very minor concerns over relevance (due to sample consisted of participants previously recruited in a feasibility RCT); serious concerns over adequacy with limited information from one study supporting the theme. Overall judgment of confidence was very low due to the methodological limitations and the insufficiency of information supporting the theme, concerns over relevance being too minor to contribute towards lowering the confidence rating.

Review finding 4 CYP: Diagnosis of ME/CFS and its communication across settings

Health professionals working with children and young people with ME/CFS reflected on how the choice of label given to a young person influenced subsequent intervention. The experience of receiving a diagnosis, and the explanation around it, seemed pivotal in families' acceptance of the diagnosis and label and the recovery process as it either facilitated engagement or provided a barrier to treatment. The pathway to recovery varied as a consequence of the label given. For example, the HCP who referred to ME/CFS as 'last straw syndrome' felt that this label guided interventions exploring the impact of stress on the body. Similarly, the participant who felt that a child could receive a diagnosis of either chronic pain or ME/CFS highlighted that different specialist teams would be involved, and rehabilitative treatment would differ in each case. Parents, teachers and health professionals talked about the importance of sharing the diagnosis across settings. Parents described the impact of diagnosis, the 'relief that somebody has listened', feeling believed and felt it was important that the clinic communicated this directly to the school. Both teachers and families identified the diagnosis as a catalyst to the school taking the health concerns seriously and implementing the necessary support. Teachers emphasised that at an organisation/policy level, teachers needed this formal diagnosis to implement treatment recommendations, such as reduced timetables.

Explanation of quality assessment: minor concerns over methodological limitations in the contributing studies with minor concerns in one study (due to potential selection bias with in the recruitment strategy as participants were recruited on the basis of how they informed and validated emerging theory) and very minor concerns in the other study (due to concerns over the influence of the researcher on the findings not being discussed); no concerns about coherence; no concerns over relevance; minor concerns over data richness with the information supporting the theme in one contributing study being mainly based on the authors' interpretation of what was reported by the health professionals in the study rather

than by the actual information reported by participants but no similar concerns in the other contributing study. Overall judgment of confidence was moderate due to minor methodological limitations and concerns over adequacy.

Review finding 5 CYP: Nature of ME/CFS

Specialist paediatric health professionals talked about the complexity of paediatric ME/CFS. They described the difficulty of treating children with 'CFS/ME' due to variability and fluctuation of the condition and environmental barriers preventing children from returning to normal; and described a number of coping strategies were employed to help children cope with the condition. They talked about the complexity of the condition with symptoms varying between children; circularity was also described as a feature of the condition; children experience a 'boom and bust' pattern with increasing symptom severity following activity which can lead to a downward spiral of reduced activity. The circularity of low mood was described as maintenance factor preventing improvement. Children can have low mood due to symptoms and a lack of participation (to school, leisure activities and social life) and can then become more vigilant to symptoms. This can then lower their thresholds for participation, further lowering their mood in a negative cycle.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the role of the researcher not being explored); no concerns about coherence; no concerns about relevance; minor concerns about adequacy with information from one study supporting the theme. Overall judgment of confidence was moderate due to very minor concerns over methodological limitations and minor concerns over adequacy.

Review finding 6 CYP: Practical accessibility

The location of therapy sessions appeared to be an issue for adolescents. The travelling and the sessions themselves left the young people feeling drained and struggling to participate fully. Sometimes the effort was perceived to impact on their health over subsequent days. Young people and their parents as well as specialist healthcare professionals reflected on the benefits of videoconferencing. They felt a benefit of videoconferencing would be that patients who either lived too far away to receive a specialist service or were too unwell to attend hospital appointments, would still be able to access evidence-based therapies. Travel was frequently cited as a potential difficulty in terms of increasing 'CFS/ME' symptoms, therefore the use of videoconferencing was seen in a positive light because it meant that patients would not have to travel long distances to access support. They talked about videoconferencing being beneficial for young people because it was more convenient and flexible and could "fit around school hours" and for parents especially if they were "struggling to get time off work". There could also be flexibility in terms of appointment times, both in terms of "length of appointment and the right time of day" for the patient. Videoconferencing was easier to fit in to the busy lives of families.

Explanation of quality assessment: very minor concerns over methodological limitations with very minor concerns in one contributing study (due to the role of the researcher not being discussed) and no concerns in the other study; no concerns about coherence, no concerns over relevance; no concerns over adequacy with sufficient information from two studies illustrating the theme. Overall judgment of confidence was high.

Review finding 7 CYP: Technical problems as a barrier to care

Technical difficulties associated with video-conferencing were considered as a barrier to effective communication with health-care professionals, especially because it could exacerbate the problems in interaction that result from a young persons' 'CFS/ME' symptoms. Those included issues with connection speed, reduced quality of the picture, reduced sound quality sometimes muting the therapist and occasions when video-conferencing would just intermittently stop working, all leading to disruptions to the session.

Although technological issues were frustrating, some participants felt that they could be dealt with and almost accepted this as part of the experience. Although the majority of discourse around technological issues was negative, for some participants there were positive experiences of using technology.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the role of the researcher not being discussed) that were too minor to lower the confidence rating; minor concerns about coherence due to participants in the study expressing conflicting views on the extent to which technical problems act as a barrier to care but the majority of participants agreeing that they do; moderate concerns over relevance due to the theme being particularly relevant to people with ME/CFS who are to receive care via videoconferencing; no concerns over adequacy with sufficient information in the study illustrating the theme. Overall judgment of quality was low due concerns over coherence and relevance.

Review findings 8 CYP: Virtual care

Patients and health-care professionals talked about communication being negatively affected by a virtual connection, and it seemed that the screen could become a “barrier” to effective communication. That with a virtual connection you “can't tell exactly how people are feeling”, voices would sound different and subtle emotional cues could be missed. For some, the inability to have direct eye contact via videoconferencing was something that was problematic. Not being able to see the whole person on videoconferencing also made things difficult. Young people, parents and healthcare professionals all talked about how subtle emotional cues may be missed via videoconferencing. They talked about how interacting via videoconferencing was inherently different from interacting face-to-face. Some young people felt that the virtual sessions constrained both the content and the depth of what they would discuss. Lack of, or reduced engagement was a potential result. Healthcare professionals wondered whether this potential lack of engagement was because a therapist was not seen as a “real person” when on screen. In contrast some reported that videoconferencing could potentially facilitate more open communication than face to face sessions. Being physically removed from the therapist was seen as a possible reason why young people may find it easier to open up.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the role of the researcher not being discussed); minor concerns about coherence due to participants in the study expressing conflicting views regarding whether a virtual connection positively or negatively influences communication but the majority of participants reporting on the potential negative implications involved; no concerns over relevance; no concerns over adequacy with sufficient information illustrating the theme. Overall judgment of quality was moderate due to the concerns over coherence with methodological limitations being too minor to further lower the confidence rating.

Review finding 9 CYP: Child-centred care

Clinicians, teachers and parents of children with ME/CFS, emphasised the importance of child-centred care. Clinicians spoke about identifying the child’s ‘goals’ and having ‘their voice in the room’ and teachers about giving them ‘ownership’ and encouraging the child to communicate. As raised by a clinician, ‘even though it’s going to be caregivers who are really following through with the plan, its’ still not going to be as successful as if you’re engaging with a young person and they have an element of understanding, appropriateness to their age, we can’t lose sight that the young person needs to be involved with their care’.

Specialist health-care professionals highlighted the importance of considering the individual functional level and priorities of children when setting treatment goals. They described how they could be working with an athletic child one minute and then a child who only wants to see their friends the next and how flexible strategies were required to treat the variable

severity of symptoms and functional ability of individual children. Explanation of quality assessment: very minor concerns over methodological limitations in the contributing studies (due to the role of the researcher not being discussed); no concerns about coherence; no concerns over relevance; no concerns over adequacy with sufficient information from two studies illustrating the theme. Overall judgment of confidence was high due to methodological limitations being too minor to lower the confidence rating.

Review finding 10 CYP: Ongoing communication across schools, families and health-care professionals

Clinicians, teachers and parents of children with ME/CFS highlighted the lack of ongoing direct communication between clinic and school. Teachers reported minimal contact from clinicians typically consisting of two or three letters. In some cases, this limited direct contact was acceptable to schools, however there were cases where families, schools and clinicians identified this minimal contact as insufficient. In the latter cases, schools viewed direct input from the clinical service as 'really vital' and were dismayed that teachers held high levels of responsibility for the child's health with little guidance.

There was a level of frustration from all parties. Teachers expressed frustration about the limited input from clinicians, families reported that schools didn't believe them and didn't adapt to the child's needs and created a lot of resistance. Equally clinicians were frustrated by the lack of support from schools.

There was agreement on the factors associated with satisfaction or dissatisfaction with the low levels of direct clinic-school contact. Firstly, the communication between parents and schools. Teachers satisfied with minimal clinical input attributed this to effective communication between parents and school which allowed teachers to gain an understanding of the condition, receive updates on clinical appointments and viewed the family's communication with the school to be very important. Clinicians believed it was important to empower patients to liaise with the school. In contrast, teachers wanting more support from clinicians reported challenges in communicating with parents and said that direct communication with clinic was needed when parents did not have the capacity to communicate. Clinicians also recognised fractious relationship between families and school was a marker to intervene directly with schools. Secondly, the goals for the child's education aligned. Those teachers satisfied without direct communication from clinicians described the parent as prioritising education while teachers wanting more health input were in tension with parents about how much the child could/should be attending. Equally parents had negative perceptions of schools when they perceived this mismatch and saw schools as more concerned about their targets. The third factor was relevant to complexity and severity. Teachers managing without direct intervention from clinicians talked about cases being straightforward, describing low levels of absenteeism, fewer concerns over emotional well-being, believed the child was keeping up academically and recovering from the illness. By contrast, those keen for more guidance were concerned with high levels of absenteeism and academic difficulties, cases of multiple diagnoses and multiple professionals involved. Equally some clinicians differentiated between simple and complex cases, in simple cases stating it was up to the parents and the school to put boundaries in place and to have really good communication links but they believed their direct intervention with school could be justified for complex children. They advocated starting without direct communication with schools, moving to direct communication if the case became challenging. Teachers, parents and clinicians who emphasised the need for direct communication between schools and clinic wanted direct conversation with professionals for clearer advice about the child's individual needs and personalised guidance on how the school could manage their health needs. They believed that telephone, emails and face to face meetings between clinicians and teachers could be beneficial. They also wanted multidisciplinary meetings, classroom observations and training sessions. Clinicians differentiated between simple and complex cases (considering complexity in terms of illness severity, co -morbidities and other professionals involved) and clinicians agreed that telephone and face to face meetings could

be beneficial for complex cases. Parents valued direct contact between clinic and school in the minority of cases where this happened.

Specialist health-care professionals also highlighted working with schools as a core part of treatment. That involved educating schools, correcting unrealistic expectations and formulating reduced timetables.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing studies (due to the role of the researcher not being discussed); no concerns about coherence; no concerns over relevance; no concerns over adequacy with a wealth of information illustrating the theme. Overall judgment of confidence was high, with the methodological limitations identified being too minor to lower the confidence rating.

Review finding 11 CYP: Lack of social support

Health professionals identified understanding, attitudes and support from others as a potential barrier to children with ME/CFS returning to normality. Due to a lack of understanding from the community, children with can be faced with negative attitudes and comments. Health professionals felt this could affect the ability of families to follow clinical advice.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the role of the researcher not being discussed); no concerns about coherence; no concerns over relevance; serious concerns over adequacy with limited information from one study illustrating the theme. Overall judgment of confidence was low due to the insufficiency of information supporting the theme, with the methodological limitations identified being too minor to further lower the confidence rating.

Review finding 12 CYP: Communication barrier

Parents of children with ME/CFS struggled to communicate an illness that wasn't visible as well as having difficulty communicating a problem that their child, and not themselves, were experiencing. They reported that their children found it hard to put their experiences into words and that it was difficult answering more probing questions in front of the child.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the role of the researcher not being discussed); no concerns about coherence; no concerns over relevance; serious concerns over adequacy with very limited information from one study illustrating the theme. Overall judgment of confidence was low due to the insufficiency of information supporting the theme, with the methodological limitations identified being too minor to further lower the confidence rating.

Review finding 13 CYP: Limited capacity to self-manage and need for support

Teachers, families and clinicians agreed that younger children with 'CFS/ME', especially those under 8 years, haven't got the capability to manage their condition independently across home, school and clinical setting. Parents described the younger children's inability to understand and adhere to treatment without support, explaining that children wouldn't comprehend the treatment plan and do not have the maturity to self-monitor and self-regulate. At clinic, most dialogue occurred between the clinician and parent, with children having little engagement, not being very responsive. At school, teachers perceived that these younger children were not as adept at regulating their own behaviour (for example unnecessarily exerting energy and then collapsing, being in pain or very upset). Children relied on the adults around them and parents, teachers and clinicians had distinct roles in the child's care.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the potential influence of the researcher on the findings not being discussed); no concerns about coherence; no concerns over relevance; no concerns

over adequacy with a wealth of information from one study supporting the theme. Overall judgment of confidence was high, with concerns over methodological limitations being too minor to lower the confidence rating.

Review finding 14 CYP: Integrated/shared care

Parents, teachers and clinicians have distinct roles in the child's care. All three reflected on the clinician's role as providing a diagnosis, developing treatment plans that spanned the home and school setting, providing advice such as reducing the school attendance. The clinician's role was to review the child's progress and revise the treatment plan as needed. All parties viewed parents as the coordinators of care, responsible for relaying information between clinic and school. They were also primarily responsible for day-to-day supervision of the child's treatment. They monitored their child's symptoms and activity levels, gave their child direct instructions to regulate activity and sleep, structured the child's environment in line with the treatment plan and administered medication. Teachers explained that they had a close and consistent relationship with the child who was usually with them most of the day, with clinicians and families also acknowledging this important relationship. All parties recognised the teachers' responsibility for day-to-day management of the child's health including accommodating reduced school timetables, maintaining a connection with the family during the child's absences, monitoring and regulating the child's activity levels, responding to cognitive, physical and emotional needs; helping the child maintain friendships and encouraging the child to communicate their needs. Clinicians recognised that making the school aware of management advice and accommodations needed, is very valuable. Considering the process of diagnosis, clinicians identified the increased complexity of assessing younger children and discussed the benefits of involving schools in this process-stating that the school's observation of the child could be really helpful in the assessment process. Teachers expressed a desire to provide formal reports (which they provided for other clinical conditions such as ADHD) to clinicians to aid assessment. They stated their privileged position of a professional perspective along with a close relationship with the child could be beneficial to the clinician. Parents did not explicitly discuss the need to involve teachers in assessment, but acknowledged the insight that teachers had about the child.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the potential influence of the researcher on the findings not being discussed); no concerns about coherence; no concerns over relevance; no concerns over adequacy with a wealth of information from one study supporting the theme. Overall judgment of confidence was high, with concerns over methodological limitations being too minor to lower out confidence.

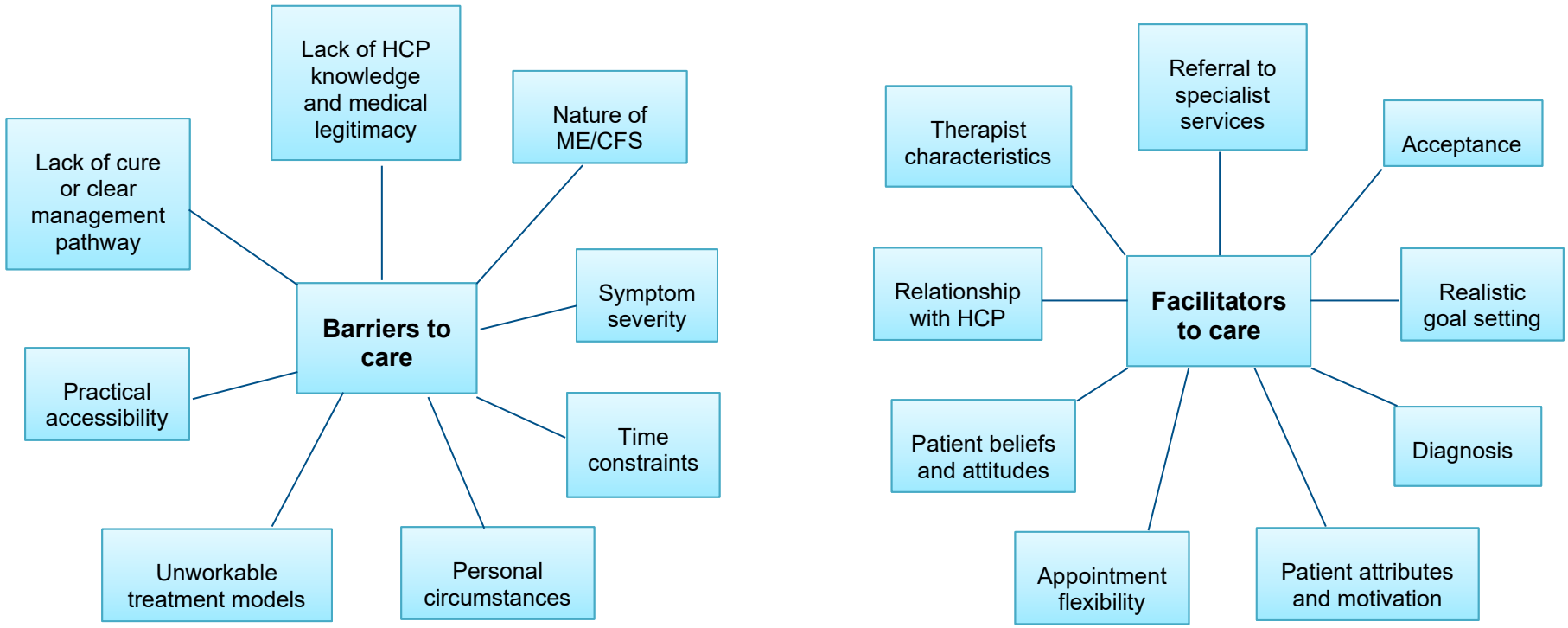
Review finding 15 CYP: Accommodations in the school setting

Clinicians, parents and teachers described the clinician's role in developing treatment plans that spanned the home and school setting, providing advice such as reducing the school attendance (for example, only doing four hours of school a day'), structuring rest breaks (e.g. recommending regular breaks), limiting physical education and making physical and social adaptations in the classroom. One clinician suggested things like a medical card so that if the child wants to leave the class, she would just hold the card up. Teachers portrayed a proactive attitude to providing support and all parties (family, teachers, clinicians) recognised their (that is, the teachers') responsibility for day-to-day management of the child's health including accommodating reduced school timetables, structuring the environment to reduce the burden on the child.

Explanation of quality assessment: very minor concerns over methodological limitations in the contributing study (due to the potential influence of the researcher on the findings not being discussed); no concerns about coherence; no concerns over relevance; no concerns over adequacy with a wealth of information from one study supporting the theme. Overall

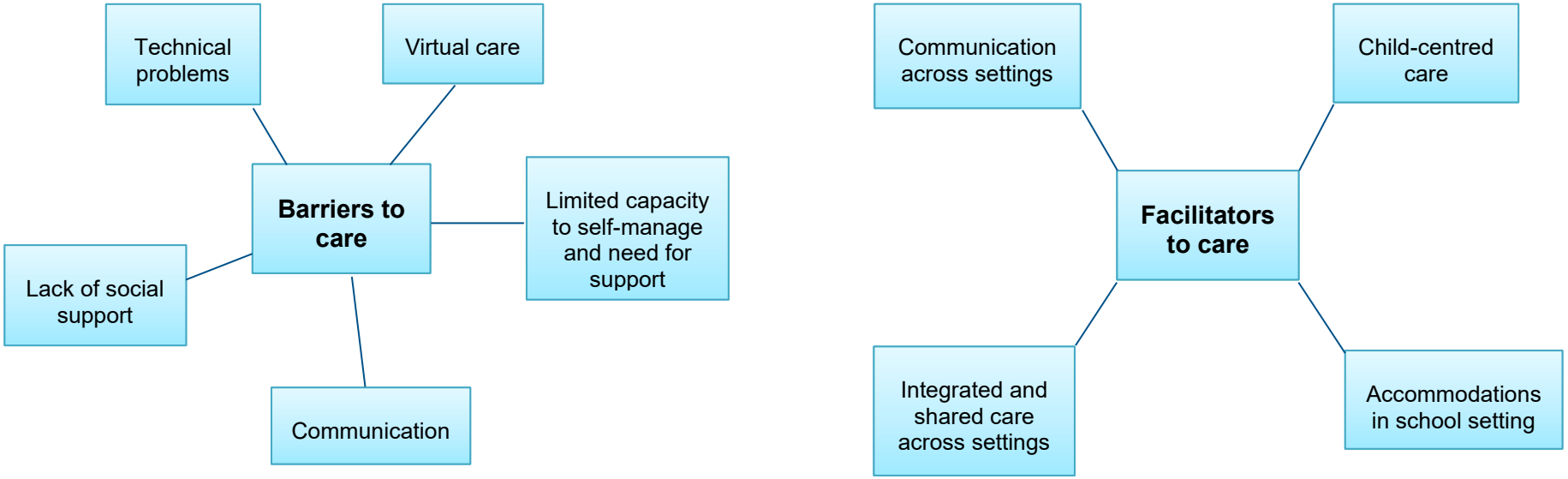
judgment of confidence was high, with concerns over methodological limitations being too minor to lower out confidence.

Figure 2: Theme map of review findings (adults)



Source/Note: Some themes may be classified as a barrier or a facilitator to care, e.g. personal circumstances can allow for investment of time and effort in treatment or can act as a barrier depending on the nature of the circumstances.

Figure 3: Theme map of review findings (additional themes in children/young people)



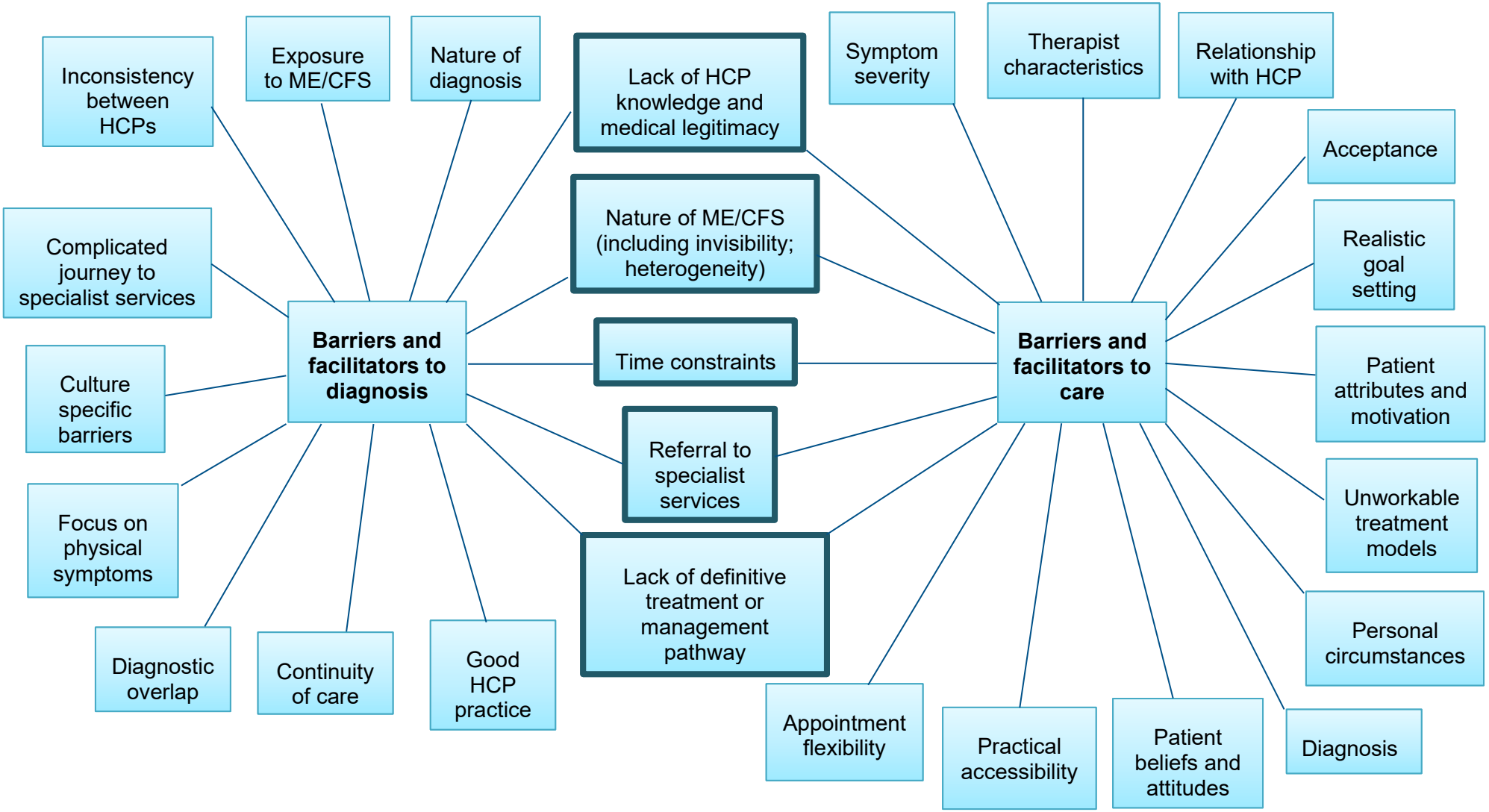
Source/Note: Some themes may be classified as a barrier or a facilitator to care, e.g. lack of social support can be a barrier, whereas good social support can be a facilitator.

Source/Note: Only additional themes that were different to those identified in adults are displayed here.

2.6.2 Economic evidence

The committee agreed that health economic studies would not be relevant to this review question, and so were not sought.

Figure 4: Map of overlapping themes in the review findings



3 The committee's discussion and interpretation of the evidence

The committee's discussion on the evidence reviews for the barriers and facilitators to diagnosis and the barriers and facilitators to care are included here.

The committee discussed this evidence with the findings from the evidence reviews on evidence report A: Information and support for people with ME/CFS, evidence report B: information for health and social care professionals, evidence report D: diagnosis and evidence report I: multidisciplinary teams and the report on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). Where relevant these sources are noted.

3.1 The quality of the evidence

Barriers and facilitators to diagnosis

Fourteen qualitative studies were included in the review. The majority of the studies were conducted with adults with ME/CFS with only two studies relevant to young people with ME/CFS.

Confidence in the review findings ranged from high to low. Main reasons for downgrading were methodological limitations, relevance and adequacy. One of the most common methodological limitations was insufficient reporting of the role of the researchers and their relationships with the study participants, making their potentially influence on the results unclear. Issues with data analysis were also common, with some studies insufficiently reporting the methodology and many studies presenting limited data, often single quotes, to support research findings.

The majority of the evidence was based on studies in which the research aim was different from the focus of this review. Several findings were directly applicable; however, confidence in some findings was reduced due to inferences being assumed.

Some findings were based on evidence from a small number of studies, which meant that there were concerns about the adequacy of data, particularly where data from these studies were not rich.

In general, the committee placed greater weight on high and moderate confidence findings than low confidence findings during discussion of the evidence, although they acknowledged that some lower confidence findings reflected their own experience and should not be disregarded. For example, the finding regarding the importance of attention to symptom presentation and rigorous history taking was rated low, but the committee agreed that it could be interpreted with a higher degree of confidence.

Barriers and facilitators to care

Twenty-six qualitative studies were included in the review. The majority of the studies were conducted with adults with ME/CFS, with seven studies relevant to the stratum of children and young people with ME/CFS. One study included both children, young people and adults with ME/CFS. This was considered to contribute to findings relevant to both the strata of adults and of children and young people. Concerns over part of the population contributing to a finding, being indirect were taken into account in the assessment of the confidence in that finding.

Confidence in the review findings ranged from high to very low. Main reasons for downgrading were methodological limitations, relevance and adequacy. The most common

methodological limitations were insufficient reporting of the role of the researchers and their relationships with the study participants; issues with data analysis, including insufficient reporting of the methodology and limited data being presented to support research findings; and recruitment strategies that could have biased the results. Studies for example that only included participants who had completed a particular treatment, or those that recruited participants via ME/CFS charities were judged to have methodological limitations in this domain. Three studies were conducted in the USA and one in the Netherlands.

Some studies had a different research aim from the focus of this review. Several findings were directly applicable; however, confidence in some findings was reduced due to inferences being assumed. Other issues regarding relevance included the exclusion of people with severe and very severe ME/CFS, recruitment of participants of RCTs trialing specific interventions and inclusion of participants across both age strata.

Some findings were based on evidence from a small number of studies, which meant that there were concerns about the adequacy of data, particularly where data from these studies were not rich.

The vast majority of studies used semi-structured interviews, two of which also included focus group discussions as their data collection method. One study used unstructured interviews and two studies used qualitative questionnaire responses to inform the research.

In general, the committee placed greater weight on high and moderate confidence findings than low and very low confidence findings during discussion of the evidence, although they acknowledged that some lower confidence findings reflected their own experience and should not be disregarded. For example, the findings regarding lack of or delayed referral to specialist services, symptom severity and practical accessibility as barriers to were rated low to very low, but the committee agreed that they could logically be interpreted with a higher degree of confidence.

3.2 Findings identified in the evidence synthesis

Overall, the committee considered that the findings identified in the reviews were consistent with their own experience and no important findings had been missed. It was suggested that several of the findings (for example, lack of medical legitimacy) could be classified under the overarching theme of epistemic incongruence, where people with lived experience of ME/CFS face difficulties in communicating their experience to healthcare professionals who lack knowledge and understanding of the condition.

However, the committee agreed it was important to consider the findings separately, in order to preserve the complexities of the themes and the potential interactions between them. Themes identified for children and young people broadly mirrored those identified for adults. Findings unique to children and young people are highlighted.

While synthesising the evidence it was clear that many of the themes in the two reviews overlapped and identified factors that impact on access to all areas of care (Figure 4 illustrates the overlapping themes). To avoid duplication the committee discussion of the findings from both reviews is reported under the following headings: barriers and facilitators to accessing care, barriers and facilitators to diagnosis, and barriers and facilitators to management. The committee noted that the majority of findings were barriers and only a few facilitators were identified.

The evidence from the separate reviews is identified in the discussion by using (R1) for barriers and facilitators to diagnosis and (R2) for barriers and facilitators to care. The review findings are labelled as in the narrative summary of the review findings. For example, in the

barriers and facilitators to diagnosis review, review finding 1 is lack of health professional knowledge & medical legitimacy. This is labelled in the discussion as (R1:RF1).

Barriers and facilitators to accessing care

Understanding and accepting ME/CFS: Health and social care professionals

Lack of knowledge and medical legitimacy from healthcare professionals (R1:RF1,: R2:RF1, RF1CYP)

Evidence suggested there was a lack of medical legitimacy, with limited health professional knowledge and understanding of ME/CFS and this is underpinned by insufficient medical training. This finding is a consistent and enduring theme in all of the qualitative reviews conducted for this guideline (see evidence review A: Information, education and support for health and social care professionals, evidence review B: Information, education and support for people with ME/CFS, their families and carers), it was highlighted in both the commissioned reports (Appendix 1 and 2) and is discussed by Dr Muirhead in her expert testimony (Appendix 3). Disbelief in the existence of ME/CFS has far reaching harmful effects for people with ME/CFS its impact starts at the beginning of the clinical pathway with difficulties and delays in getting a diagnosis. If ME/CFS is not recognised or understood by healthcare professionals, it will not be diagnosed or managed appropriately. This reflected the committee's experience and they made recommendations raising awareness about what ME/CFS is and the importance of acknowledging this to the person with ME/CFS.

The committee noted the experience of not being believed can impact on the way people with ME/CFS engage with health and social care services. The committee were aware of people that had spent a long time trying to get recognition of their or their child's ME/CFS. This was frustrating and for some people had resulted in a loss of faith and trust in health and social care services. This was highlighted in the report on Children and Young people, where the limited understanding of ME/CFS by health-care professionals and their lack of empathy often meant parents had to make a lot of effort to convince clinicians there was a problem, this was characterised by multiple appointments and a repeated explanation of symptoms. This was unhelpful in terms of coping with the condition, often delayed the diagnosis and created anguish for people with ME/CFS and their families. The committee agreed the impact of not being believed on people with ME/CFS and their families and carers was important for health and social care professionals to consider and take into account when building a relationship with the person with ME/CFS and their families and made recommendations to reflect this. The committee considered this particularly relevant to children and young people and made a separate recommendation highlighting this (also see the discussion on safeguarding in evidence report B: information for health and social care professionals).

The committee decided to prioritise awareness of ME/CFS and its impact and place it at the front of the guideline. The first section of the guideline sets out principles of care for people with ME/CFS clearly stating that healthcare professionals should be aware that ME/CFS is a real condition that is complex and this reality should be acknowledged to the person with ME/CFS.

Nature of ME/CFS and lack of a clear management pathway (R1:RF7:R2:RF5)

Evidence suggested that the nature of ME/CFS in terms of its uncertain aetiology, complicated diagnostic process, non-specific symptoms and the absence of cure made the role of health professionals difficult in supporting people with ME/CFS (R2:RF5). Some health care professionals reported diagnosing ME/CFS as a last resort because making the diagnosis did not lead to obvious treatment and could have a negative effect resulting in a lack of access to care (R1:RF7. R2:RF5). This can lead to people remaining undiagnosed.

This invisibility of the illness often meant patients' need for help remained unrecognised and made them reluctant to ask for help. The complexity of ME/CFS and the frustration reported by health care professionals that there is not a clear management pathway is a consistent theme in the qualitative reviews conducted for this guideline (see evidence review A: Information, education and support for health and social care professionals, evidence review B:Information, education and support for people with ME/CFS, their families and carers).It was highlighted in both the children and young people, and people with severe ME/CFS reports (Appendix 1 and 2) and is discussed by Nina Muirhead in her expert testimony (Appendix 3).

The committee agreed that to address the lack of understanding of ME/CFS and its management health and social care professionals need better training and education and this supported the recommendations on training and education, which are discussed in evidence report B: information for health and social care professionals.

Relationship with the healthcare professional (R1:RF13, RF15. R2:RF15)

Evidence suggested that an established, on-going relationship with a health care professional (GP, family physician or therapist delivering care) who took the time to listen to the patient influenced care positively. It affected people's ability to demonstrate their symptoms, communicate their experiences and their engagement to primary care. The committee considered the issue of continuity of care to be common to many health conditions, however it was agreed that the implications are particularly significant for people with ME/CFS because access to many professionals can have both favourable and unfavourable consequences for someone with ME/CFS. This can result in a person having contact and appointments with several different people with a negative impact on the person's health potentially worsening symptoms. To avoid this unintended consequence, it is important there is one point of contact to co-ordinate care. This was common practice in the committee's experience in specialist care and they noted that although during specific treatments one professional is predominantly involved, other team members are easily accessible and can be more involved if the need arises. The committee made recommendations to provide a named contact in the person's primary care or specialist team to coordinate their care and support plan, help them access services and support them during periods of relapse.

People with ME/CFS and their families and friends

Acceptance of ME/CFS and pre-existing beliefs (R2:RF10, RF16, RF17, RF3 CYP, RF4 CYP)

Evidence suggested that being believed, acceptance of the diagnosis by the person with ME/CFS and its implications was crucial for engaging with treatment and health services to gain the most benefit. The importance of receiving a diagnosis and understanding around it was seen as pivotal in families' acceptance of the diagnosis and label and the recovery process and parents described a relief at being listened and believed. Evidence suggested that pre-existing beliefs about the illness and the treatment offered can influence decision to seek medical advice and treatment acceptance or engagement. Adolescents found accepting and adapting to ME/CFS management strategies to be challenging.

The committee considered that acceptance of the condition and its impact is a personal process and that each person with ME/CFS will have their own experience. The committee noted that it is important that people with or with suspected ME/CFS are given up to date information throughout the diagnostic and care pathway. This information should be tailored to the person's individual circumstances. The committee agreed the recommendations raising awareness about the reality and impact of ME/CFS and on providing information to people with ME/CFS would increase understanding of ME/CFS, which in turn may facilitate

the process of acceptance. The committee were aware that a person's experience and knowledge of other's experiences about support offered for ME/CFS has resulted in a hesitation to engage with health and social are services. The committee considered that making recommendations for patient led care, including explaining that the person with ME/CFS is in charge of their care and that they have the right to decline any part of their care and support plan without it affecting other aspects of their care would reassure and support people with ME/CFS to engage in services and to access the care they require.

Lack of social support (R2:RFCYP11)

Evidence suggested that negative attitudes from the social environment can act as a barrier to improvement implicating the family's ability to follow clinical advice. Although this finding was identified in children and young people, the committee considered that in their experience, disbelief and lack of social support could also act as a barrier to care in adults with ME/CFS. The committee hoped that the guideline would raise general awareness of ME/CFS, which would lead to wider acceptance of the condition and support for those living with it. This is also reflected in the recommendations raising awareness about the impact of not being believed.

Organisational factors that impact on care

Time constraints in primary care (R1:RF12, R2:RF4)

Evidence suggested that time constraints in primary care were a barrier to care and this was highlighted by both people with ME/CFS and health care professionals. The committee discussed that time constraints are an important barrier for all people with complex health conditions accessing care, but considered that due to the unpredictable and fluctuating nature of the condition people with ME/CFS may require additional flexibility around the timing, length and frequency of appointments The committee recommended that service providers should ensure people with ME/CFS can access health and social care services in several ways, including adapting the timing, length and frequency of appointments and treatments according to reasonable adjustments.

Accessibility (R2:RF13, RF6CYP)

Evidence suggested that the geographical location of healthcare providers, transportation links as well as the availability of appointments can impact people's ability to attend health care services. This finding was echoed in the evidence on children and young people, which showed that the location of therapy or health services can negatively impact young people's health and their ability to fully engage in therapy, while the flexibility of videoconferencing could overcome the barriers to care posed by the distance of healthcare services, the family's availability and symptom severity.

The committee were familiar with this issue from their own experience of ME/CFS as well as other chronic health conditions. The committee considered that although this barrier to care is not specific to ME/CFS, the journey may present more challenges for people with ME/CFS and potentially exacerbating their symptoms. In addition to the recommendations for a flexible approach to the timing, length and frequency of appointments and methods of delivering care, the committee made a recommendation to ensure people with ME/CFS can access health and social care services by taking into account physical accessibility, such as the distance to travel, availability of suitable transport, parking and the location of rooms where appointments and treatments are held. This also included specific considerations for people who need inpatient care, such as situation of the hospital bed, accessibility of toilets and washrooms and environmental factors.

The committee discussed the finding that videoconferencing could overcome some of the barriers to care faced by children and young people. The committee noted the COVID-19

pandemic has meant that HCPs have needed to change the way in which they interact with patients day-to-day. Most GPs and other HCPs are now set-up to deliver video consultations, and this may make this a more accepted and accessible method of monitoring/reviewing people with ME/CFS. The committee acknowledged the limitations and potential problems with videoconferencing, including difficulty with physical examinations and exposure of people with ME/CFS to blue light, which could exacerbate symptoms. The committee considered that videoconferencing can be a valuable alternative to face-to-face appointments in some circumstances but should not replace them altogether.

Children and young people: communication (R2: RFCYP9, RFCYP12)

Evidence suggested that parents of children with ME/CFS struggled to communicate an illness that was not visible and symptoms that their child, and not themselves, were experiencing. They also reported their children found it hard to put their experiences into words and it was difficult answering more probing questions in front of the child. Care should be child centred and the child with ME/CFS should have ownership and be heard. This was described by one clinician as 'even though it's going to be caregivers who are really following through with the plan, its' still not going to be as successful as if you're engaging with a young person and they have an element of understanding, appropriateness to their age, we can't lose sight that the young person needs to be involved with their care'.

The committee considered it important that health care professionals take these findings in to account in order to help tailor consultation styles, interpret reported experiences appropriately and to ensure effective management. A recommendation was made to ensure that care was child centred and to be aware that children and young people may find it difficult to describe their symptoms.

The committee were aware that the Royal College of Paediatrics and Child Health have developed resources, with input from children and young people, to aid their communication with health professionals. The 'Being Me' resources help children and young people to share who they are, how they are feeling and what support they would like. The materials include: feelings poster, children's health and wellbeing passport and top tips for doctors. These tools are especially effective for children and young people that do not feel comfortable to freely share their experiences, as described by this young person: "Emojis are an easy and fun way for us to tell doctors how we are feeling when we can't fully explain or don't want to. Children can point to an emoji or draw with their doctor." RCPCH &Us Voice Bank, 2018.

Children and young people: Barriers *of a virtual connection (R2:RF7CYP, RF8CYP)*

Evidence on children and young people's experiences of specialist treatment delivered by videoconferencing showed that this technology could be a barrier to care. Technical difficulties, such as issues with connection speed, reduced picture and sound quality and occasions when videoconferencing would intermittently stop working, were a barrier to effective communication between young people and health-care professionals. Despite the benefits that can be provided by a virtual connection with health professionals, communication can be compromised compared to face-to-face interactions with emotional cues being missed, the content and depth of discussions being limited.

The committee considered that findings related to children and young people's experiences of videoconferencing could also be applied to adults. The committee noted that there were concerns regarding the coherence of both findings, due to participants in the study expressing conflicting views on the extent to which technical problems and a virtual connection act as barriers to care. The committee agreed that technical issues are a limitation of videoconferencing, but that when the technology works well it can be of great value in certain circumstances. The committee also emphasised that no alternative method of care delivery should replace face to face contact altogether, but that when a person is too ill to attend in person, finding alternative ways to offer care is preferable to the person not

being able to access the care at all. Therefore, the committee did not wish to remove the option of videoconferencing as an alternative method of care delivery.

Language (R1:RF10)

Evidence suggested that health professionals, patients, carers and community leaders agreed that not speaking English acts as a barrier to the diagnosis and management of ME/CFS, with some BME patients not being able to adequately describe their symptoms or understand their GP during consultation.

The committee discussed the difficulties that non-English speaking people with or suspected ME/CFS can have in accessing health and social care services. They noted that although this barrier is not specific to people with ME/CFS, the complexity of ME/CFS and the non-specific nature of some of the symptoms makes them difficult to describe and for HCPs to understand. This adds to the difficulty in obtaining a diagnosis and then accessing care in non-English speaking people. To remind health and social care professionals about the importance of ensuring non-English people speaking are not disadvantaged the committee referenced the NICE guidelines on patient experience in adult NHS services and people's experience in adult social care services in the information and support section of the guideline.

Personal circumstances and symptom severity (R2:RF11, RF12, RF14,RF17)

Evidence suggested personal circumstances and availability, including work commitments, childcare, symptom severity and comorbidities can be barriers to accessing and benefitting from treatment. Evidence also showed that personal attributes such as being proactive, determined and positive can facilitate treatment access and motivation to engage in and benefit from treatment.

These findings were considered to support recommendations for patient led care and flexibility of treatment and appointments for all people with ME/CFS regardless of the severity of their symptoms. The committee agreed that being able to initiate treatment when people have the capacity and motivation to fully engage and offering flexibility around the timing, length and frequency of appointments and methods of delivering care should help minimise the impact of symptoms and other personal factors. Evidence showed that flexibility in the frequency and mode of medical appointments was valued by patients. Specific examples mentioned were later appointments, appointments via telephone and videoconference and home visits. These were suggested as examples of alternative and flexible methods of delivering care in the recommendation (also noted above).

The committee discussed that the unpredictability of the severity of people’s symptoms can sometimes prevent reliable planning ahead meaning that scheduled appointments (or work) may be missed or cancelled with little notice. The committee were aware that this could result in people being discharged from services under local ‘did not attend’ (DNA) policies. The committee agreed it was important to discuss with the person c the reasons for not attending and explore how the person could be supported to attend appointments. The expert testimony from Dr Husain noted that DNA rates in the service he worked in had reduced during the COVID-19 pandemic and suggested this may be due to increased videoconference appointments (see evidence report I: multidisciplinary care). Alongside this recommendation the committee noted that people with ME/CFS are unlikely to be seen at their worse and might be unable to have contact with services until their symptoms improve.

<u>People with severe or very severe ME/CFS</u>

Throughout the guideline reference is made to the breadth of symptoms (from being able to carry out most daily activities to severe debilitation) that people with ME/CFS can have. In the evidence specialist health-care professionals reported that a very small proportion of the people they saw were living with a severe or very severe condition and were significantly unwell, confined to home, or bedbound in a darkened room, and unable to communicate.

This was seen as extremely challenging for professionals who may have few helpful suggestions to support people with severe or very severe ME/CFS. Health care workers reported that people with severe or very severe ME/CFS often struggle with a low level of energy and concentration, which was described as a 'low load capacity', which made it difficult for some to read the texts in the programs or to even sit behind a computer. This resonated with the committee's experience and the committee discussed their experience and these findings alongside the report for people with severe ME/CFS.

The nature of severe or very severe ME/CFS means that this group of people can be invisible to health and social care services, throughout the guideline reference is made to the invisibility of people with severe and very severe ME/CFS. This was supported by the 'involving people with severe ME/CFS' report (appendix 2) with many of the respondents reporting being unwell for years or decades with few people reporting improving. The majority of people were housebound, some bedbound with all experiencing difficulties with activities of daily living and needing support from family members.

The committee recognised there is a lack of understanding about how people with severe or very severe ME/CFS are affected and the impact on their lives. This results in people with severe and very severe ME/CFS not receiving appropriate care and potentially receiving care that is harmful. In the people with severe ME/CFS report although some participants receive some form of disability benefit, many reported difficulties and delays accessing such payments. Nearly 2/3rds of the participants report a lack of social care support, other than disability benefits.

People with severe or very severe ME/CFS are a group for special consideration in this guideline and the committee agreed it was important to make recommendations to address the difficulties that people with severe or very severe ME/CFS have accessing health and social care services.

The committee noted that health and social care professionals rarely encountered people with severe or very severe ME/CFS and this results in a lack of knowledge and awareness about the severity of their symptoms. The committee agreed it was important to raise awareness about this and made recommendations describing the severity of symptoms and what this means in all aspects of their lives and the support they need. For example, people with severe or very severe ME/CFS can experience severe and constant pain and need careful physical contact taking into account possible sensitivity to touch. The committee noted that the experience of living with severe symptoms can significantly affect a person's emotional wellbeing and the committee commented that people with ME/CFS, particularly those with severe or very severe may be at higher risk of depression and suicide and healthcare professionals people caring for this population need to be aware of this. They noted the initial assessments and the scheduled review recommended in the guideline include wellbeing and this should be explored.

Taking into account the impact of severe or very severe symptoms the committee made specific recommendations in the following area highlighting where particular care was needed for people with severe or severe ME/CFS. These are also discussed in the guideline reports discussing the management of care and symptoms.

The committee discussed the importance of energy management for people with ME/CFS and the prioritisation of daily activities. They commented that this is heightened in people with severe and very severe ME/CFS where even the smallest action or interaction may result in worsening of symptoms. People with severe or very severe ME/CFS report they can be hypersensitive to noise and even people whispering can be very painful (see appendix 2). The committee recommended that all interactions should be risk assessed to ensure that any benefits are not at the result of worsening symptoms.

Advocacy and safeguarding are discussed in evidence report B: information for health and social care professionals.

The committee noted that admission to hospital was very difficult for people with severe or very severe ME/CFS and were aware of people that had described this as a frightening painful experience. The committee made a specific recommendation about planning hospital care for people with ME/CFS and what a transfer to and care in hospital for people with severe ME/CFS should look like to minimise discomfort and post exertional symptom exacerbation, this could include requesting an ambulance for transfer to hospital.

Although access to appointments is discussed above and the committee made recommendations to consider home visits for people with ME/CFS, the committee considered this should be strengthened in people with severe or very severe ME/CFS and recommended offering home visits, particularly to carry out their holistic assessment and to develop a care and support plan. This was supported by the findings in the report on people with severe ME/CFS (Appendix 2).

Managing severe or very severe ME/CFS (also in the management reports F and G).

The committee discussed the sensitivities and difficulties of implementing energy management in people with severe ME/CFS due to the severity and impact of their symptoms. The committee noted energy management strategies for people with severe or very severe ME/CFS should be supported by a physiotherapist or occupational therapy service that specialises in ME/CFS as the potential for causing harm by inappropriately managing activity is greater. In addition, the committee noted when agreeing energy management strategies with people with severe ME/CFS (and their families and carers as appropriate) that changes in activity are smaller and any increases (if possible) much slower. The committee noted people with severe or very severe ME/CFS have limited mobility and are often house or bedbound and agreed that it is important that they are assessed at every contact for pressure ulcers and risk of contractures.

The committee noted that none of the clinical effectiveness evidence included or reflected the needs of people with severe or very severe ME/CFS. They recognised that CBT could be supportive for people with severe or very severe ME/CFS but because of the severity of their symptoms it is important to adapt the delivery of CBT to accommodate the limitations of those with severe or very severe ME/CFS. This might include shorter, more infrequent sessions, and longer-term goals. To reflect this the committee also noted that those delivering CBT to a person with severe ME/CFS should seek supervision and consultation with those more experienced in working with ME/CFS, to enable an understanding of the process and pace of CBT for the severely affected, including realistic expectations and goals of therapy.

The committee discussed whether there were any specific considerations for people with severe or very severe ME/CFS related to dietary management/strategies. The committee considered that this group are particularly at risk of problems associated with eating and are likely to require additional support. Therefore, the committee recommended that people with severe or very severe ME/CFS are referred to a dietitian who specialises in ME/CFS for a full dietetic assessment. The committee also discussed some general dietary strategies that could be helpful for people with severe or very severe ME/CFS from their own experience. These included eating little and often, having nourishing snacks and drinks, finding easier ways of eating to conserve energy and using modified eating aids. The committee made a recommendation to be aware of the types of dietary issue that people with severe or very severe ME/CFS may face and the possible strategies to support them.

The committee discussed whether there were any specific considerations for people with severe or very severe ME/CFS related to dietary supplements. They considered that people with severe or very severe ME/CFS are at a higher risk of vitamin D deficiency. However, the committee decided that the recommendations in the NICE guideline on vitamin D adequately deal with the management of deficiency and no additional recommendations specific to this population were required.

Barrier and facilitators to a diagnosis

Lack of knowledge and complexity of diagnosing ME/CFS (R1:RF1, RF8, RF9, RF11, RF15, RFCYP2, RFCYP6)

The committee discussed why healthcare professionals doubt the existence of ME/CFS as a legitimate medical condition. Healthcare professionals including GPs, practice nurses and family physicians described their struggle to make sense of ME/CFS symptoms and admitted their limited clinical knowledge and understanding of ME/CFS (R1:RF1). This was echoed in the experience of patients and carers and the belief that they often knew more than their GPs and provided them with information, and this is a cross cutting theme across the reviews in the guideline. Healthcare professionals' struggle to make sense of symptoms was highlighted (R1:RF8, RF9) with the acknowledgement that the fluctuating nature of the condition and the inability to measure symptoms (often running tests with only negative results) was bewildering and frustrating. This was supported by the findings there was an inconsistency in the terms used to describe ME/CFS and that health care professionals were uncertain what label to use with some HCPs using the term medically unexplained symptoms because of being unable to provide a clear aetiology (R1:RFCYP6). In addition, physicians reported that the variability in different diagnostic criteria is confusing and the variability of symptoms means that in some criteria it is possible for two patients to have a diagnosis of CFS without having any of the same symptoms (except for fatigue) (R1:RF11). It is clear this results in a lack of confidence in health professionals and compounds the reluctance to diagnose ME/CFS. One of the few facilitators identified was exposure to new and different presentations of ME/CFS, this enables practitioners to recognise the condition and develop confidence in their diagnostic skills (R1:RF15).

The committee agreed that health and social care practitioners needed to be better informed about the key symptoms of ME/CFS and how to diagnose ME/CFS. Addressing lack of understanding and confusion about how to identify ME/CFS the committee made recommendations about when to suspect ME/CFS. To support health care professionals better identify people with suspected ME/CFS the committee agreed on criteria based on the IOM (2015). The differences and inconsistencies in the many case definitions of ME/CFS was identified as confusing (RF1:RF11) and this is also further discussed in evidence report D: diagnosis where the different case definitions are reviewed in detail. The committee agreed that to support health and social care professionals to diagnose ME/CFS they need better training and education, and this supported the recommendations on training and education, which are discussed in evidence report B: information for health and social care professionals.

Focus on physical symptoms (R1:RF3)

Evidence suggested people from BME groups may focus on describing physical symptoms and their healthcare professionals focus on identifying physical symptoms in people from BME groups and as a result may miss other important symptoms such as fatigue, loss of concentration and sleep problems and miss a diagnosis of ME/CFS. The committee noted this finding was only identified in one study but acknowledged that research in people with ME/CFS in BME groups is sparse and considered it an important finding. The committee hoped that the recommendations on the principles of care and suspecting ME/CFS would provide guidance that should be applied to anyone with or suspected ME. The committee discussed how this finding highlights the importance of good relationships between patients and health care professionals, careful history taking and listening to the presentation of symptoms (R1: RF13, RF14) in facilitating a diagnosis.

*Diagnostic overlap and co-morbidities (R1:RF6, RF5CYP)*The committee discussed the finding that people with ME/CFS report being initially misdiagnosed, with many people being

referred to psychiatrists. This finding concurred with their experiences noting that non-specific symptoms such as fatigue, loss of concentration and sleep problems can frequently be misinterpreted as another condition, such as depression. The committee noted how this finding supports the importance of good relationships between patients and health care professionals, careful history taking and listening to the presentation of symptoms (R1: RF13, RF14) in facilitating a diagnosis.

Referral to specialist services (R1:RF4, RF5, RF12, RF3CYP, RF4CYP, R2:RF3)

Evidence suggested that referral to specialist services or secondary care facilitates the diagnosis, providing access to experts that can confirm the diagnosis and support GPs and HPs who may lack the confidence to diagnose ME/CFS (R1:RF4). This was supported by the finding that ten minute consultations with a patient with ME/CFS can be challenging due to the variety and complexity of symptoms. A ten minute consultation was seen as a potential barrier to diagnosis particularly by ME/CFS specialists reporting that GPs may not be able to gain a complete understanding of the variety of symptoms patients can experience and the impact of those on their life (R1:RF12).

The committee agreed with the findings that specialist services can facilitate a diagnosis of ME/CFS but recognised the finding that pathway to referral can be long and difficult with a lack of specialist services with some people self-diagnosing their illness (R1:RF5, RF4CYP, R2, RF3). The committee discussed the relationship between these findings and the potential implications of a recommendation to refer people with symptoms suggestive of ME/CFS to specialists. The committee agreed that the benefits of a quicker diagnosis of ME/CFS would mean people access appropriate care sooner and enable better symptom management. The finding from this review supported the recommendations that people with ME/CFS should be referred to a specialist ME/CFS service to have a provisional diagnosis confirmed and a personalised care and support plan developed. This is discussed evidence report D: diagnosis and evidence report I: multidisciplinary care.

Barriers and facilitators to management *Lack of diagnosis (R1:RF2)*

A lack of diagnosis, a delayed diagnosis or a misdiagnosis was identified in the evidence as an important barrier to care and people may self-diagnose as a result of the delay (evidence report C: access to care). Until an accurate diagnosis is made, people with ME/CFS find themselves unable to access appropriate treatments, or worse, may be exposed to inappropriate treatments which can make their condition worse. A similar finding was identified for children and young people with ME/CFS (Appendix 1).

The committee weighed the benefit of a timely diagnosis ensuring that people with ME/CFS receive appropriate care against the risk of missing other differential diagnoses if a diagnosis is made too early. Further discussion of the duration of symptoms necessary to diagnose ME/CFS can be found in evidence report D: diagnosis. The qualitative evidence reflected the committee's experience that many people experience a delay in diagnosis, and it was considered that awareness should be raised about the importance of early diagnosis. The committee decided to include a recommendation within the general principles of care to raise awareness that ME/CFS requires early diagnosis to start appropriate care to prevent potential deterioration of condition and worsening of symptoms.

Children and young people: communication between schools and health-care professionals (R2:RF4CYP, RFCYP10, RF13CYP, RFCYP14, RFCYP15)

Evidence suggested that communication of a diagnosis to schools was important. Both teachers and families identified the diagnosis as a catalyst to the school taking the health concerns seriously and implementing the necessary support. Teachers emphasised that at an organisation/policy level, teachers needed this formal diagnosis to implement treatment

recommendations, such as reduced timetables. There was a level of frustration from all parties. Teachers expressed frustration about the limited input from clinicians and the difficulties in supporting particularly young children. Families reported that schools did not believe them and did not adapt to the child's needs and created a lot of resistance. Equally clinicians were frustrated by the lack of support from schools. Specialist health-care professionals working with schools was a core part of treatment for children and young people, which involved educating schools, correcting unrealistic expectations and formulating reduced timetables. The committee discussed how important these findings were and how they reflected their experience. Recommendations related to training and education are discussed in evidence report A: information for people with ME/CFS.

Nature of ME/CFS and lack of a clear management pathway (R2: RF5, RF6, RF4CYP, RF5CYP, RFCYP12, RFCYP15)

Evidence suggested the nature of ME/CFS in terms of its uncertain aetiology, complicated diagnostic process, non-specific symptoms and the absence of cure made the role of health professionals difficult in supporting people with ME/CFS. HCPs described their frustration in not being able to measure how people with ME/CFS were responding to their care and described the condition as invisible on good days. This resulted in people's needs being unrecognised and made them reluctant to ask for help. This was highlighted by specialist paediatricians, who described the difficulty they found in helping children with 'CFS/ME' due to variability and fluctuation of the condition. This was particularly highlighted in younger children and the difficulties in explaining self-management and the importance of understanding the consequences of over exertion.

HCPs reflected on the importance of the diagnosis 'label' used and how this made a difference to the clinical pathway and access to services and the interventions available. An example given was of a diagnosis of either chronic pain or ME/CFS and that depending on diagnosis given different specialist teams would be involved, and rehabilitative treatment would differ in each case. Some health care professionals reported using the label ME/CFS as a last resort because making the diagnosis did not lead to obvious treatment.
The committee considered that this finding demonstrated the need for better training and education for health care professionals and supported the recommendations on training and education, which are discussed in evidence report B: information for health and social care professionals. The theme of invisibility is echoed in evidence report B and reinforces the importance of ensuring that HCPs understand that they may not see people with ME/CFS at their worst and may not understand they extend of the care they need.

Referral to specialist services (R2:RF3, RF2CYP)

Evidence suggested that people with ME/CFS would be better managed by a specialist ME/CFS service. GPs highlighted the complexity of the condition and people with ME/CFS recognised that GPs did not have the time to manage their condition. People who had accessed specialist services felt they had benefited with diagnosis being confirmed and better management of their symptoms. GPs described the limited number of specialist services and the difficulty in accessing and referring people. This finding reflected the committee's experience and is reflected above in the discussion about the findings about referral to specialist services for diagnosis. This is also supported in evidence report D: diagnosis and evidence report I: multidisciplinary care and reflected in the recommendations on referral.

Accessibility of treatment options (R2:RF7)

Evidence suggested that people with ME/CFS lack access to helpful treatment options due to the unavailability in primary care or due to the strict acceptance criteria in some specialist services. The committee considered this finding in relation to the lack of evidence of

effectiveness identified for many of the treatments reviewed in this guideline. Despite there not being any known cure for ME/CFS, the committee considered there are interventions that are helpful for managing the ME/CFS symptoms and these should be accessible to people with ME/CFS. Recommendations related to symptom management are discussed in the management reports (F and G). Taking into account the complexity of the ME/CFS, the committee recommended that all health care professionals caring for people with ME/CFS should have training that is relevant to their role (see evidence report B: information for health and social care professionals). The committee noted that some therapies, such as CBT should be delivered by professionals with experience and training in ME/CFS and require supervision by a specialist in ME/CFS. Recommendations related to symptom management are discussed in the management reports (F and G).

Experiences of interventions (R2:RF8, RF9,RF15)

Evidence suggested that a nurse-led rehabilitation intervention was difficult to apply to everyday life, which was identified as a barrier to care. Realistic goal setting towards management rather than cure was seen as vital for treatment success. The committee discussed that a negative experience can result in a person disengaging from health and social care services. The committee discussed the importance of the availability of good care provided by health and social care professionals trained in ME/CFS (see evidence report B: information for health and social care professionals).

Individual characteristics of the therapists such as their attitude towards treatment, the ability to flexibly tailor the intervention to the needs of the individual and to effectively communicate with them were seen as important factors influencing the implementation of interventions. The committee noted concerns about applicability as evidence was based on one study on therapists and managers implementing internet-based CBT. However, the importance of a good therapeutic relationship to the experience of treatment and individualised care were strong themes identified across many interventions in the review of people's experiences of interventions for ME/CFS and is discussed further in the management reports (F and G). The committee considered that recommendations for patient led care, including explaining that the person with ME/CFS is in charge of their care and that they have the right to decline any part of their care and support plan without it affecting other aspects of their care would reassure and support people with ME/CFS to engage in services and to access the care they require.

3.3 Cost effectiveness and resource use

Barriers and facilitators to diagnosis

Cost effectiveness evidence was not sought as this was a qualitative review.

The recommendations describe barriers to diagnosis of ME/CFS that health care professional should be aware of when managing people who might have this illness. The committee considered that the review's findings demonstrated the need for better training and education for health care professionals and supported the recommendations on training and education, which are discussed in evidence report B: information for health and social care professionals.

Barriers and facilitators to care

Cost effectiveness evidence was not sought as this was a qualitative review.

The review evidenced the challenges and negative impact of healthcare attendances. The committee therefore recommended that providers make reasonable adjustments to the timing and length of appointments and treatments. They specifically mentioned later appointments, appointments via telephone and videoconference and home visits. In 2013, a

survey of all 49 ME/CFS services in England showed that 19 services did not normally provide services for severely affected people and another 3 did not provide home visits or inpatient services.[96] Therefore, more resources could be required in some areas.

They also recommended improving physical accessibility, by considering the distance to travel, availability of suitable transport, parking and the location of rooms where appointments and treatments are held. Some of these adjustments might require extra staff time or other healthcare resource use and the cost effectiveness of these adjustments is uncertain. However, for equity reasons, ME/CFS patients need the same access to healthcare as other NHS patients that is commensurate with the severity of their illness, which for many is very limiting. There is evidence that people with ME/CFS have very poor quality of life, worse than most other chronic conditions.[53]

The committee made a recommendation to allocate a single point of contact to the person with ME/CFS. The cost effectiveness of this recommendation is uncertain. This could be implemented differently in different regions according to local service structures and needn't necessarily require the addition of new staff. It could improve the efficiency of patient care by reducing the burden of repeated appointments.

Another theme was the need for specialist services as a source of information and support for health care professionals but also the need for a clear clinical management pathway. This was echoed in the reviews of patient information needs and health care professional information needs. The committee recommended that specialist multidisciplinary teams should be used to confirm diagnosis, establish a treatment plan and provide support for primary care services. The cost effectiveness of a specialist multidisciplinary team is uncertain, but the uneven provision of specialist services has been identified by patients and professionals as a key contributor to delayed diagnosis and poor patient outcomes.

The committee also concluded that better training and education for health care professionals would reduce barriers to care – see evidence report B: information for health and social care professionals.

3.4 Other factors the committee took into account

The committee discussed the lack of evidence exploring access to social care and the support needed to enable people with ME/CFS to maintain their independence. The committee agreed this was an important area of care that was neglected in people with ME/CFS.

Accessing social care and maintaining independence

The committee recommended that all people with ME/CFS should have their needs and preferences for social care discussed as part of the personalised care and support plan to support people to maintain their independence at home. This should explore the person's energy limits and the capacity to carry out activities of daily living and any other activities. Then if a person needs support a social care assessment should be conducted and include an assessment of: personal care needs to enable them to carry out activities of daily living, potential adaptions to their home (such as environmental controls to avoid glare from lights), equipment to maintain independence. They should be asked about any practical support needs, such as financial support and advice. Where needs are identified an assessment should be undertaken and support and guidance given on how to access the services. The committee were aware that people with ME/CFS have difficulties in accessing the equipment they need to participate in activities of daily living and maintain their quality of life and made a recommendation to provide the equipment identified in the personalised care and support plan without delay. The committee discussed aids, particularly wheelchairs, and the hesitancy of some health and social care professionals to facilitate access to them due to the incorrect belief that deconditioning is the main cause of symptoms in ME/CFS and a lack of

understanding of post-exertional symptom exacerbation. The committee considered that aids, such as wheelchairs, may allow some people to preserve energy, that would otherwise be wasted on walking, for more meaningful activities whilst remaining within their energy limits (for example, being able to attend a social activity or medical appointment).

Pregnancy, childbirth and post-natal care

The committee discussed the lack of research including pregnant women, childbirth and post-natal care in all areas of the guideline. This committee noted there is a general lack of information available about how to support women with ME/CFS and their partners during pregnancy through to the post-natal period. The committee agreed that women with ME/CFS can have very different experiences of pregnancy and childbirth on their symptoms. The committee agreed they did not have the expertise to make any specific recommendations but considered that the focus in the guideline on personalised care and regular review of care should prompt the necessary planning required for pregnant women through to and including the post-natal period.

To raise awareness of this gap in the evidence pregnant women and women in the post-natal period have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations.

Appendices

Appendix A Review protocols

Review protocol for barriers and facilitators to the diagnosis

ID	Field	Content
0.	PROSPERO registration number	CRD42019138129
1.	Review title	What are the barriers and facilitators to the diagnosis of ME/CFS?
2.	Review question	What are the barriers and facilitators to the diagnosis of ME/CFS?
3.	Objective	People with ME/CFS report delays in diagnosis, and research has highlighted that many GPs lack the confidence and knowledge to recognise and diagnose ME/CFS. This review aims to identify the barriers and facilitators of the process of diagnosing people with ME/CFS.
4.	Searches	The following databases will be searched: • Embase • MEDLINE • CINAHL • PsychINFO Searches will be restricted by:

		• English language The searches may be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion if relevant. The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	ME/CFS
6.	Population	• Adults, children and young people who are diagnosed with ME/CFS, or who are suspected of having ME/CFS by their primary clinician. • Clinicians caring for people with ME/CFS, or people suspected to have ME/CFS
7.	Intervention/Exposure/Test	Perceptions of patients and clinicians of the barriers and facilitators to the smooth and effective running of the diagnostic process. What slowed it down or got in the way? What aspects of care helped? What were the preconceived attitudes?

8.	Comparator/Reference standard/Confounding factors	N/A
9.	Types of study to be included	Qualitative studies (e.g. transcript data collected from focus groups / semi structured interviews)
10.	Other exclusion criteria	Exclusion: Quantitative studies (i.e. closed questionnaire surveys)
11.	Context	N/A
12.	Primary outcomes (critical outcomes)	Themes emerging from qualitative data
13.	Secondary outcomes (important outcomes)	Not applicable
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract information from studies (see Developing NICE guidelines: the manual section 6.4). Once saturation is considered to have been reached (all the themes are already covered in the data extraction) data from other included papers will

		not be extracted or critically appraised, but the paper will still be read to check for any additional themes and will be noted in the included studies. The point at which data extraction is reached will be noted within the review.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. For this review the CASP qualitative checklist will be used to assess risk of bias of individual studies. A sample of 10% of the critical appraisals will be quality assured by a second reviewer. Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
16.	Strategy for data synthesis	The synthesis of qualitative data will follow a thematic analysis approach. Information will be synthesised into main review findings. Results will be presented in a detailed narrative and in table format with summary statements of main review findings. GRADE CERQual will be used to synthesise the qualitative data and assess the certainty of evidence for each review finding.
17.	Analysis of sub-groups	Stratification: • Adults, young people and children • People with severe ME/ less severe ME
	Type and method of review	☐ Intervention

18.		☐ Diagnostic ☐ Prognostic ☒ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)		
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	01/05/19		
22.	Anticipated completion date	01/03/20		
23.	Stage of review at time of this submission	**Review stage**	**Started**	**Completed**
		Preliminary searches	☐	☑
		Piloting of the study selection process	☐	☑

		Formal screening of search results against eligibility criteria	☐	☐
		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	**5a. Named contact** [Give development centre name] **5b Named contact e-mail** [Guideline email]@nice.org.uk [Developer to check with Guideline Coordinator for email address] **5e Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE) and the National Guideline Centre		
25.	Review team members	From the National Guideline Centre: • Dr Kate Kelley • Ms Maria Smyth • Dr Mark Perry		

		• Ms Melina Vasileiou • Dr Karin van Bart • Mr David Wonderling • Ms Agnes Cuyas • Ms Amy Kesley
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10091
29.	Other registration details	N/A
30.	Reference/URL for published protocol	[Give the citation and link for the published protocol, if there is one.]

31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: Notifying registered stakeholders of publication Publicising the guideline through NICE's newsletter and alerts Issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32.	Keywords	
33.	Details of existing review of same topic by same authors	N/A
34.	Current review status	☒ Ongoing ☐ Completed but not published ☐ Completed and published ☐ Completed, published and being updated ☐ Discontinued
35..	Additional information	N/A
36.	Details of final publication	www.nice.org.uk

Review protocol for barriers and facilitators to care for people with ME/CFS

ID	Field	Content
0.	PROSPERO registration number	CRD42019152096
1.	Review title	What are the barriers and facilitators to the care of people with ME/CFS?
2.	Review question	What are the barriers and facilitators to the care of people with ME/CFS?
3.	Objective	To identify the barriers and facilitators of the care of people with ME/CFS
4.	Searches	The following databases will be searched: • Embase • MEDLINE • CINAHL • PsychINFO Searches will be restricted by: • English language The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review.

5.	Condition or domain being studied	**ME / CFS**
6.	Population	• Adults, children and young people who are diagnosed with ME/CFS, or who are suspected of having ME/CFS by their primary clinician and their families/carers. • Health and social care professionals caring for people with ME/CFS, or people suspected to have ME/CFS
7.	Intervention/Exposure/Test	Perceptions, experiences and views of patients, health and social care professionals of the assisting factors and hurdles during the process of care.
8.	Comparator/Reference standard/Confounding factors	NA
9.	Types of study to be included	Qualitative studies (e.g. transcript data collected from focus groups / semi structured interviews)
10.	Other exclusion criteria	Exclusion: Quantitative studies (ie closed questionnaire surveys)
11.	Context	N/A
12.	Primary outcomes (critical outcomes)	Themes emerging from qualitative data
13.	Secondary outcomes (important outcomes)	Not applicable
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be

		reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract information from studies (see Developing NICE guidelines: the manual section 6.4). Additional qualitative studies will be added to the review until themes within the analysis become saturated; i.e. studies will only be included if they contribute towards the development of existing themes or to the development of new themes. The point at which data saturation is reached will be noted within the review.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual: For this review the CASP qualitative checklist will be used to assess risk of bias of individual studies. A sample of 10% of the critical appraisals will be quality assured by a second reviewer. Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary.
16.	Strategy for data synthesis	The synthesis of qualitative data will follow a thematic analysis approach. Information will be synthesised into main review findings. Results will be presented in a detailed narrative and in table format with summary statements of main review findings.

		GRADE CERQual will be used to synthesise the qualitative data and assess the certainty of evidence for each review finding.		
17.	Analysis of sub-groups	Stratification: • Children/young people vs. adults • People with severe ME/ less severe ME (as defined by the studies) • People with ME/CFS/families/carers vs. clinicians		
18.	Type and method of review	☐ Intervention ☐ Diagnostic ☐ Prognostic ☒ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)		
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	01/05/19		
22.	Anticipated completion date	01/03/20		
23.	Stage of review at time of this submission	**Review stage**	**Started**	**Completed**
		Preliminary searches	☐	☑

		Piloting of the study selection process	☐	☑
		Formal screening of search results against eligibility criteria	☐	☐
		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	**5a. Named contact** [Give development centre name] **5b Named contact e-mail** [Guideline email]@nice.org.uk [Developer to check with Guideline Coordinator for email address] **5e Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE) and the National Guideline Centre		
25.	Review team members	From the National Guideline Centre: • Dr Kate Kelley • Ms Maria Smyth		

		• Ms Melina Vasileiou • Dr Richard Clubbe • Dr Karin van Bart • Mr David Wonderling • Ms Agnes Cuyas • Ms Amy Kelsey
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10091
29.	Other registration details	N/A
30.	Reference/URL for published protocol	[Give the citation and link for the published protocol, if there is one.]

31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: Notifying registered stakeholders of publication Publicising the guideline through NICE's newsletter and alerts Issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
32.	Keywords	
33.	Details of existing review of same topic by same authors	N/A
34.	Current review status	☒ Ongoing ☐ Completed but not published ☐ Completed and published ☐ Completed, published and being updated ☐ Discontinued
35..	Additional information	N/A
36.	Details of final publication	www.nice.org.uk

Appendix B Literature search strategies

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

- What are the barriers and facilitators to the diagnosis of ME/CFS?
- What are the barriers and facilitators to the care of people with ME/CFS?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[102]

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

B.1 Clinical search literature search strategy

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

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

Table 7: Database date parameters and filters used

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

Medline (Ovid) search terms

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

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

Embase (Ovid) search terms

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

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

Cochrane Library (Wiley) search terms

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

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

CINAHL (EBSCO) search terms

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

PsycINFO (ProQuest) search terms

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

Epistemonikos search terms

1.	(advanced_title_en:((advanced_title_en:((chronic* fatigue* syndrome*) OR (fatigue* syndrome* OR fatigue* disorder* OR postviral fatigue* OR post viral fatigue* OR fatigue* immune dysfunction OR post infection fatigue* OR postinfection fatigue*) OR (encephalomyelitis OR encephalopathy) OR ("ME/CFS" OR "CFS/ME" OR "CFIDS"

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

Appendix C Qualitative evidence study selection

Figure 5: Flow chart of qualitative study selection for the review of Barriers and facilitators to the diagnosis

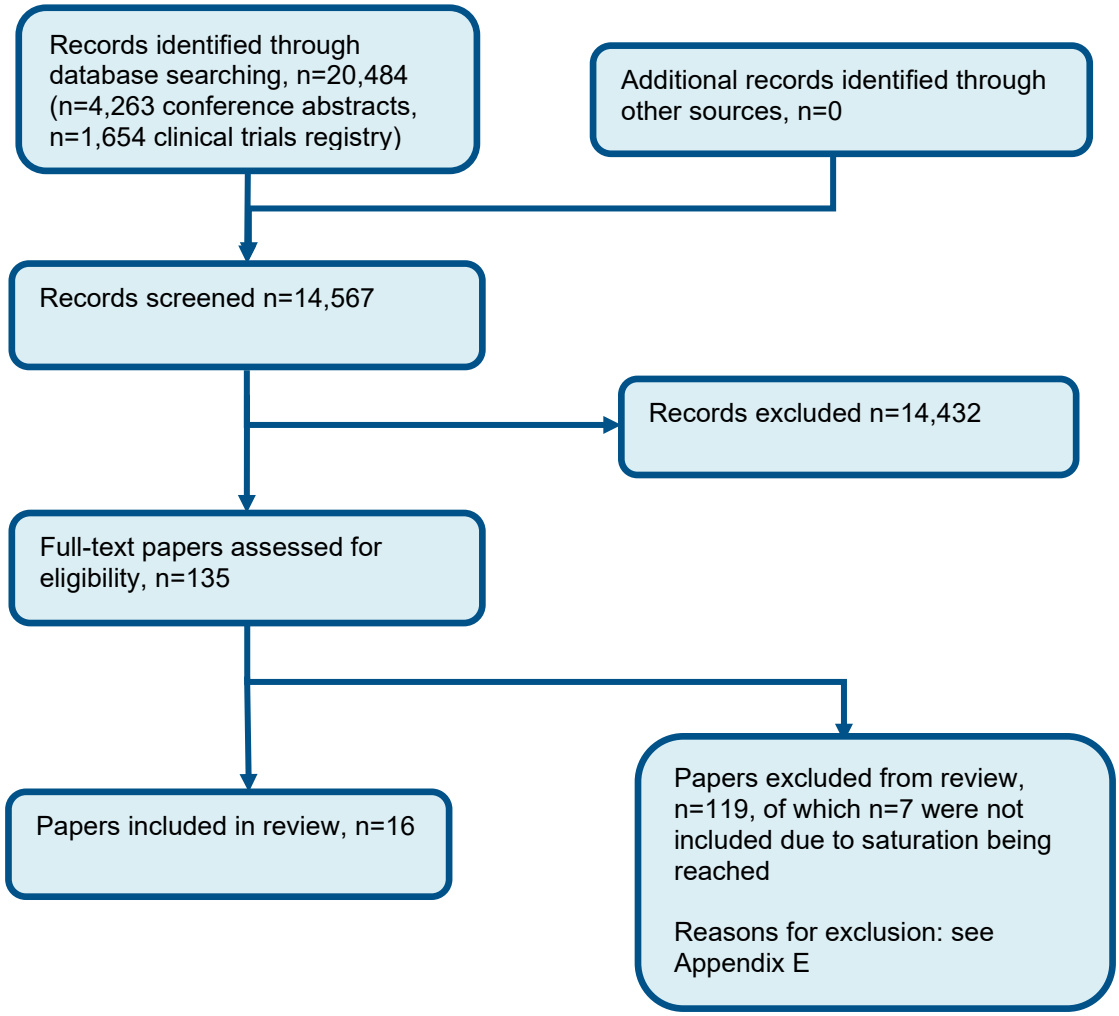
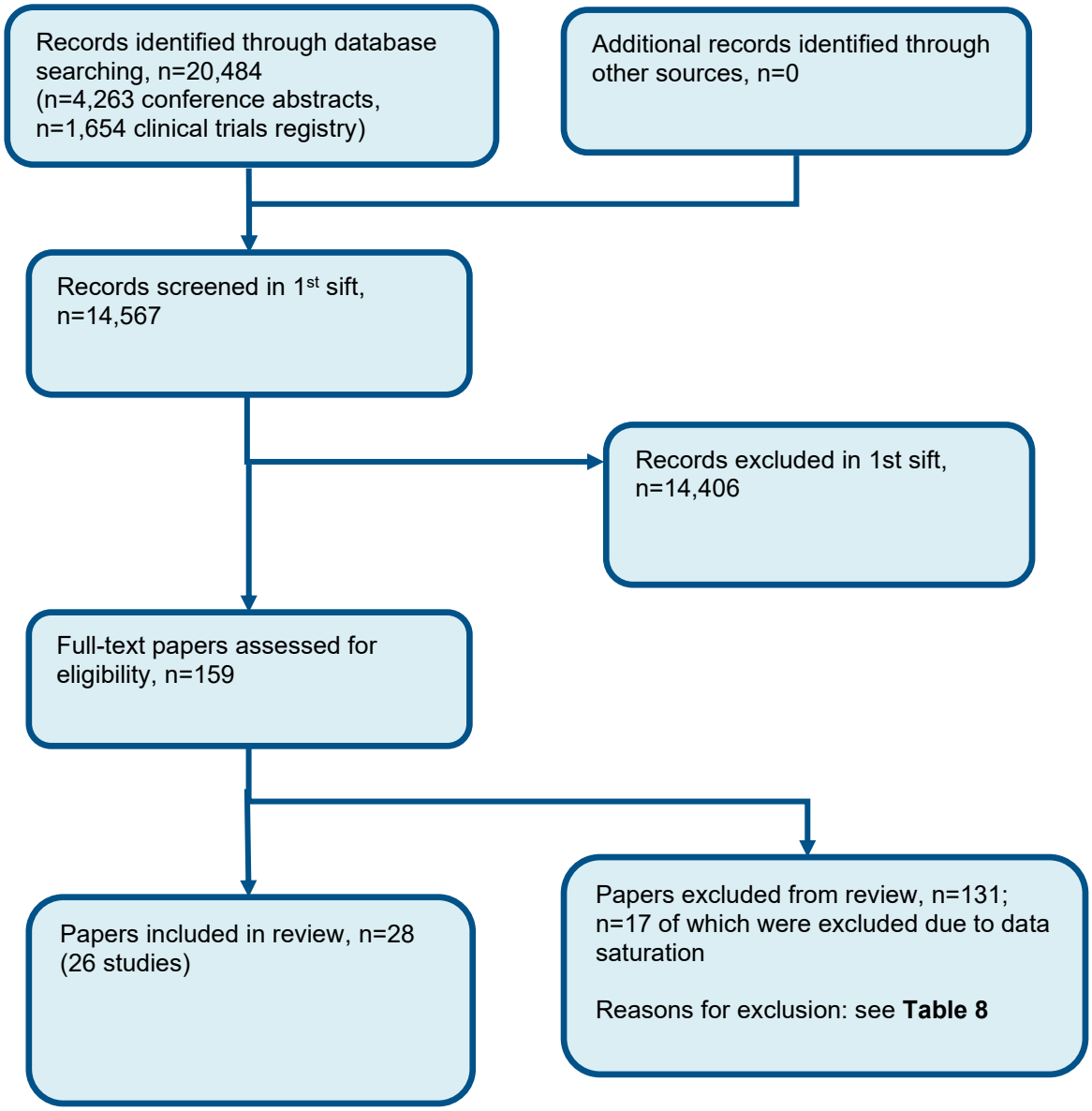


Figure 6: Flow chart of qualitative study selection for the review of barriers and facilitators to care of people with ME/CFS



Appendix D Qualitative evidence

Barriers and facilitators to the diagnosis

Study (primary & secondary analysis)	Bayliss 2014[18, 44]
Aim	To explore the possible reasons for the lower levels of diagnosis of 'CFS/ME' in the Black Minority Ethnic group (BME) population and the implications for management. Secondary analysis: To explore making the diagnosis and managing 'CFS/ME' in the UK form the perspectives of patients, carers, community leaders and primary care practitioners, to understand why 'CFS/ME' may not be commonly diagnosed is South Asia (SA).
Population	35 key stakeholders in NW England: BME patients (n=11), carers (n=2), community leaders (n=5) and GPs (n=9); recruited via purposive sampling.
Setting	Patient and carers were recruited through existing 'CFS/ME' support groups and South Asian community groups in North West England; Other participants were recruited through specialist 'CFS/ME' services in the NHS. GPs were recruited through GP practices.
Study design	Qualitative interview study
Methods and analysis	Face-to-face semi-structured interviews were conducted using topic guides: BME patient/carer interviews focused on experiences of accessing primary care, illness models, attitudes of family and community and sources of support; community leaders' interviews explored understanding of 'CFS/ME' and role of family, community, primary care and religion in the diagnosis and management of 'CFS'; HP interviews focused on current practice, attitudes towards CFS and perceived barriers faced making the diagnosis and managing 'CFS/ME' in people in BME groups. Interviews were digitally recorded and analysed in parallel with interviewing using components of thematic analysis that were in line with modified grounded theory. In the secondary analysis, a new analytic framework was developed on culture and barriers to diagnosis. The secondary researcher was naïve to the original research findings. The process of refinement and validation of findings was conducted through a collaborative exercise creating feedback loops between the secondary researcher and the primary researchers. Further discussion between authors resulted in the identification of themes specifically relevant to BME patients presented in the paper.
Findings	**Focus on physical symptoms** a) **Patients' biomedical illness model:** Community leaders and HPs described how they perceived that many BME patients held biomedical models of illness and therefore would focus on presenting physical symptoms such as headaches and muscle pain when consulting with their GP, suggesting BME people would be more likely to refrain from seeking medical advice about non-specific symptoms such as fatigue, loss of concentration and problems with sleep- fatigue was reported to be part of the expected aging process is some BME communities.

Study (primary & secondary analysis)	Bayliss 2014[18, 44]
	b) **HP focus on physical symptoms:** Patients and community leaders suggested that HPs might focus on physical symptoms and patients might not be encouraged to discuss nonspecific symptoms such as fatigue, with the majority of GPs describing 'CFS/ME' as a set of symptoms which they found hard to understand but alluded to a 'biopsycho-social' etiology and impacting on function.
	GP turnover
	High turnover of GPs in the inner city practices that may provide care for people in BME communities was cited as a reason why some people may not receive a diagnosis of 'CFS/ME'. Patients believed that a lack of continuity meant that they were unable to build a long-term relationship with their health professional and GPs were unable to take the holistic approach considered necessary for the diagnosis of 'CFS/ME' to be made.
	Language & understanding
	HPs, patients, carers and community leaders agreed that not speaking English acts as a barrier to the diagnosis and management of 'CFS/ME', with some BME patients not being able to adequately describe their symptoms or understand their GP during consultation. Community leaders also described how a person's lack of understanding of English limits their ability to research their symptoms using the internet or books resulting in a lack of awareness of 'CFS/ME' compared to the white population.
	Culture specific issues
	a) **Community expectations:** The expectation to fulfil certain roles within the family or community was described as a barrier to the diagnosis and management of 'CFS/ME', with some patients commenting on pressures from the family for high academic achievement and the perceived stigma attached to low achievement which pushed patients to ignore symptoms of 'CFS/ME' until they reached a crisis point. GPs suggested that patients of BME origin present with vague physical complaints, with somatisation being more common; culturally BME communities do not consider tiredness or fatigue a symptom that requires medical assistance, instead other physical symptoms are reported.
	b) **Religion and culture:** Patients and community leaders described how some BME people would turn to religion or spiritual healers rather than primary care when experiencing fatigue, believing that spirits or black magic may be causing the condition. Religion and prayer were also cited as motivators for patients to attempt to manage their symptoms and not seek medical advice. White British health professionals in the study were not aware of the barriers in the diagnosis and management of 'CFS/ME' in primary care.
	c) **Racial stereotypes & stigmatisation:** HPs recognised the possible influence of racism and stereotypes in preventing the diagnosis of 'CFS/ME'. Patient, carers and community leaders described how they believed some GPs may hold stereotypical views of people from certain cultures such as being 'lazy', 'complainers' that might prevent the diagnosis of 'CFS/ME'. Community leaders also described how people with 'CFS/ME' could be given stigmatising labels such as 'lazy', 'liars' or 'crazy' by their community and may therefore want to avoid this potentially stigmatising diagnosis.
	Lack of HP knowledge

Study (primary & secondary analysis)	Bayliss 2014[18, 44]
	Some GPs described uncertainty and unwillingness to make a diagnosis of 'CFS/ME', attributed to their lack of knowledge about the condition and its management.
	Nature of diagnosis
	'CFS/ME' was described as a diagnosis of exclusion, a difficult diagnosis to make.
Limitations and applicability of evidence	Very minor limitations due to the role of the researcher Minor concerns over applicability due to the study population that was limited to BME groups potentially limiting the relevance of emerging themes to BME populations.

Study	Beasant 2014[21]
Aim	To understand the experiences of adolescents and families in accessing and using a specialist service, and explore whether or not they value referral to a specialist service for young people with 'CFS/ME'
Population	Mothers and adolescents diagnosed with 'CFS/ME' by paediatric 'CFS/ME' specialist service (aged 12-18 years, mildly or moderately affected i.e. not house bound), referred to large regional specialist 'CFS/ME' service in South West England, participating in the SMILE study (designed to test the feasibility and acceptability of recruiting adolescents to a RCT comparing specialist medical care with specialist medical care and the Lighting Process). Mothers n=13; adolescents n=12, male: 3 (25%), female: 9 (75%), mean age (SD): 13.9 (1.6); median illness duration (IQR): 13 (9 to 18) months
Setting	Large regional specialist 'CFS/ME' service in South West England.
Study design	Qualitative interview study
Methods and analysis	In-depth qualitative interviews were conducted using a topic guide to ensure similar areas were covered but with sufficient flexibility to enable participants to raise topics of interest to them, covering questions concerning experiences of the initial clinical assessment appointment, study participation and the interventions that young people received. Families were interviewed at three possible time points: after initial assessment, at the specialist clinic and before randomisation, after randomisation but before the intervention, and after the intervention. Adolescents were interviewed once at one of these time points for not more than 20 minutes. Parent interviews lasted for 20-60 min and were conducted at a convenient location, usually at the participant's home. Interviews were audio-recorded and transcribed verbatim. Data were analysed using thematic analysis using techniques of constant comparison. Data analysis was an ongoing and iterative process, commencing soon after data collection started and informing further sampling and data collection. Two members of the

Study	Beasant 2014[21]
	research team analysed ~10% of the data independently to compare coding and enhance its reliability. Descriptive accounts were produced, and theoretical explanations for behaviours, opinions and decisions were developed.
Findings	**(Complicated) Journey to the specialist service**
	a) Long waiting times: Most mothers described a long and difficult journey to the 'CFS/ME' service, that was deemed complex and frustrating with numerous interactions with healthcare professionals at various locations and long periods of waiting
	b) Diagnostic procedures: Mothers described how long period of waiting were intensified by repeated blood tests to rule out serious acute illnesses and reported how various tests such as blood tests and brain scans were initially conducted to rule out different conditions, which required a lot of time. The fact that ME/XFS symptoms such as extreme tiredness could be associated with various different illnesses causing confusion and uncertainty was also expressed.
	c) Access to services/funding: A small number of mothers reported having to wait for funding to be agreed before their child could access the specialist 'CFS/ME' service.
	d) Co-morbidities: co-morbid conditions further complicated the journey to the 'CFS/ME' service by introducing complexity to the process of diagnosis or masking 'CFS/ME'. Nearly all mothers suggested that other conditions, such as behavioural issues or depression, had developed because of prolonged illness with 'CFS/ME'.
	Lack of knowledge of health professionals (HPs)
	a) Mothers felt they had to be proactive and persistent, using additional knowledge sources to bypass potential gatekeepers who acted as barriers because of lack of knowledge about either 'CFS/ME', potential treatment or availability of specialist services. This was felt to be the case for both GPs and paediatricians.
	Referral to specialist 'CFS/ME' service
	a) Referral to specialist service gave families access to an informative team of experts, for some a formal diagnosis and for all, a tailored, patient-cantered specialist medical intervention that had not been available earlier.
Limitations and applicability of evidence	Minor limitations due to the role of the researcher and concerns over data richness with findings mostly supported by single quotes. Minor concerns over applicability due to the research aim of the study and minor concerns over the representativeness of the sample considering sample consisted of feasibility RCT participants which may differ from eligible patients not recruited to a trial.

Study	Broughton 2017[29]
Aim	To explore the experiences of 'CFS/ME' patients who were completing programmes of treatment at three NHS specialist 'CFS/ME' services in England.
Population	Adults completing/concluding treatment at one of three outpatient NHS specialist 'CFS/ME' services (median age 43, range 24-62 years; median self-reported illness duration 7.5 years, range 1-17).

Study	Broughton 2017[29]
	N=16; male: 12.5%, female: 87.5% median age (range): 43 (24-62) years; median self-reported illness duration (range): 7.5 (1-17) years Participants recruited between July-September 2014, who completed a course of treatment within this period, returning a Consent to Contact Form. Exclusion criteria: age <18 years; too severely affected to be able to participate in interviews; unable to provide informed consent; unable to read and understand the patient information sheet and consent forms; or not diagnosed with 'CFS/ME' as a primary diagnosis.
Setting	Three outpatient NHS specialist 'CFS/ME' services in England.
Study design	Cross-sectional design using semi-structured interviews to explore patients' experiences.
Methods and analysis	Six face-to-face (conducted at the participant's home) and 10 telephone semi-structured interviews lasting from 23 to 57 min (mean length 32 min) with questions about the patient journey before, during and at the end of receiving specialist medical care. All interviews began with the open question: "Tell me about your CFS/ME" and participants were encouraged to guide discussion and introduce their own topics of interest. Interviews were audio-recorded, transcribed and analysed thematically (by two researchers).Techniques of constant comparison informed the analysis and identification of themes.
Findings	**Journey to the specialist service:**
	a) Lengthy referral and diagnostic procedures: Four participants reported that referral to the specialist service had been a lenghty process, mainly because diagnostic procedures required ruling out other medical conditions, involved numerous medical tests and appointments with multiple clinicians.
	Barriers and facilitators to specialist service access:
	a) Misdiagnoses: Participants discussed factors that delayed referral to specialist services for 'CFS/ME'. Some were initially misdiagnosed, for example with depression, multiple sclerosis or glandular fever.
	b) Role of GPs and lack of HP knowledge: All participants were referred to 'CFS/ME' specialist services by their GPs. Participants with positive experiences reported their GPs had been 'very supportive', 'brilliant' and 'fantastic', they valued 'being taken seriously' and recognised the key role their GP had played. Participants with less positive experiences described a number of barriers to accessing specialist services including a lack of information, having to take a proactive role in asking for diagnostic tests, and GP's lack of 'awareness', 'knowledge' or 'belief' in 'CFS/ME'.
	Referral to specialist service:
	a) Many participants had their 'CFS/ME' diagnosis confirmed when they were assessed by the specialist services. For many participants specialist services provided information and explanation of 'CFS/ME', simultaneously validating and normalising participants' experiences and symptoms. All participants felt they had benefited from accessing specialist service. The majority recalled having had hopes and expectations of referral and treatment including to confirm diagnosis and manage symptoms better.

Study	Broughton 2017[29]
Limitations and applicability of evidence	No concerns over methodological limitations No concerns over applicability

Study	Chew-Graham 2008[37]
Aim	To explore how patients with 'CFS/ME' and family physicians conceptualise this condition and understand it and how their understanding might affect the primary care consultation.
Population	Family physicians: n=14; 7 male, 7 female; mean age: 48, SD: 12 years; one of the family physicians' practice was not participating in the FINE trial. Patients: n=24; 11 male, 13 female; mean age: 48, SD: 12 years; months since CFS diagnosis range: 1-240, median: 40.5
Setting	Family physicians and registered patients were from 44 primary care trusts in North West England
Study design	Qualitative interview study
Methods and analysis	Semi-structured interviews were conducted by one author at the patients' home and physicians place of work (1 physician was interviewed at home). Interviews lasted between 16 and 72 minutes (median duration= 38 minutes). An interview guide providing a flexible framework for questioning and exploring a number of areas: models of illness, appearance of symptoms, reaching a diagnosis, the consultation and doctor-patient encounters, was used. The interviewer combined open-ended questions to elicit free responses with focused questions for probing and prompting. Digitally recorded interviews were transcribed verbatim by a professional transcribing service, with transcripts checked against the tape by the interviewing author. Analysis proceeded in parallel with the interviews and was inductive taking an interpretative stance. Coding was iterative and informed by the accumulating data and continuing thematic analysis. Coding and interpretation was undertaken individually by four authors.
Findings	**Invisibility of the illness**
	Family physicians expressed frustrations that they could not measure how the patient was affected by their condition. It was so-called 'invisible' and the symptoms seemed out of proportion to the signs leading some to doubt the condition and the genuineness of its presentation. The inability to demonstrate the extent of their condition beyond the snapshot view revealed in the consultation meant that patients were unable to establish that symptoms come and go and that the condition is invisible on good days. Family physicians described how they ran a battery of tests, which invariably returned negative results. With no manifest sign of patients' symptoms and no confirmation of a diagnosis, the physicians would often reach clinical impasse. Patients were aware their condition was invisible from a biomedical perspective.
	Limited medical knowledge & doubt
	Family physicians admitted having limited clinical understanding about 'CFS/ME' available to them, causing them to question the existence of the condition. Patients were aware that the medical community disagreed over the existence of the condition and also that

Study	Chew-Graham 2008[37]
	family physicians had limited clinical knowledge about 'CFS/ME'. They believed they were unprepared by their medical training and continuing education to diagnose and manage 'CFS/ME' and they acquired evidence from sources outside the clinical domain. Their training enabled them to exclude a physical cause for the patients' symptoms but doubt and limited knowledge about 'CFS/ME' made the diagnosis uncertain.
	Relationship with physician
	Some patients believed it was important in both the diagnosis and management of their condition to have an established relationship with their family physician: Not having such an ongoing relationship with their family physician was reported by the patients to make it difficult to achieve agreement about the symptoms and the diagnosis, because the primary physician had no prior knowledge of them.
Limitations and applicability of evidence	Minor limitations due to concerns over data richness with some findings supported by limited quotes. Minor concerns over applicability due to the research aim and sample which consisted of people recruited in a RCT (FINE trial).

Study	Chew-Graham 2010[36]
Aim	To explore GPs' beliefs about the value of the label of 'CFS/ME', implications of the diagnosis and attitudes towards patients suffering with this condition.
Population	GPs (n=22) recruited via purposive sampling through practices participating in the FINE trial. 46 GPs were invited by letter but 22 agreed to be interviewed.
Setting	GP practices in North-West England
Study design	Qualitative interview study
Methods and analysis	Semi-structured interviews lasting between 10 to 72 minutes (median duration 34 minutes) were conducted using an interview guide. This provided a flexible framework for questioning and explored a number of areas: ideas about the cause of 'CFS/ME', previous experience of patients with 'CFS/ME', how the diagnosis of 'CFS/ME' was achieved, and their role in management of those patients. The interviewer combined open questions to elicit free responses with focused questions for probing and prompting. Interviews were digitally recorded and transcribed verbatim. Analysis proceeded in parallel with the interviews and was inductive, taking an interpretative stance. Coding was iterative and was informed by the accumulating data and continuing thematic analysis. Thematic categories were identified at initial interviews which were then tested or explored at subsequent interviews were disconfirmatory evidence was sought. Interpretation and coding of data was undertaken by three researchers individually and themes were agreed through discussion with the whole team.
Findings	**Difficulty defining 'CFS/ME' / Lack GP confidence about making the diagnosis & uncertainty about CFS as a medical condition**

Study	Chew-Graham 2010[36]
	GPs described a struggle, trying to make sense of a difficult set of symptoms and attributed different causes to the illness. There was also some debate over whether 'CFS/ME' actually existed as a medical condition. Such beliefs about 'CFS/ME' necessarily will lead to difficulties in labelling the symptoms or making a diagnosis.
	GPs' view of diagnosis: harm of the label/ Lack of clear management pathway
	The majority of GPs felt that the label of 'CFS/ME' could be harmful because it did not offer a clear management pathway for either the GP or the patient. This can cause GPs to be reluctant to make the diagnosis of 'CFS/ME'.
	Referral to secondary care/ places for support
	a) **Role of referral**: Those GPs who felt that making the diagnosis or labelling the patient's condition, was helpful suggested that referring the patient to secondary care could potentially assist in achieving a diagnosis and providing support to GPs who lack confidence in making the diagnosis alone.
	b) **Limited availability:** GPs however reported experiences of limited availability of potentially helpful places to support them in either making the diagnosis or managing the patient.
Limitations and applicability of evidence	No methodological limitations Minor concerns over applicability due to the sample which consisted of people recruited in a RCT.

Study (& subsidiary paper)	Clarke 1999[38]; Clarke 2000[39]
Aim	Study 1: To compare the experience of men and women with CFS; both their self-perceived illness experiences and their relationships with medical practitioners, in order to investigate the two major explanations for the gender difference in morbidity rates and the anomalous findings regarding the difference between the genders with respect to morbidity as compared to mortality. Study 2: To examine the process and some of the consequences of diagnosis-seeking in the experiences of people with chronic fatigue syndrome
Population	'CFS/ME' patients N=59; 18 male, 41 female; mean age: 45 years, range 18 – 80 years, representing all occupational arenas; 62.5% had symptoms from 1 to 5 years. 20% were well enough at the time of the interview to return to work after a lengthy leave and only on a part-time basis, 80% were tired, unemployed or on sick leave.
Setting	Patients were recruited through 'CFS/ME' support groups based in Ontario, Canada.
Study design	Qualitative interview study

Study (& subsidiary paper)	Clarke 1999[38]; Clarke 2000[39]
Methods and analysis	Telephone interviews were conducted at a time and location selected by the participant. Interviews lasted approximately an hour and were conducted using an open-ended focused interview schedule raising topics for discussion and asking respondents to describe their experiences with emphasis on what each considered to be their most salient concerns. Topics covered included major symptoms; when signs and symptoms were first noted; reactions of significant others, preferred diagnostic labels, impact of symptoms on the rest of life, views of causes of disease, impact of disease on self-concept and identity and the process of seeking and finding diagnoses. Analysis: Study 1: Constant comparative method was used for analysis. Data were analysed separately by sex and involved open and axial coding. This involved reading one interview transcript and noting and coding phrases, sentences and sometimes paragraphs which reflect a particular aspect of participant's experience. This first set of codes ('open' codes) was then used to analyse the next interview transcript and new codes were added as necessary. Then 'axial' coding was undertaken which involved the search of linkages among the first open codes. At the same time, the researcher wrote analytic memos regarding the procedures used and developed and insights to inform later analysis. Study 2: The researcher used the method of cross-case analysis which involved reading one interview transcript and noting coding phrases, sentences and sometime paragraphs reflecting a particular aspect of the participant's experience, which were then used to analyse the next interview transcript and new codes added. 'Open' coding was followed by 'axial' coding, involving the search of linkages among the first open codes or the discovery of themes.
Findings	**Variability of symptoms:**
	Almost all the men and women reported that their symptoms varied from day to day, week to week, month to month, and even at times from hour to hour. Extreme fatigue, muscle pain and cognitive problems were ranked as the most common symptoms by men and women, while visual disturbance, low grade fever, auditory disturbance and respiratory symptoms were ranked as the least common.
	Lack of medical legitimacy
	Most people had to seek a diagnosis through more than three different doctors while the remainder sought help from 1-3 practitioners. All began their search through contact with a general practitioner, then all men and 89% of women went to specialists. Because of the controversial nature of the disease and its lack of medical legitimacy, people relied less on the medical profession for information and more on their support groups or their own research.
	Overlap with psychiatric disorders & symptoms
	Many people were referred to psychiatrists when they first presented their doctors with their symptoms. A greater percentage of women were referred to psychiatrists at the diagnostic stage and a greater percentage of men were referred to a psychiatrist to improve coping.
	Dissatisfaction with doctors & doctor shopping

Study (& subsidiary paper)	Clarke 1999[38]; Clarke 2000[39]
	At first, participants often searched from doctor to doctor to get help with their symptoms. The majority of patients (62%) sought a diagnosis from more than 3 doctors to confirm their diagnosis and 90% sought help from (at minimum) a GP, a specialist and a support group. For most participants, the first stages involved doctor-shopping because of personal dissatisfaction with the lack of adequate explanation for their suffering,
	Diagnostic process/ nature of diagnosis
	a) **Multiple referrals:** For most participants, the first stages involved referral from doctor to doctor in search for the specialist who was responsible for one of the organs or systems that was felt to be affected by the sufferer; 50% were referred to a psychiatrist and 38% tried at least one type of alternative health care.
	b) **Insufficiency of tests:** Participants had gone to a number of different doctors and been tested for a variety of different diseases. The tests were usually inconclusive and led rather than to an answer, to more tests by different specialists
	Conflicts and disagreement between doctors
	Often times in the early stages where participants searched from doctor to doctor to get help with their symptoms, they observed differences of opinion and even disputes and contradictions between different doctors, with different specialists focussing on the possible problems associated with different organ symptoms and offering different sorts of potential explanations. In these cases the lay people were forced to decide on their own whether any of these doctors were correct or helpful for them.
	'Bad' and 'good' doctors
	In their search for a diagnosis, persons with CFS often developed a calculus of 'good and 'bad' doctors. The former may not be able to diagnose the disease but still believed the patient. The latter is the one that does not take the symptoms seriously, does not believe the lay person or suggest that it is all in their head. 75% of the participants felt that they had to deal with a 'bad' doctor, one who aggravated their suffering as they sought a diagnosis and treatment. A strategy for dealing with the new, unusual feelings was to get the name of an expert (or at least a believing) doctor from support group, a friend, acquaintance, family member or media-report. There are a few doctors scattered across the country, who have become known because they are 'believers' and willing to diagnose the disease. People get their names and often travel to see them, hopeful that their bodily experiences will be labelled and explained.
Limitations and applicability of evidence	Very minor limitations due to the role of the researcher not being discussed. No concerns over applicability.

Study	Devendorf 2019[46]
Aim	To explore physicians' views on the challenges to studying and approaching recovery, to examine these challenges in-depth and provide recommendations that will improve how researchers and practitioners approach the study and quantification of ME and CFS recovery.

Study	Devendorf 2019[46]
Population	Physicians specialising in ME/CFS of diverse medical specialties (n=10), recruited via non-probabilistic, purposive sampling. Specialists were defined by their extensive patient experience, research contributions and significant involvement in the field. Other physicians (n=3), not identified as ME/CFS specialists (one paediatrician, two psychiatrists) were also recruited. n=13, males: 9, females: 4; mean age 60 years. For years in practice, three physicians had 30 or more years, seven had 20-29 years, one had 10-19 years and two had 1-9 years of medical experience. The sample was diverse in their medical specialties: epidemiology (n=1), geriatrics (n=1), infectious diseases (n=1), neurology (n=1), internal medicine (n=2), psychiatry (n=2), general medicine (n=3), and paediatrics (n=5); three physicians identified with two medical specialties.
Setting	The place of work of the recruited physicians is not specified. The study was conducted at DePaul university in the USA.
Study design	Qualitative interview study
Methods and analysis	Semi-structured phone-based interviews (one via email) (mean duration 31 minutes). Interviews asked physicians about their general thoughts on recovery from ME/CFS-defining, measuring and studying recovery. Questions were inspired by online, patient discussion boards discussing the PACE trial. Interviews were audio-recorded, transcribed verbatim and verified for accuracy. Transcripts were analysed using deductive thematic analysis by two researchers.
Findings	**Variability/Heterogeneity of ME/CFS**
	a) Lifespan differences in the illness experience: Physicians noted that ME and CFS may present differently in children than adults but there is little if any research that demarcates these differences. E.g. in terms of symptoms and how they affect daily life, prognosis. Cognitive abilities and self-awareness also develop with age. Young children may lack awareness that they are sick, or the ability to articulate their experience. Symptoms such as fatigue, orthostatic intolerance, and memory issues may be difficult to detect in pediatric populations. Symptom screenings should be sensitive to these developmental issues.
	b) Lack of consensus in case definitions: Case definitions affect whether a patient is diagnosed with ME or CFS and may select more or less severe cases. Physicians alluded to this issue. They felt that compared to other chronic illnesses, there is more variability with ME/CFS patients (e.g. with the Fukuda et al criteria it is possible for two patients to have a diagnosis of CFS without having any of the same symptoms (except for fatigue). This issue confused physicians to the point where a few questioned their patient's symptoms. Depending on the case definition used by the physician, patients may be diagnosed differently between providers
	Misdiagnosis
	a) Health professionals acknowledged that the patients they see often exhibit depressive symptoms and mentioned that misdiagnosis occurs on both ends. Patients may be diagnosed with depression when they really have ME or CFS. This may have detrimental effects as this process is stigmatising, delegitimising and damaging to the patients because they may inadvertently seek inappropriate care.
	Diagnosis of exclusion

Study	Devendorf 2019[46]
	c) Specialist physicians reported that they screened patients for exclusionary diagnoses, like anemia, with a few mentioning 'landing' on a ME or CFS diagnosis when no cause was discovered.
Limitations and applicability of evidence	Minor limitations due to the role of the researcher, data analysis with themes mostly supported by single quotes Minor concerns over applicability as main findings emerging are driven by the study's original aims to explore physicians' views on recovery.

Study	Gilje 2008[60]
Aim	To explore obstructions for quality care from experiences by patients suffering from CFS
Population	Patients who had suffered from CFS for at least 1 year, one of them the last 20 years, recruited via purposive sampling being considered as people who might be especially aware of questions related to quality care. Diagnosis had been confirmed by various doctors. n=12; 2 male, 10 female; mean age (range): 41 (22-54) years
Setting	Local patient organisation (West Norway)
Study design	Qualitative case study with data drawn from a focus group, written answers to a questionnaire and a follow-up meeting.
Methods and analysis	A group interview according to focus group principles was conducted. The moderator invited participants to share their experiences from encounters with health care providers and to describe episodes from everyday life where the symptoms made a difference as compared to life before illness onset. The conversation was audiotaped, transcribed and supported by field notes. Qualitative analysis was conducted with systematic text condensation: a) reading all material to obtain an overall impression and bracketing previous preconceptions, b) identifying units of meaning, representing different aspects of participants' experiences of health care and coding of these; c) considering the contents of each of the coded groups to generalize descriptions and concepts concerning health care experiences. The questionnaire intended to complement the interview, contained similar issues as the interview, expressed as open-ended questions and also some quantitative issues such as duration of illness. Questions beyond the scope of this study were also included such as beliefs about etiology. Due to the limited amount of time, these matters were not introduced in the interview, and were omitted from analysis. The follow-up meeting 1 year later was attended by 5 of the 12 participants, all women. The major findings from the initial analysis were then presented and discussed in depth. Fieldnotes from this meeting and the questionnaires were used to clarify and supplement issues from the group interview.
Findings	**Lack of GP knowledge & effort/support**

Study	Gilje 2008[60]
	A common impression among participants was that their GPs held a low level of knowledge about CFS. Two women told about doctors who never examined them properly, even after having seen them for several years, claiming that they did no efforts at all to find out whether they were ill or not. Some of the participants were not even able to tell their doctor what was wrong with them before he gave them a prescription. Many participants felt that the doctors psychologized too much, interpreting exhaustion as depression and trivialising the symptoms and described how doctors' lack of knowledge about the condition would lead to long-term uncertainty or maltreatment.
	Diagnostic procedures/ Nature of diagnosis
	Even with doctors who were supportive and believed in the patients, it would usually take months and sometimes years until a medical conclusion would be reached, or other disorders were ruled out.
	Referral to specialists
	Many GPs had more or less reluctantly referred their patients to specialists for investigation, and most of the participants had been seen by neurologists at a hospital department with a special interest in CFS. This was usually the place where the diagnosis had been concluded.
Limitations and applicability of evidence	Very minor limitations due to the role of the researcher. No concerns over applicability..

Study	Hannon 2012[66]
Aim	To develop an education and training intervention to support practitioners in making an early diagnosis of 'CFS/ME' and supporting patients in the management of their symptoms.
Population	Health practitioners (GPs n=9, practice nurses n=5, 'CFS/ME' specialists n=4), Carers (n=10), patients (n=16), aged 28-71 Patients and carers included n=12 BME (black minority ethnic) group participants.
Setting	Patients and carers were recruited through 'CFS/ME' support groups, community groups, specialist 'CFS/ME' services in the NHS. A purposive sample of BME group patients were also recruited from South Asian third sector groups in General Manchester and personal visits to community groups. Practitioners were recruited via a purposive sample of GP Practices and Primary Care Trusts.
Study design	Qualitative interview study
Methods and analysis	Semi-structured interviews were conducted face-to-face using topic guides: patient/carer interview focus included experiences of being diagnosed, support received in primary care; practitioner interviews focused on current practice in the diagnosis and management of patients with ME/CFS, attitudes towards ME/CFS and training and education needs; Specialist 'CFS/ME' practitioner interviews focused on the needs of patients and asked for comments on existing 'CFS/ME' resources. Initially inductive analysis was conducted

Study	Hannon 2012[66]
	using thematic analysis in line with modified grounded theory approach, using open coding; a deductive approach was then taken when data fully analysed.
Findings	**Lack of HP knowledge/understanding/recognition of ME/CFS** **a)** The GP and practice nurse respondents expressed varying degrees of understanding of 'CFS/ME' and some questioned whether 'CFS/ME' was a legitimate illness; they were unaware of the evidence base for this condition or believed the symptoms could be explained by a psychological problem or secondary gains. Those who did recognise it as a legitimate illness were aware that some of their colleagues fail to identify this condition which can lead to inappropriate diagnosis. Some GPs and practice nurses used the label as a last resort and with reluctance due to their own lack of knowledge, but also because making the diagnosis did not lead to obvious treatment. Patients and carers explained how they took information to their GP in an attempt to raise their awareness of the condition. A gap in knowledge was also recognised by 'CFS/ME' specialists who highlighted a training need in primary care **Uncertainty around ME/CFS** **a)** **Lack of definitive treatment for ME/CFS:** Some GPs and practice nurses used the label as a last resort and with reluctance because making the diagnosis did not lead to obvious treatment and they believed that there was no cure for 'CFS/ME'. **b)** **Diagnostic issues (exclusion, lack of criteria):** Practitioners described how the diagnosis of 'CFS/ME' was made by exclusion due to the lack of positive diagnostic criteria **Consultation duration** **a)** HPs recognised that a 10 minute consultation with a patient with 'CFS/ME' can be challenging due to the variety and complexity of symptoms. A ten minute consultation was also seen as a potential barrier to diagnosis by 'CFS/ME' specialists as GPs may not be able to gain a complete understanding of the variety of symptoms patients can experience and the impact of those on their life.
Limitations and applicability of evidence	Minor limitations due to the role of the researcher, data analysis with findings mostly supported by single quotes No concerns over applicability

Study	Horton 2010[76]
Aim	To describe from the perspective of health care practitioners (HCPs) judged by people with ME/CFS as having been particularly helpful and effective, practices that: enable participants to establish the legitimacy of their condition; impact positively on the process of diagnosis and care; and enable patients to overcome experiences of social isolation and other negative effects.
Population	6 HCPs (3 specialist and 3 non-specialists) working with patients with ME/CFS, nominated by 'CFS/ME' patients as having provided them with particularly helpful or effective care, based on their perceptions of the quality of care they had received. Participants were nominated by people with 'CFS/ME' who had taken part in an associated England-wide study of their support needs (Social inequalities in the impact of living with 'CFS/ME': 'CFS/ME' Observatory project)
Setting	Participants were from the East of England and London
Study design	Qualitative interview study
Methods and analysis	Semi-structured individual interviews (5 face-to-face, 1 telephone) were conducted by two of the authors based on a topic guide covering topics such as: general experiences of working with people with ME/CFS; enabling people to access information and resources; recognising and responding to the needs of people with 'CFS/ME', including coping with uncertainty, unpredictability and stigma; enabling people to take an active role; experiences of working with people from ethnic minorities, or from manual or routine occupations or who had a sever condition. Interviews lasted between half to a full hour and were all audio-recorded. Audio-recordings were transcribed in full using English orthography, according to an agreed protocol. Thematic analysis followed, employing methods of peer triangulation in between researchers to validate the analysis.
Findings	**HCPs experience of ME/CFS**
	a) **Lack of experience:** It was generally acknowledged that reaching a firm diagnosis of 'CFS/ME' can be challenging for GPs working in primary care who may have little experience of the condition.
	b) **Exposure to presentations of ME/CFS:** Exposure to new presentations of 'CFS/ME' was considered important for improving primary care practice. It enabled practitioners to recognise the condition and develop confidence in their diagnostic skills. Specialist practitioners develop awareness of the wide range of symptoms, whether physical or psychological that can be associated with the condition, and their significance through extensive exposure to 'CFS/ME'.
	c) **Disbelief:** Specialist HCPs reported many GPs did not understand 'CFS/ME' and see it as a psychological rather than physical condition. They reported whole practices as having decided that 'CFS/ME' did not exist and how some patients told them that their GP openly stated their lack of belief in the existence of 'CFS/ME'.
	d) **Education for HCPS/ Ignorance:** Specialist HCPs emphasised that there is a need for specialist services to provide education for other HCPs, GPs especially, because there is quite a lot of ignorance about 'CFS/ME' in the GP population, which was potentially due GPs lack of frequent exposure to patients with the condition.
	Lack of a diagnostic test

Study	Horton 2010[76]
	a) Several HCPs saw the lack of any diagnostic test giving conclusive proof of the condition as impacting on practitioners and patients alike. One view was that until such a test is developed the existence of the condition will remain in doubt amongst some medical practitioners and policy-makers.
	Good HP practice
	a) Very careful case history-taking, listening carefully and patiently to presentation of symptoms, with appropriate investigation were all considered vital elements of practice.
	Between-patient variability
	HCPs emphasised that the variability between patients presenting with symptoms apart from the fatigue and where other symptoms such as headaches, gut symptoms or muscle may be predominant for some individuals.
	Access to specialist services
	a) **Hindered access:** Specialists identified a core minority group of GPs in their region who made referrals to their services and contrasted these to the many who did not understand ME/CFS. They reported that many GPs would never make a referral to a specialist service and acknowledged how much pressure some people had had to exert just to get a referral to their service. They emphasised that there is a need for specialist services to be more visible and to provide education for other HCPs.
	b) Specialists had both experience and expertise to be able to support GPs and other HCPs in reaching or confirming a diagnosis.
Limitations and applicability of evidence	Minor methodological limitations due to the role of the researcher not being discussed and concerns over data analysis with some themes supported by single quotes. No concerns over applicability

Study	Lovell 1999[93]
Aim	To study the perceptions of overseas workers who had developed CFS
Population	Overseas workers diagnosed with CFS by a GP or medical consultant and fulfilling the Oxford diagnostic criteria for CFS at the time of interview, recruited through a travel health clinic for overseas aid workers in London, England. N=12; 7 female; mean age (range) 40.33 years (27 to 61); Mean duration of CFS symptoms (range): 25 months (12-50 months)
Setting	Travel health clinic for overseas aid workers in London, England
Study design	Qualitative interview study
Methods and analysis	Open-ended, one-to-one interviews were conducted by the same psychologist, which lasted approximately 2 hours (from 1-2.5 hours). Interviews were tape recorded and transcribed verbatim and analysed using grounded theory approach. Interviewees were asked:

Study	Lovell 1999[93]
	'Could you please tell me about yourself and your experience of chronic fatigue syndrome? Further interview prompts were used as necessary. Tapes were transcribed verbatim and analysed using methodological principles of grounded theory. Findings were sent to participants who were asked to offer comments for validation purposes.
Findings	**Waiting times**
	Several participants said that they found it frustrating to wait months or even years before being given a diagnosis of CFS.
	Misdiagnosis
	Some participants stated they had initially been misdiagnosed
Limitations and applicability of evidence	Serious limitations due to the role of the researcher, concerns over data collection method as the study lacked detail and over data richness with limited information to support overall findings. Very minor concerns over applicability due to the aim of the study.

Study	Marks 2016[94]
Aim	To explore HCPs experiences of working with children and adolescents with 'CFS/ME' so as to develop an understanding of the process relating to how they understand the condition.
Population	Paediatricians, physiotherapists and clinical psychologists, working in two NHS organisations in the UK: a hospital outpatient paediatric service and a specialist centre providing inpatient and outpatient care for young people with 'CFS/ME'. All had a minimum 3 years' experience of working with ≥ 3 young people with 'CFS/ME'. Consistent with theoretical sampling, participants were selected on the basis of how they informed and validated emerging theory. (n=10; 3 male, 7 female; 5 specialists: inpatient and outpatient care, 5 non-specialists: hospital based-outpatient care)
Setting	Hospital outpatient paediatric service and a specialist centre providing inpatient and outpatient care for young people with 'CFS/ME'
Study design	Qualitative interview study
Methods and analysis	Semi-structured interviews were conducted, using a semi-structured interview schedule developed by the research team. This focused on how participants referred to and understood 'CFS/ME', exploring thoughts about aetiology, maintaining factors and effective recovery. Following data analysis, the schedule was modified and focussed on the emerging theory. The audio-recorded interviews were conducted by the primary researcher and varied between 28 and 83 minutes. Interviews were transcribed and analysed consecutively by the primary researcher and transcripts were simultaneously analysed by two of the researchers. Concepts were constantly compared within and between transcripts and grouped together into categories. Axial coding was used to explore the relationship between categories. The theory was refined through selective coding where a core

Study	Marks 2016[94]
	category emerged and a provisional model is proposed outlining how concepts produce particular beliefs which generate certain actions and consequences.
Findings	**Uncertainty around 'CFS/ME'**
	a) Lack of HCP understanding: HCPs acknowledged a lack of understanding of 'CFS/ME' compared to other health conditions. An unknown aetiology, limited evidence and research contradictions contributed to uncertainty and 'CFS/ME' was described as 'ambiguous' and 'a bit of an enigma'. Working with 'CFS/ME' was described as difficult and challenging compared to other chronic conditions.
	b) Inconsistent terminology: There was inconsistency in the use of the terms 'Chronic fatigue' and 'CFS' For some these were synonymous but others felt the latter conveyed increased symptom severity or that terms differentiated between fatigue rooted in psychological factors and fatigue stemming from psychosocial issues. Young people presenting to the services with medically unexplained fatigue could receive one of a range of labels, including 'CFS/ME', CFS, Chronic fatigue, Chronic Pain and MUPS; difficulties could also be conceptualised and labelled as depression and anxiety. Within the context of working with uncertainty participants described 'finding a label that fits' with how they conceptualised the young person's difficulties.
	c) Absence of diagnostic test: In absence of a diagnostic test for ME/CFS, HCPs described uncertainty in appropriately identifying and labelling 'CFS/ME'. This ambiguity combined with differing beliefs, gave rise to variability in the 'Diagnosis and Choice of label' given to a young person
	d) Impact on diagnostic process: Because of uncertainty and the lack of an empirically grounded understanding, HCPs endeavoured to 'make sense of CFS/ME' by developing their own understanding which then influenced clinical practice. HCPs could conceptualise the difficulties differently and participants described significant 'diagnostic variability' that resulted in a 'difficult' and 'challenging' diagnostic process given the need to safely diagnose in the absence of a definitive medical test, illustrating how 'working with uncertainty' impacts on the formal diagnostic process and how HCPs conceptualise and label a young person's difficulties
	Personal beliefs & HCP confidence in diagnosis:
	a) Aetiology: Although participants used the 'official term CFS/ME', they held their own beliefs about the condition, and these varied between HCPs. With regard to Aetiological Beliefs all recognised the contribution of physiological and psychological factors; however, differences appeared in the emphasis given to these. Some HCPs described feeling more comfortable giving a diagnosis of medically unexplained physical symptoms (MUPS) rather than 'CFS/ME', because of not being able to provide a clear aetiology
	b) Past-experiences: The role of clinical judgment appeared to be shaped by HCPs reflecting on labels they had given previously. One participant described feeling uncomfortable giving a label of 'CFS/ME' due to concerns that it may 'reinforce an illness behaviour', illustrating how personal beliefs influenced by past experience can influence label choice.
Limitations and applicability of evidence	Minor methodological limitations due to small sample size and recruitment skewing towards HCPs with positive attitudes towards ME/CFS (as participants were recruited on the basis of how they informed and validate emerging theory).

Study	Marks 2016[94]
	No concerns over applicability.

Study	McCue 2004[95]
Aim	To explore the illness experience of a group of people who had achieved substantial recovery from CFS.
Population	Participants who had previously suffered from CFS but regarded themselves as recovered, recruited through 'CFS/ME' support groups in the North East of England and through contacts at M E North East, using purposeful sampling. All but one participants had previously been diagnosed with CFS by a GP or specialist consultant. N=14; 100% female; mean age (range) 42 years (21 to 70); illness duration range: 2 to 17 years; range of time recovered: 6months to 10 years
Setting	'CFS/ME' support groups in the North East of England
Study design	Qualitative interview study
Methods and analysis	Semi-structured open-ended individual interviews conducted at the participant's home. These were tape-recorded or in cases where the participants were uncomfortable notes were taken. Participants were asked to describe their experiences while having CFS, and their opinions on what lead to eventual recovery. The following open-ended questions were used: 1. Could you tell me about how your illness began, and what happened in the early days of your illness? 2. Could you give me some idea of how this affected your life? Interviews were transcribed verbatim. Interviews were analysed using a grounded theory approach. Data was initially open-coded, axial coding (developing sub-categories) was then used to ascertain connections between categories. A small sample of transcripts was sent to participants to check for accuracy of recording of data.
Findings	**Doctors and health care professionals** **a) Uncertainty:** There is a great deal of uncertainty about CFS which often appears to translate into a diagnostic dilemma for many GPs. (single quote) **b) Lack of acceptance:** All 14 participants described having had problems of acceptance of the illness from GPs, initially at least. **Overlap with psychiatric disorders/ Diagnostic overlap** **a)** Seven out of 14 participants reported having been given anti-depressants either at the outset or at some point during the course of their illness. Nine of the 14 participants expressed the opinion that their doctors ignored their physical symptoms and focussed more on the depressive symptoms, which 8 felt were due to the effects the illness had on their lives. 11/14 participants felt that their more physical symptoms were disregarded in favour of any that could be described as pertaining to depression or to mental health issues. They expressed that many doctors had actually symptom picked at some point. Five participants initially believed they had

Study	McCue 2004[95]
	some kind of psychological disorder rather than a physical one as a result of the numerous indefinable symptoms they were experiencing.
Limitations and applicability of evidence	Very minor limitations due to the role of the researcher not being discussed. No concerns over applicability.

Study	Taylor 2005[143]
Aim	To determine what aspects of the disability experience of persons with CFS are explained by the social model of disability, and what aspects of disability fall outside or contradict central tenets of the social model.
Population	Adults meeting the Fukuda criteria for CFS, recruited prospectively from local CFS self-help organisations, physicians specializing in the treatment of persons with CFS, and advertisements posted in CFS newsletters, local newspapers, on CFS Web sites and listervs, and on local cable TV station. n=47; male: 4%, female: 96%; mean age 46.9 years, SD 10.4
Setting	Centre of independent living
Study design	Qualitative study involving focus groups and qualitative response questionnaires
Methods and analysis	For each client, qualitative data were collected over a period of 12 months through Focus groups and End-of-Group Reflections Form. During Focus groups participants were educated about the social model and were asked about their experiences with CFS within social contexts of home, work and community, their interactions with health care providers, family, friends and peers with and without disabilities. End-of-Group Reflections Form questionnaire was distributed at the end of each group meeting and included questions such as 'Was there anything in particular about the independent living philosophy, advocacy, empowerment, or sense of community that you learned in today's group?' Analysis was based on the grounded theory approach and followed a qualitative comparative method. Triangulation was used to achieve confidence in the findings by comparing information within and across data collection methods, across participants, and across time.
Findings	**Role of HPs** **a) Lack of knowledge and disbelief:** Participants consistently reported that when they sought help for their condition by health care providers, most health professionals were either relatively ignorant or incredulous of CFS, leading to disbelief in the legitimacy of CFS as a medical entity, lack of validation of participants' impairments and symptoms, tendency to overemphasise psychological and social variables as plausible causes of symptoms and overprescribe psychotropic medications.

Study	Taylor 2005[143]
	b) Lack of specialisation: Most participants reported continued and ongoing dissatisfaction with their treatment, particularly when it was administered by a physician that did not specialise in CFS. Along the way they encountered misinformation, misdiagnosis, and inappropriate treatment recommendations
	Access to services
	a) Most participants described long and frustrating histories of their attempts to access necessary information and services to help them address the consequences of their impairment. Participants reported that they sought treatment for their CFS symptoms and impairments from an average of six physicians before they were ultimately diagnosed with CFS.
Limitations and applicability of evidence	No concerns over applicability or methodological limitations.

Barriers and facilitators to care

Study	Arrol 2008[8]
Aim	To investigate the process by which individuals conceptualise their bodily signs and sensations as consistent with the label CFS/ME.
Population	Patients with 'CFS/ME' from two East of England 'CFS/ME' support groups, recruited via group listings held by the ME Association. N=10; mean age (SD): 55.5 (9.4); male/female: 3/7; mean length of time with 'CFS/ME' (SD, range): 21.4 years (16.3, 6-53 years)
Setting	Primary care?
Study design	Qualitative interview study
Methods and analysis	Semi-structured telephone interviews consisting of a range of open-ended questions were conducted by the researcher. The general question: 'Can you please describe to me how you became ill with CFS/ME?' was posed to commence the interview, with more specific lines of enquiry following. Additional topics included in the interview schedule were the cause of 'CFS/ME', the effect on one's life, the process of diagnosis and advice that one would give another individual who believed that he/she might be suffering from 'CFS/ME'. The duration of the interview was between 26 and 90 minutes with an average length of 40.8 minutes (SD= 20.6). The eight good quality recordings were transcribed verbatim; two were discarded due to poor quality. Data was analysed with Interpretative phenomenological analysis (IPA), following a process of a case-by-case analysis followed by comparison across cases. To begin with, one transcript was read thoroughly and repeatedly, which permitted the researcher to become

Study	Arrol 2008[8]
	familiar with the account, as each additional reading tended to evoke new insights. Initial coding then entailed noting down anything of interest, interpretations and maki9ng summaries of ideas. From this stage, recurrent themes were extracted, with key words or phrases that captured the essence of the content acting as codes. This procedure was repeated for each transcript, with the researcher aiming to identify repeated patterns emerging in the subsequent transcripts whilst allowing additional topics to be identified. The next stage involved looking for thematic connections both within and across transcripts. Themes were then clustered and developed into a consolidated list of master or superordinate themes. Transcripts were reread to ensure that the themes and sub-themes could be undoubtedly recognised in the verbatim transcripts. Finally, transcript quotations were noted for each theme and a file created.
Findings	**Nature of the illness**
	The nature of the illness particularly led a patient to believe her symptoms were associated with a relatively innocuous and brief pathology. However the insistence of these symptoms brought about query in her mind as to whether they were a sign of a common infection or perhaps something more serious. It was the persistence of symptoms that directed patients towards the evaluative process. Patients appeared to initially attempt to normalise their symptoms by rationalising them e.g. as general complaints cause by stress. The wilderness of ambiguous bodily signs and severe ill health led participants to use internal cues such as the frequency of their disturbances and external information to provide lay theories of understanding. However, additional information was not enough on its own for all participants to come to the conclusion that their condition was 'CFS/ME' due to the nature of the symptomatology. For example a patient found it difficult to accept that her poor health was other than a virus as this appeared more consistent with her knowledge and experience.
	Attributes of CFS/ME/ Uncertain aetiology
	New information from external sources presented the possibility that patients' ill health may be due to 'CFS/ME'. In some cases this was accepted, although others had difficulty in associating this illness with their own experience, potentially due to the attributes of 'CFS/ME' as it is an illness of unknown aetiology and at best is defined as a cluster of symptoms. The uncertain aetiology of the illness had an impact on the diagnostic process. Due to the uncertainty also reflected in terms of the name used for the condition (CFS, ME, post-viral fatigue syndrome, chronic fatigue etc.), it was reported that doctors could not supply patients with a definitive response. The first step towards reaching a diagnosis requires the exclusion of all possible causes of the presenting symptomatology and if no active disease process can be found, the practitioner must use their experience and knowledge to conclude that the patient is suffering from 'CFS/ME'.
	Diagnostic delay/ GP unhelpfulness
	It was reported that patients may not receive satisfactory assistance not being given a diagnosis or further advice, having to consult another GP who then referred them to a specialist which later provided them with a diagnosis. This lengthened the period between initial symptom occurrence and treatment and the search for a diagnosis was often a lengthy ordeal with numerous unfruitful meetings which often led to difficult relationships between participants and care providers.
	Lack of effective treatment

Study	Arrol 2008[8]
	Following on from the process of gaining a diagnosis, participants looked to their medical practitioners for treatment options, but this was not a straightforward progression. There was a deficiency in conventional treatment, apart from anti-depressants, that together with limited guidance led patients to search for self-treatment methods.
	Limited or inappropriate treatment advice
	A patient reported her doctor had suggested meditation at a point in her illness where she did not feel able to follow it. Even in the case of a patient that had found a compassionate doctor, advice was reported to be limited.
Limitations and applicability of evidence	Minor limitations due to the role of the researcher and risk of selection bias as two interviews were discarded due to poor quality. No concerns over applicability.

Study (primary & secondary analysis)	Bayliss 2014[18, 44]
Aim	To explore the possible reasons for the lower levels of diagnosis of 'CFS/ME' in the Black Minority Ethnic group (BME) population and the implications for management. Secondary analysis: To explore making the diagnosis and managing 'CFS/ME' in the UK form the perspectives of patients, carers, community leaders and primary care practitioners, to understand why 'CFS/ME' may not be commonly diagnosed is South Asia (SA).
Population	35 key stakeholders in NW England: BME patients (n=11), carers (n=2), community leaders (n=5) and GPs (n=9); recruited via purposive sampling.
Setting	Patient and carers were recruited through existing 'CFS/ME' support groups and South Asian community groups in North West England; Other participants were recruited through specialist 'CFS/ME' services in the NHS. GPs were recruited through GP practices.
Study design	Qualitative interview study
Methods and analysis	Face-to-face semi-structured interviews were conducted using topic guides: BME patient/carer interviews focused on experiences of accessing primary care, illness models, attitudes of family and community and sources of support; community leaders' interviews explored understanding of 'CFS/ME' and role of family, community, primary care and religion in the diagnosis and management of 'CFS'; HP interviews focused on current practice, attitudes towards CFS and perceived barriers faced making the diagnosis and managing 'CFS/ME' in people in BME groups. Interviews were digitally recorded and analysed in parallel with interviewing using components of thematic analysis that were in line with modified grounded theory. In the secondary analysis, a new analytic framework was developed on culture and barriers to diagnosis. The secondary researcher was naïve to the original research findings. The process of refinement and validation of findings was conducted through a collaborative exercise creating feedback loops between the secondary researcher and the primary researchers. Further discussion between authors resulted in the identification of themes specifically relevant to BME patients presented in the paper.

Study (primary & secondary analysis)	Bayliss 2014[18, 44]
Findings	**Focus on physical symptoms**
	d) **Reluctance to seek help:** Community leaders and HCPs described how they perceived that many BME patients held biomedical models of illness and therefore would focus on presenting physical symptoms such as headaches and muscle pain when consulting with their GP, suggesting BME people would be more likely to refrain from seeking medical advice about non-specific symptoms such as fatigue, loss of concentration and problems with sleep- fatigue was reported to be part of the expected aging process is some BME communities.
	e) **HCP focus on physical symptoms:** Patients and community leaders suggested that HCPs might focus on physical symptoms and patients might not be encouraged to discuss nonspecific symptoms such as fatigue, with the majority of GPs describing 'CFS/ME' as a set of symptoms which they found hard to understand but alluded to a 'biopsycho-social' etiology and impacting on function.
	Patients' lack of awareness of ME/CFS
	Patients and health professionals described how BME patients were often unaware of CFS/ME and would not seek further support from primary care if they are told that there was nothing physically wrong with them.
	GP turnover & lack of continuity in care
	High turnover of GPs in the inner city practices that may provide care for people in BME communities was cited as a reason why some people may not receive a diagnosis of 'CFS/ME'. Patients believed that a lack of continuity meant that they were unable to build a long-term relationship with their health professional and GPs were unable to take the holistic approach considered necessary for the diagnosis of 'CFS/ME' to be made.
	Negative experiences with health-care professionals
	As a result of negative experiences with the GP around the presentation of non-specific symptoms such as fatigue, some patients reported that they had chosen not to consult in the future and would prefer to manage symptoms themselves.
	Language & understanding
	HCPs, patients, carers and community leaders agreed that not speaking English acts as a barrier to the diagnosis and management of 'CFS/ME', with some BME patients not being able to adequately describe their symptoms or understand their GP during consultation. Some patients described visiting the GP with English speaking family members, or using brief notes written by community leaders to outline symptoms. Others relied on professional interpreters who may not understand their regional dialect, or misinterpret their symptoms. Health professionals stated the use of interpreters can present a barrier when trying to achieve a diagnosis or advice about management. Community leaders also described how a person's lack of understanding of English limits their ability to research their symptoms using the internet or books resulting in a lack of awareness of 'CFS/ME' compared to the white population. Some patients reported a preference to see the Hakim or herbalist if they experienced symptoms of 'CFS/ME' as they speak their language and are able to spend more time with the patient.
	Culture specific issues

Study (primary & secondary analysis)	Bayliss 2014[18, 44]
	c) **Community expectations & attitudes:** The expectation to fulfil certain roles within the family or community was described as a barrier to the diagnosis and management of 'CFS/ME', with some patients commenting on pressures from the family for high academic achievement and the perceived stigma attached to low achievement which pushed patients to ignore symptoms of 'CFS/ME' until they reached a crisis point. GPs suggested that patients of BME origin present with vague physical complaints, with somatisation being more common; culturally BME communities do not consider tiredness or fatigue a symptom that requires medical assistance, instead other physical symptoms are reported. Community leaders and health professionals described how some people turn to their family rather than a GP when they feel unwell and it was suggested that large families adapt to accommodate or manage fatigue in one member.
	d) **Religion and culture:** Patients and community leaders described how some BME people would turn to religion or spiritual healers rather than primary care when experiencing fatigue, believing that spirits or black magic may be causing the condition. Religion and prayer were also cited as motivators for patients to attempt to manage their symptoms and not seek medical advice. White British health professionals in the study were not aware of the barriers in the diagnosis and management of 'CFS/ME' in primary care.
	f) **Racial stereotypes & stigmatisation:** HPs recognised the possible influence of racism and stereotypes in preventing the diagnosis of 'CFS/ME'. Patient, carers and community leaders described how they believed some GPs may hold stereotypical views of people from certain cultures such as being 'lazy', 'complainers' that might prevent the diagnosis of 'CFS/ME'. Community leaders also described how people with 'CFS/ME' could be given stigmatising labels such as 'lazy', 'liars' or 'crazy' by their community and may therefore want to avoid this potentially stigmatising diagnosis.
	Lack of HP knowledge / reluctance to diagnose
	Some GPs described uncertainty and unwillingness to make a diagnosis of 'CFS/ME', attributed to their lack of knowledge about the condition and its management.
Limitations and applicability of evidence	Very minor limitations due to the role of the researcher not being discussed. Minor concerns over applicability due to the study population that was limited to BME groups potentially limiting the relevance of emerging themes to BME populations.

Study	Bayliss 2016[17]
Aim	Following the development of an online training module for GPs, and an information pack and DVD for patients, this study explored the extent to which these resources can be implemented in routine primary care, leading to a better understanding of the barriers and facilitators to the adoption and integration of new practices associated with medically unexplained conditions.
Population	Individuals with an existing diagnosis of 'CFS/ME', recruited from participating GP practices. Patients with other conditions, or other factors that may account for their fatigue were excluded by the participating GPs.

Study	Bayliss 2016[17]
	GPs from practices from seven PCTs in North West England who were given access to an online 'CFS/ME' training module (hosted by the Royal College of General Practitioners RCGP website) that involved patient resource packs for use in consultation with new and existing 'CFS/ME' patients, who had completed training. Patients (n=11); male/female 2/9; mean age (range): 46 (27-74) years; GPs (n=8) GPs (n=8); 6/8 had participated in the training, although not all had completed the online test and downloaded their completion certificate.
Setting	Participants' homes, UK
Study design	Semi structured interviews with thematic analysis.
Methods and analysis	Face-to-face semi structured interviews took place. Patients were interviewed in their own home while GPs were interviewed at their practice. Not all GPs had fully engaged in the training or research. Patient interviews focused on their views on the 'CFS/ME' patient resource and their experience with their GP before and after the practice had access to the online training. Interviews were digitally recorded and transcribed. GP interviews explored the experience of managing people with 'CFS/ME' before the participating in the study and their opinions on the training and the patient resource pack. Analysis was conducted in parallel with the interviews and was inductive, using components of thematic analysis. Thematic categories were identified in initial interviews and then explored in subsequent interviews. Main categories were compared across interviews and reintegrated into common themes. Interview transcripts were read, annotated, and categorised independently by researchers of different professional backgrounds and patient and carer research partners to increase reliability of the analysis. Open coding was used initially. It was agreed that theoretical saturation across the data sets was achieved when no new themes emerged during the final interviews.
	Management in secondary care/ role of referral to secondary care
	For some GPS, the level of commitment required to manage patients over the longer term is too much for a primary care professional, and 'CFS/ME' should be managed in secondary care by specialists. Limited referral options were seen as a barrier to successfully working with patients to manage CFS/ME. Most GPs highlighted the complexity of the condition and believed that it would be more appropriate for 'CFS/ME' to be managed by a specialist service. Patients also wanted more access to specialist services with some recognising that GPs didn't have time to manage their condition.
Findings	**Barrier/Facilitator: Role of health professionals**
	Patients wanted their GP to be accessible and actively involved in the longer term management of their condition. Where support was not received, patients reported disengaging from primary care. Patients also recognised a continued lack of commitment to the

Study	Bayliss 2016[17]
	management of the condition by GPs. As a result of not receiving information about the study from GPs, many patients reported disengaging from primary care as this reinforced beliefs that GPs do not prioritise 'CFS/ME'.
	Lack of experience with ME/CFS cases.
	GPs completing the training module reported that they had difficulty remembering the key messages due to limited opportunities to diagnose the condition because it was seen relatively rare.
	Limited consultation duration
	GPs and patients reported a lack of time within a ten minute consultation. Patients felt unable to explain the complexity of their condition to their GP. Without the opportunity to relay this information, patients struggled to work with their GP to manage their symptoms.
	Information from GPs
	Patients with varying severity and time since diagnosis described how the provision of reliable evidence based information meant that the GP was validating their 'CFS/ME' and enabled them to self-manage their condition.
	Online resources as a barrier and facilitator to management
	GPs and patients reported that the training and resources provided as part of the study could have a positive impact on the management of CFS/ME in primary care but suggested these should be made available online and therefore accessible to all. However, some patients were concerned that by placing the resources online, GPs would be let off managing the condition in primary care and sceptical attitudes would continue. Patients therefore reported that they wished to bring information from the internet to the consultation in order to gain a diagnosis from a health professional. Participants had done this in the past, and GPs welcomed this where information was from a reliable source.
Limitations and applicability of evidence	Very minor methodological limitations due to the role of the researcher not being discussed No concerns regarding applicability.

Study	Beasant 2014[21]
Aim	To understand the experiences of adolescents and families in accessing and using a specialist service and to explore whether or not adolescents and their mothers value referral to a specialist service for young people with 'CFS/ME'.
Population	Adolescents taking part in the Specialist Medical Intervention and Lightning Evaluation (SMILE) study and their mothers. Participants were eligible for the SMILE study if they had been diagnosed with 'CFS/ME', were aged between 12 and 18 years and were mildly or moderately affected by the condition; that is, they were not house bound (NICE, 2007). Purposive sampling to ensure that interviews included a range of participants in terms of age, sex, socioeconomic circumstance and ethnicity as well as families from both intervention arms.

Study	Beasant 2014[21]
	N=12 adolescents; male/female 3/9; age mean (SD) 13.9 (1.6) years; illness duration median (IQR) 13 (9 to 18) months; 5 were interviewed post randomisation but before receiving the intervention, and 7 after the intervention. N=13 mothers; 5 mothers were interviewed at all three time points, 8 took part in one-off interviews: 4 post randomisation and 4 after their child received an intervention.
Setting	Participants' homes, UK
Study design	Semi structured interviews with thematic analysis
Methods and analysis	Families were interviewed at three possible time points: after initial assessment before randomisation, after randomisation before the intervention, and after the intervention. Adolescents with 'CFS/ME' were interviewed once at one of these time points for not more than 20 min; parent interviews lasted for 20–60 min. A checklist of topics was used to ensure that similar areas were covered in each interview (experiences of the initial clinical assessment appointment, study participation and the interventions) but with sufficient flexibility to enable participants to raise topics of interest to them. Interviews were audio-recorded and transcribed. Data items were systematically assigned codes using the qualitative data organisation package NVivo and analysed thematically using techniques of constant comparison. Data analysis was an ongoing and iterative process, commencing soon after data collection started and informing further sampling and data collection. Two members of the research team analysed, 10% of the data independently to compare coding and enhance its reliability.
Findings	**Referral to specialist services (for recognition, diagnosis, information & management)**
	The majority of mothers reported the initial assessment appointment as a positive experience. The service recognised and acknowledged the young person's condition, resulting in a sense of relief and reassurance. Mothers felt that symptoms were now being understood and they would receive help. Referral to a specialist service gave families access to an informative team of experts, for some a formal diagnosis, and for all a tailored, patient centred specialist medical intervention that had not been available earlier. This enabled positive change and steps towards a managed recovery. Some mothers felt that the 'CFS/ME' service reinforced symptom management strategies that they had been trying to get their child to follow, and that they felt their child would be more likely to listen if techniques were legitimised by a health-care professional. Half the adolescents reported that specialist medical care was positive, as it enabled them to talk about their illness and gave guidance on how to manage their condition, which brought structure and a sense of normality back into their lives.
	Difficulty with acceptance and integration of medical care strategies to their life
	Half the adolescents reported that, although specialist medical care resulted in better symptom management, accepting that for a time they must reduce activity levels and adopt a routine was challenging. A few mothers noted that specialist medical care strategies had an impact on the whole family and could be difficult to integrate with their lifestyle.

Study	Beasant 2014[21]
Limitations and applicability of evidence	Minor methodological limitations due to unclear relationship between the researcher and the findings, data richness (some findings supported by single quotes). Minor concerns over applicability due to the research aim of the study and representativeness of the sample considering it consisted of feasibility RCT participants which may differ from eligible patients not recruited to a trial.

Study	Brigden 2020[26]
Aim	To examine the extent to which the care of children (aged 5-11 years) with 'CFS/ME' is integrated across settings (home, education and health settings), in order to understand barriers and generate recommendations for integrating care.
Population	Participants were sampled from two studies with embedded qualitative interviews. EXPLORER is a mixed-methods study investigating the epidemiology and qualitative experiences of 'CFS/ME' in younger children. EXPLORER recruited children with a diagnosis of 'CFS/ME' aged 5-11. MAGENTA is an RCT evaluating two behavioural treatments for paediatric 'CFS/ME'. MAGENTA participants were invited to take part in additional interviews for EXPLORER if they were aged between 8 and 11. Families: Children aged 5-11 years and their parent/carers, were sampled from the EXPLORER and MAGENTA, purposefully sampled for variety in terms of the child's gender, age, school attendance and duration of illness. Clinicians: Clinicians working in the specialist paediatric 'CFS/ME' service were recruited as part of the EXPLORER study, purposefully sampled with the aim of recruiting a range of multi-disciplinary professionals. School personnel: Families in EXPLORER were given an information sheet about school interviews and were invited to opt-in and provide written consent to this element of the study. 56% of the families (n=28/50) consented. Schools were purposefully sampled for variety in terms of pupils' age and level of school attendance. School personnel were referred as teachers as all but one staff member was a teacher. Parents: N= 14 Children: N=8; mean age (range) 8.5 (5-11) years; school attendance mean (range) 60% (0%- 100%); illness duration range 9-63 months, mean 24 months. Teachers/School staff: N=11 (7 class teachers, 3 head of year/lead teachers, 1 Specialist Educational Needs Coordinator (SENCO), 1 deputy head, 1 intervention officer (safeguarding and pastoral care)- some staff members had dual roles); from 9 state schools and 2 private schools.

Study	Brigden 2020[26]
	Clinicians: N=9 (5 psychologists, 2 doctors, 2 physiotherapists)
Setting	Specialist Paediatric 'CFS/ME' service
Study design	Qualitative interview study
Methods and analysis	The study's initial focus was on children, their parents/carers and clinicians, exploring their views and experiences of the condition and its treatment. Data were collected and analysed simultaneously and from early analysis it became apparent that the role of the school in the child's care was an important issue and the protocol was emended to extend interviews to school staff. The lead author (AB) undertook face-to-face, semi-structured interviews using a topic guide. Separate topic guides were developed for each participant group, based on literature, the aims of the study and in consultation with two patient and public advisory groups (a 'CFS/ME' young person's advisory group and a public involvement group based in a primary school). Data collection was an iterative process and subsequent topic guides were informed by earlier analyses. A range of locations were offered for the qualitative interviews, including the university premises, the participants' home (families) or workplace (clinicians and teachers) or via Skype (all participants). Interviews were designed to last one hour with adults and 30 minutes with children. The child could choose to be interviewed alone or interviewed in a dyad with their parent (2 children were interviewed alone, 6 with their parent). Interviews were audio-recorded and transcribed. Anonymised transcripts were imported into the data management software Nvivo. Analysis was thematic. Firstly, the datasets were analysed separately (within-group analysis of family, clinician and teacher data), beginning with familiarisation with the transcripts, followed by systematic line-by-line coding of transcripts. Codes were reviewed and grouped into broader themes, which were discussed and refined within the research team. The three datasets were analysed by reviewing the within-group themes and comparing and contrasting perspectives across these groups to draw out key areas of convergence and divergence. Analysis focused on themes relating to integrating care across settings. Interpretation of data was informed by the socio-ecological perspective.
Findings	**Limited capacity to self-manage & need for treatment support**
	Teachers, families and clinicians agreed that younger children with 'CFS/ME', especially those under 8 years, haven't got the capability to manage their condition independently across home, school and clinical setting. Parents described the younger children's inability to understand and adhere to treatment without support, explaining that children wouldn't comprehend the treatment plan and do not have the maturity to self-monitor and self-regulate. At clinic, most dialogue occurred between the clinician and parent, with children having little engagement, not being very responsive. At school, teachers perceived that these younger children were not as adept at regulating their own behaviour (for example unnecessarily exerting energy and then collapsing, being in pain or very upset). Children relied on the adults around them and parents, teachers and clinicians had distinct roles in the child's care.
	Child-centred care

Study	Brigden 2020[26]
	Participants emphasised the importance of child-centred care. Clinicians spoke about identifying the child's 'goals' and having 'their voice in the room' and teachers about giving them 'ownership' and encouraging the child to communicate. As raised by a clinician, 'even though it's going to be caregivers who are really following through with the plan, its' still not going to be as successful as if you're engaging with a young person and they have an element of understanding, appropriateness to their age. we can't lose sight that the young person needs to be involved with their care.
	Integrated/shared care
	Children relied on the adults around them and parents, teachers and clinicians had distinct roles in the child's care. Participants described the **clinician's role as providing a diagnosis, developing treatment plans that spanned** the home and school setting, providing advice such as reducing the school attendance (e.g. only doing four hours of school a day'), structuring rest breaks (e.g. recommending regular breaks), limiting physical education and making physical and social adaptations in the classroom. One clinician suggested things like a medical card so that if the child wants to leave the class she would just hold the card up. **The clinician's role was to review the child's progress and revise the treatment plan as needed. All parties viewed parents as the coordinators of care, responsible for relaying information between clinic and school. They were also primarily responsible for day-to-day supervision of the child's treatment.** They monitored their child's symptoms and activity levels, gave their child direct instructions to regulate activity and sleep, structured the child's environment in line with the treatment plan and administered medication. **Teachers** explained that they had a close and consistent relationship with the child who was usually with them most of the day, with clinicians and families also acknowledging this important relationship. All parties recognised the teachers' responsibility for day-to-day management of the child's health including accommodating reduced school timetables, maintaining a connection with the family during the child's absences, monitoring and regulating the child's activity levels, responding to cognitive, physical and emotional needs; helping the child maintain friendships and encouraging the child to communicate their needs. Clinicians recognised that 'having schools on board with those kinds of things is just so valuable'. Considering the process of diagnosis, clinicians identified the increased complexity of assessing younger children and discussed the benefits of involving schools in this process- stating that the school's observation of the child could be really helpful in the assessment process. Teachers expressed a desire to provide formal reports (which they provided for other clinical conditions such as ADHD) to clinicians to aid assessment. They stated their privileged position of a professional perspective along with a close relationship with the child could be beneficial to the clinician. Parents did not explicitly discuss the need to involve teachers in assessment, but acknowledged the insight that teachers had about the child.
	Accommodations at school
	Participants described the **clinician's role in developing treatment plans that spanned** the home and school setting, providing advice such as reducing the school attendance (e.g. only doing four hours of school a day'), structuring rest breaks (e.g. recommending regular breaks), limiting physical education and making physical and social adaptations in the classroom. One clinician suggested things like a medical card so that if the child wants to leave the class, she would just hold the card up. Teachers portrayed a proactive attitude to providing support and all parties (family, teachers, clinicians) recognised their (i.e. the teachers') responsibility for day-to-day management of the child's health including accommodating reduced school time-tables, structuring the environment to reduce the burden on the child.

Study	Brigden 2020[26]
	Role and communication of diagnosis across home, school and clinical setting
	Across the datasets, participants talked about the importance of sharing the diagnosis across settings. Parents described the impact of diagnosis, the 'relief that somebody has listened', feeling believed and felt it was important that the clinic communicated this directly to school. Both teachers and families identified the diagnosis as a catalyst to the school taking the health concerns seriously and implementing the necessary support. Teachers emphasised that at an organisation/policy level, teachers needed this formal diagnosis to implement treatment recommendations, such as reduced timetables.
	Ongoing communication across settings (home, school, clinical setting)
	All parties highlighted the lack of ongoing direct communication between clinic and school. Teachers reported minimal contact from clinicians typically consisting of two or three letters. In some cases, this limited direct contact was acceptable to schools, however there were cases where families, schools and clinicians identified this minimal contact as insufficient. In the latter cases, schools viewed direct input from the clinical service as 'really vital' and were dismayed that teachers held high levels of responsibility for the child's health with little guidance. There was a level of frustration from all parties. Teachers expressed frustration about the limited input from clinicians, families reported that schools didn't believe them and didn't adapt to the child's needs and created a lot of resistance. Equally clinicians were frustrated by the lack of support from schools. There was agreement on the factors associated with satisfaction or dissatisfaction with the low levels of direct clinic-school contact; 1) relationship/ communication between parents and schools: Teachers satisfied with minimal clinical input attributed this to effective communication between parents and school which allowed teachers to gain an understanding of the condition, receive updates on clinical appointments and viewed the family's communication with the school to be very important. Clinicians believed it was important to empower patients to liaise with school. In contrast, teachers wanting more support from clinicians reported challenges in communicating with parents and said that direct communication with clinic was needed when parents did not have the capacity to communicate. Clinicians also recognised fractious relationship between families and school was a marker to intervene directly with schools; 2) Goals for the child's education aligned: Those teachers satisfied without direct communication from clinicians described the parent as prioritising education while teachers wanting more health input were in tension with parents about how much the child could/should be attending. Equally parents had negative perceptions of schools when they perceived this mismatch and saw schools as more concerned about their targets; 3) Complexity and severity: Teachers managing without direct intervention from clinicians talked about cases being straightforward, describing low levels of absenteeism, fewer concerns over emotional well-being, believed the child was keeping up academically and recovering from the illness. By contrast, those keen for more guidance were concerned with high levels of absenteeism and academic difficulties, cases of multiple diagnoses and multiple professionals involved. Equally some clinicians differentiated between simple and complex cases, in simple cases stating it was up to the parents and the school to put boundaries in place and to have really good communication links but they believed their direct intervention with school could be justified for complex children. They advocated starting without direct communication with schools, moving to direct communication if the case became challenging. Teachers, parents and clinicians who emphasised the need for direct communication between schools and clinic wanted direct conversation with professionals for clearer advice about the child's individual needs and personalised guidance on how the school could manage their health needs. They believed that telephone, emails and face to face meetings between clinicians and teachers could be beneficial. They also wanted multidisciplinary meetings, classroom observations and training sessions. Clinicians differentiated between simple and complex cases (considering complexity in terms of

Study	Brigden 2020[26]
	illness severity, co -morbidities and other professionals involved) and clinicians agreed that telephone and face to face meetings could be beneficial for complex cases. Parents valued direct contact between clinic and school in the minority of cases where this happened.
Limitations and applicability of evidence	Very minor concerns associated with the potential influence of the researcher on the findings not being discussed. No concerns over applicability.

Study	Broughton 2017[29]
Aim	To explore the experiences of 'CFS/ME' patients who were completing programmes of treatment at three NHS specialist 'CFS/ME' services in England.
Population	Adults completing/concluding treatment at one of three outpatient NHS specialist 'CFS/ME' services (median age 43, range 24-62 years; median self-reported illness duration 7.5 years, range 1-17). N=16; male: 12.5%, female: 87.5% median age (range): 43 (24-62) years; median self-reported illness duration (range): 7.5 (1-17) years Participants recruited between July-September 2014, who completed a course of treatment within this period, returning a Consent to Contact Form. Exclusion criteria: age <18 years; too severely affected to be able to participate in interviews; unable to provide informed consent; unable to read and understand the patient information sheet and consent forms; or not diagnosed with 'CFS/ME' as a primary diagnosis.
Setting	Three outpatient NHS specialist 'CFS/ME' services in England.
Study design	Cross-sectional design using semi-structured interviews to explore patients' experiences.
Methods and analysis	Six face-to-face (conducted at the participant's home) and 10 telephone semi-structured interviews lasting from 23 to 57 min (mean length 32 min) with questions about the patient journey before, during and at the end of receiving specialist medical care. All interviews began with the open question: "Tell me about your CFS/ME" and participants were encouraged to guide discussion and introduce their own topics of interest. Interviews were audio-recorded, transcribed and analysed thematically (by two researchers).Techniques of constant comparison informed the analysis and identification of themes.
Findings	**Role of health professionals**
	All participants were referred to 'CFS/ME' specialist services by their GPs. Participants with positive experiences reported their GPs had been 'very supportive', 'brilliant' and 'fantastic', they valued 'being taken seriously' and recognised the key role their GP had played. Participants with less positive experiences described a number of barriers to accessing specialist services including a lack of

Study	Broughton 2017[29]
	information, having to take a proactive role in asking for diagnostic tests, and GP's lack of 'awareness', 'knowledge' or 'belief' in 'CFS/ME'.
	Acceptance of diagnosis & adaptation:
	Although some patients described feeling relieved that diagnosis provided an answer and ruled out other conditions, it was a difficult time for the majority. Participants recalled feeling angry, distressed, frustrated and fearful and that the diagnosis represented a life sentence. Accepting diagnosis of a contested condition was difficult for some; because of participants own negative preconceptions about 'CFS/ME' and the reactions of others. These patients discussed feeling under pressure to convince or prove the validity of their experiences. Time appeared to influence acceptance, with some participants recalling a gradual acceptance that treatment might not be curative. The importance of acceptance in obtaining the most benefit from treatment was highlighted and participants discussed a need to accept changes to their lives as a result of developing ME/CFS, and reflected upon what they had lost or relinquished, including social networks, employment, career and study aspirations and independence.
	Personal attributes-being open and accommodating
	Half the participants recalled finding initial stages of treatment difficult. Many discussed personal responses they believed were key to overcoming challenging periods during treatment. Characteristics described included being open, positive, proactive, willing to try anything, being able to take a leap of faith and having perseverance. They explained how during early stages of treatment advice given by clinicians felt counter-intuitive, and was a departure from the way that symptoms and 'boom and bust cycles' had been self-managed prior to accessing services. Participants highlighted the importance of being 'willing to change' and being prepared to say goodbye to their old life completely in order to engage fully with treatment.
	Realistic goal setting (towards management instead of cure)
	Participants recalled that clinicians assisted with and encouraged the development of new goals which had not been held prior to accessing specialist services. Some viewed these as vital to treatment success, representing a shift in focus towards management rather than cure. New goals were described as smaller, a lot more realistic and more sensible, involving breaking down existing goals, lowering expectations and focusing on the day to day rather than the future.
	Accessibility of medical care (appointments):
	Participants discussed accessibility in terms of being able to attend appointments and accommodate treatment programmes around their commitments. The majority of participants were pleased with the practical accessibility of clinics, describing journeys as being manageable or easy. However all participants mentioned accessibility could be a barrier to attendance. Whilst all reported the ease of access to the clinic improved overtime as symptoms improved, travel during the early stages could be incredibly hard with participants finding the journey stressful and needing to recover after appointments. Some discussed the importance of good public transport links to the specialist service, whilst others felt that they would not have been able to attend appointments without use of a car. Some participants discussed the need for assistance to attend appointments, including help from partners or friends, particularly when symptoms were severe. Others said that work commitments could be a barrier to attending appointments; they noted accessing the clinic would have been difficult if experiencing severe symptoms and concerns were raised about the ability of those severely affected

Study	Broughton 2017[29]
	by CFS/ME to access specialist services. Flexibility in the frequency and mode of appointments was valued by participants; with two saying they appreciated being offered later appointments because of travel burden and symptom fluctuation. The option of having some appointments by telephone was highly valued, particularly when symptom severity or travel problems made attendance difficult. Skype was also mentioned as a possibility
	Referral to specialist services:
	Many participants had their 'CFS/ME' diagnosis confirmed when they were assessed by the specialist services. For many participants specialist services provided information and explanation of 'CFS/ME', simultaneously validating and normalising participants' experiences and symptoms. All participants felt they had benefited from accessing specialist service. The majority recalled having had hopes and expectations of referral and treatment including to confirm diagnosis and manage symptoms better. Participants discussed factors that delayed referral to specialist services for 'CFS/ME'. Some were initially misdiagnosed, for example with depression, multiple sclerosis or glandular fever. Four participants reported that referral to the specialist service had been a lengthy process, mainly because diagnostic procedures required ruling out other medical conditions, involved numerous medical tests and appointments with multiple clinicians.
Limitations and applicability of evidence	Very minor limitations due to the role of the researcher not being explored. No concerns over applicability.

Study	Cheshire 2020[34]
Aim	To explore patient experiences of Guided graded Exercise Self-help (GES) delivered as part of a randomised controlled trial (GETSET) for people with ME/CFS to answer the research question: 'What are the differences and similarities in treatment perceptions and experiences of GES among 'CFS/ME' participants reporting an improvement compared with those reporting deterioration in their condition?'
Intervention details	Guided graded Exercise Self-help (GES) Self-help booklet describing a 6-step programme of graded exercise self-management, based on the approach of GET developed for the PACE trial and NICE recommendations. Six steps: stabilising a daily routine, starting regular stretching, deciding on a physical activity goal and choosing a type of activity with which to start, setting a physical activity baseline, increasing the duration of physical activity and finally the intensity. If symptoms increased after an incremental change in activity, participants were advised to maintain activity at the same level until symptoms had settled, before considering another incremental increase. In the first 30 minute session (face-to-face, by Skype or by phone), a physiotherapist provided guidance on following the booklet and answered any questions. Up to

Study	Cheshire 2020[34]
	3 further 20 minute appointments by skype/telephone were offered over 8 weeks by 2 experienced physiotherapists who were trained to support participants in using the booklet, but explicitly told not to provide therapy. Physiotherapists inquired about progress, answered questions, with a focus on moving forward to the next step, recognised achievements and provided feedback, with the aim of increasing motivation and self-efficacy. A therapy leader trained the two physiotherapists until they were deemed competent and then provided regular individual supervision. Physiotherapists followed a manual and all participant guidance sessions were audio-recorded for supervision, feedback, and monitoring of treatment integrity. If a participant could not be contacted by telephone or Skype, an email was sent to re-engage them. Duration 8 weeks. Concurrent medication/care: Before randomisation, all patients had at least one specialist medical care consultation, delivered by doctors with specialist experience in chronic fatigue syndrome. SMC could involve prescriptions or advice regarding medication, as indicated for symptoms or comorbid conditions such as insomnia, pain, or depressive illness. Although not routinely scheduled during the trial, further SMC sessions were available after randomisation for patients who required it, but it was not a standardised intervention.
Population	People who had participated in the GES arm of the GETSET trial and had rated themselves as improved or deteriorated after the intervention (using clinical global impression of change scale); severely affected patients were not included in the trial. N=19 (n=9 reported feeling 'much better', n=10 reported feeling 'a little worse' – initial aim to recruit 10 reporting 'much better' or 'very much better' and 10 reporting 'much worse' or 'very much worse', but none reported feeling 'much worse' or 'very much worse', so inclusion criteria were expanded to include 'a little worse'); majority Caucasian (17/19); male/female 2/17; mean age (IQR) for 'much better' group 39 (21-54) years, for the 'a little worse group 43 (28-66) years; median (IQR) length of time since symptom onset for the 'much better' group 4 (3-5) years, for the 'a little worse' group 13 (8-21) years.
Setting	Interviews conducted by telephone (n=11), at patients' homes (n=6), at patients' place of work (n=1) and at the University (n=1); trial setting secondary care, UK.
Study design	Qualitative one-to-one interview study with thematic analysis.
Methods and analysis	Semi-structured interviews. Topics included before and after trial wellbeing, expectations of GES, barriers and facilitators to GES and any outside influences on the trial or GES participation. Interviews lasted between 13 and 80 minutes (mean 45 mins). Interviews were audiotaped, transcribed and returned to the participant for checking. Thematic analysis conducted by researchers independent of the implementation of the GETSET trial. Transcripts were analysed, a list of themes was compiled and examined by two researchers. The data were coded and explored using NVivo (qualitative data analysis software) to generate reports for each group for each theme, enabling a systematic comparison between the groups for each topic. Analysis and draft manuscript were critiqued and contributed to by the other authors, independent researchers and the patient representatives.
Findings	**Capacity to follow treatment programme (GES-specific)**
	It was important for participants to have time and space in their lives to follow the GES programme. GES seemed to work best for participants who had fewer commitments that interfered with GES (e.g. life responsibilities, such as work, looking after children, housework, food shopping; lifestyle changes participants were making; or other activities which supported them emotionally). If a

Study	Cheshire 2020[34]
	supportive partner or workplace could relieve the participant of other commitments, then they seemed to be better placed to benefit from GES.
	Motivation (GES-specific)
	Belief: A key factor for maintaining motivation to do GES was participants' belief that it could actually help their ME/CFS, to some extent. For many participants this was the first time they had been offered an NHS treatment for their ME/CFS and they had few other treatment options, and this increased their motivation to try GES. **Understanding:** An understanding of the theory behind GES helped participants understand and therefore engage in GES. For many participants, this understanding was established when GES was explained to them at the beginning of the trial, or from a previous experience of using GET. Participants who had previously unsuccessfully tried GET, or attempted to increase their levels of activity without support, found it useful to have an explanation for the possible failure of previous attempts (e.g. baseline set too high, tried to increase level of activity too quickly), this explanation could motivate them to stick to their GES programme and do it "correctly." **Other motivating factors:** Other factors that participants from both groups reported as being important motivators included: personal attributes (stubbornness, determined, or positive), life philosophies (e.g. taking personal responsibility for their own destinies, preferring not to be on medication), or overcoming fears/scepticism about GES.
	Support from other people
	Participants described how their partner, family and friends also helped them to maintain their motivation. These significant others could provide practical and emotional encouragement and support.
Limitations and applicability of evidence	No significant methodological limitations noted. No concerns about applicability.

Study	Chew-Graham 2008[37]
Aim	To explore how patients with 'CFS/ME' and family physicians conceptualise this condition and understand it and how their understanding might affect the primary care consultation.
Population	Family physicians: n=14; 7 male, 7 female; mean age: 48, SD: 12 years; one of the family physicians' practice was not participating in the FINE trial. Patients: n=24; 11 male, 13 female; mean age: 48, SD: 12 years; months since CFS diagnosis range: 1-240, median: 40.5
Setting	Family physicians and registered patients were from 44 primary care trusts in North West England
Study design	Qualitative interview study

Study	Chew-Graham 2008[37]
Methods and analysis	Semi-structured interviews were conducted by one author at the patients' home and physicians place of work (1 physician was interviewed at home). Interviews lasted between 16 and 72 minutes (median duration= 38 minutes). An interview guide providing a flexible framework for questioning and exploring a number of areas: models of illness, appearance of symptoms, reaching a diagnosis, the consultation and doctor-patient encounters, was used. The interviewer combined open-ended questions to elicit free responses with focused questions for probing and prompting. Digitally recorded interviews were transcribed verbatim by a professional transcribing service, with transcripts checked against the tape by the interviewing author. Analysis proceeded in parallel with the interviews and was inductive taking an interpretative stance. Coding was iterative and informed by the accumulating data and continuing thematic analysis. Coding and interpretation was undertaken individually by four authors.
Findings	**Invisibility of the illness**
	Family physicians expressed frustrations that they could not measure how the patient was affected by their condition. It was so-called 'invisible' and the symptoms seemed out of proportion to the signs leading some to doubt the condition and the genuineness of its presentation. The inability to demonstrate the extent of their condition beyond the snapshot view revealed in the consultation meant that patients were unable to establish that symptoms come and go and that the condition is invisible on good days. Family physicians described how they ran a battery of tests, which invariably returned negative results. With no manifest sign of patients' symptoms and no confirmation of a diagnosis, the physicians would often reach clinical impasse. Patients were aware their condition was invisible from a biomedical perspective.
	Limited medical knowledge & doubt
	Family physicians admitted having limited clinical understanding about ‘CFS/ME’ available to them, causing them to question the existence of the condition. Patients were aware that the medical community disagreed over the existence of the condition and also that family physicians had limited clinical knowledge about ‘CFS/ME’. They believed they were unprepared by their medical training and continuing education to diagnose and manage ‘CFS/ME’ and they acquired evidence from sources outside the clinical domain. Their training enabled them to exclude a physical cause for the patients’ symptoms but doubt and limited knowledge about ‘CFS/ME’ made the diagnosis uncertain. Some patients described the experience of the family physicians who had been unable to offer any advice to help them understand or manage their condition. Given the failure of science and medical training to meet their needs, family physicians and patients looked to a range of alternative sources of evidence about ‘CFS/ME’.
	Relationship with physician
	Some patients believed it was important in both the diagnosis and management of their condition to have an established relationship with their family physician: Not having such an ongoing relationship with their family physician was reported by the patients to make it difficult to achieve agreement about the symptoms and the diagnosis, because the primary physician had no prior knowledge of them. They reported on their inability to demonstrate the extent of their condition beyond the snapshot view revealed in the consultation being unable to establish that symptoms come and go and that the condition is invisible on good days.
	Proactive patients

Study	Chew-Graham 2008[37]
	Some family physicians recognised that patients sought out scientific evidence to support their stance and brought such evidence to the consultation. Patients seemed to use this method of discourse to engage family physicians in a dialog and as a means of accessing other treatments and services.
Limitations and applicability of evidence	Minor limitations due to concerns over data richness with some findings supported by limited quotes Minor concerns over applicability due to the sample which consisted of people recruited in a RCT.

Study	Chew-Graham 2010[36]
Aim	To explore GPs' beliefs about the value of the label of 'CFS/ME', implications of the diagnosis and attitudes towards patients suffering with this condition.
Population	GPs (n=22) recruited via purposive sampling through practices participating in the FINE trial. 46 GPs were invited by letter but 22 agreed to be interviewed.
Setting	GP practices in North-West England
Study design	Qualitative interview study
Methods and analysis	Semi-structured interviews lasting between 10 to 72 minutes (median duration 34 minutes) were conducted using an interview guide. This provided a flexible framework for questioning and explored a number of areas: ideas about the cause of 'CFS/ME', previous experience of patients with 'CFS/ME', how the diagnosis of 'CFS/ME' was achieved, and their role in management of those patients. The interviewer combined open questions to elicit free responses with focused questions for probing and prompting. Interviews were digitally recorded and transcribed verbatim. Analysis proceeded in parallel with the interviews and was inductive, taking an interpretative stance. Coding was iterative and was informed by the accumulating data and continuing thematic analysis. Thematic categories were identified at initial interviews which were then tested or explored at subsequent interviews where disconfirmatory evidence was sought. Interpretation and coding of data was undertaken by three researchers individually and themes were agreed through discussion with the whole team.
Findings	**Lack of clear management pathway**
	The majority of GPs felt that the label of 'CFS/ME' could be harmful because it did not offer a clear management pathway for either the GP or the patient. This can cause GPs to be reluctant to make the diagnosis of 'CFS/ME'. A number of GPs reported frustration with supporting patients once a diagnosis was made implying that 'CFS/ME' was difficult to manage as no 'cure' was possible.
	Referral to secondary care, diagnosis & management
	Those GPs who felt that making the diagnosis or labelling the patient's condition was helpful suggested that referring the patient to secondary care could potentially assist in achieving a diagnosis and providing support to GPs who lack confidence in making the diagnosis alone. GPs however reported experiences of limited availability of potentially helpful places to support them in either making the diagnosis or managing the patient.
	Nature of ME/CFS (difficulty of the condition & lack of cure)
	GPs alluded to the difficulties they had experienced working with patients with 'CFS/ME' once the diagnosis was agreed. The role of supporting the patient was stressed by respondents with a number of GPs reporting frustrations with this work implying that 'CFS/ME' was difficult to manage as no 'cure' was possible and that the work invested in working with such patients is largely unrecognised. GPs articulated a process of diagnosis that prioritised excluding physical causes for a patient's symptoms and presentation, which they

Study	Chew-Graham 2010[36]
	viewed as treatable, implying that some may feel 'CFS/ME' is not treatable, making their role in managing people whose symptoms are not easily categorised challenging.
Limitations and applicability of evidence	No concerns over methodological limitations. Minor concerns over applicability due to the sample which consisted of people recruited in a RCT.

Study	Chew-Graham 2011[35]
Aim	To establish what factors are important for patients to engage in a new intervention for chronic fatigue syndrome/myalgic encephalomyelitis ('CFS/ME') and make recommendations to general practitioners GPs on preparing a patient for referral/ the referral process to such a service.
Population	Patients participating in a RCT of two nurse led interventions for 'CFS/ME' in primary care: the FINE trial, who had received pragmatic rehabilitation (PR) for 18 weeks; recruited from 44 primary care trusts in the North West of England. Inclusion criteria: being 18 or above, fulfilling the Oxford criteria for 'CFS/ME', score of 70% or less on the SF-36 physical functioning scale and four or more on the 11-item Chalder Fatigue scale N=19; male/female: 6/ 13; age range: 20-61, months since diagnosis range: 9 months to 18 years
Setting	Primary care
Study design	Qualitative study
Methods and analysis	Semi-structured interviews were conducted by members of the research team in participants' own home, using interview guides exploring areas including patients' views on the treatment interventions. Interviews lasted between 30 and 90 minutes and were digitally recorded and transcribed verbatim. Inductive analysis proceeded in parallel with the interviews. Coding was informed by the accumulating data and continuing thematic analysis. Transcripts were read and discussed by researchers from different professional backgrounds (primary care and psychology). Thematic categories identified in initial interviews were tested or explored in subsequent interviews, where disconfirmatory evidence was sought. Interpretation and coding of the data were undertaken by all authors and the themes were agreed upon through discussion.
Findings	**Disbelief of health-care professionals / Invisibility of the illness**
	Feeling understood by the therapist was described as a novel experience and in stark contrast to the disbelief and scepticism encountered elsewhere in their encounters with health professionals. This was often attributed to the invisibility of the condition.
	Feeling accepted by the therapist

Study	Chew-Graham 2011[35]
	The belief that they were fully understood by the nurse therapist both personally and in terms of their illness condition emerged as a key factor determining whether patients continued to engage with the therapy and found the intervention offered acceptable. Talking to someone who listened and understood was described by a number of patients as the most positive part of the treatment intervention. Being believed and feeling understood by the therapist emerged as key factors in the formation of a positive relationship. Being heard and understood seemed to be of greater value than the professional medical knowledge attributed to the therapist.
	Own acceptance of diagnosis
	Some patients described the treatment intervention offered as having been especially helpful in terms of their accepting the diagnosis. Engaging with the therapy was dependent upon the patient accepting what their symptoms represented and the diagnostic that was applied. Some described their interactions with the nurse therapist as validating the illness, and the diagnosis, convincing them as to the reality and seriousness of their condition. Accepting their condition and diagnosis was described as being necessary to allow progress with treatment. Acceptance of the label of CFS, enabled the patient to believe that the intervention might be appropriate for them.
	Acceptance of the model of 'CFS/ME' implied by treatment
	Acceptance of the model of the condition ('CFS/ME') implied by the treatment offered emerged as key in engagement in the intervention. Whether or not patients perceived the nurse therapist as having a model of the illness, which matched with their own was vitally important. Where patients adopted the model presented in the intervention, their reasoning for doing so was based on the extent to which the patient perceived the model as making sense. When patients rejected the rationale for the treatment offered, there were a number of reasons; some held models of the illness before treatment which were contradictory to that being presented by the nurse therapist and remained unconvinced by the PR model and the rationale for the treatment intervention that it provides. For example several patients held a model of the illness which implied that activity was potentially damaging, so patients were fearful of relapse.
	Patients' Illness beliefs/ perception
	Some patients regarded the treatment intervention as unsuitable for them because they perceived their condition as being individual and unique and importantly not amendable to treatment. These patients described themselves as experts in their own condition and did not feel there was anything new they could usefully learn.
	Difficulty applying to daily living/ Unworkable models of treatment
	Patients who could not work the management plan into their everyday life felt that it was not a workable model. It was reported that although it sounded logical some had difficulty applying it
Limitations and applicability of evidence	Very minor limitations due to the role of the researcher not being explored. Minor concerns over applicability due to the sample which consisted of people recruited in a RCT

Study	De Carvalho Leite 2011[43]
Aim	To investigate the impact of 'CFS/ME' on people from varied social background, including those from ethnic minorities, and what challenges may be posed to health care practitioners in providing appropriate and equitable care for this condition.
Population	Adults with 'CFS/M', recruited through relevant support groups, community organisations and centres, purposively selected to include a diverse range of illness severity, duration, social variation (age, gender, ethnic background and socio-economic conditions) and year of diagnosis. n=35; aged 18-55; male/female: 8/27; illness duration for the majority was 7≤ than years
Setting	Participants recruited via ME/CFS support groups, community organisations and centres and interviews conducted at the participants' home.
Study design	Qualitative inquiry using in-depth semi-structured interviews
Methods and analysis	In depth semi-structured one-to-one interviews (n=35) and focus group discussions: six of the 35 participants were purposively selected (to include a diverse range of illness severity), for both an initial focus group discussion and the later one-to-one interview. These were tape-recorded and transcribed verbatim. The Focus group with six people with 'CFS/ME' was used to identify the main themes and issues to be explored more deeply in the subsequent interviews. It took place in a quiet room and lasted for two hours, with a break for refreshment and rest. The group was conducted by a researcher, while another researcher supported the group dynamics, observed and took notes to facilitate later analysis. The discussion was managed as a conversation, encouraging participants to tell their own stories to help articulate their ideas about the experience of living with 'CFS/ME'. Three broad areas of inquiry reflected in guide questions were used as starting points to encourage story-telling and discussion to facilitate the emergence of story line narratives within these areas: a) becoming ill and being diagnosed; b) the impact of living with 'CFS/ME'; and c) self-management and being managed within health and social care services. Story telling allowed themes to emerge, without being fixed to a set research agenda. The sequence and wording of questions were decided in the course of the discussion to respond to participants' preferences and conversational styles. One-to-one semi-structured interviews of about 45 minutes (up to a maximum of 3 interviews per participant (45 interviews in total) were conducted with the 35 participants by a researcher at the participant's home or another place convenient for them. Thematic analysis was used on both the focus group and interview datasets. The focus group data transcripts were analysed by four researchers, who together identified the main storylines and emerging thematic areas of support needs, and then adapted question guides for one-to-one interviews. The interviews transcripts were analysed by five researchers who first independently read and re-read the transcripts to identify and extract words and text sections which appeared to describe experiences of living with 'CFS/ME' and encountering health and social services. They independently selected, focused and condensed the data in tabulated written notes with codes. Three researchers met

Study	De Carvalho Leite 2011[43]
	to compare the reliability of codes and agree the developed coding scheme. New codes were developed before comparative subject analysis. Finally a wider group of researchers drew conclusions for the whole dataset
Findings	**Gaining illness recognition**
	a) By practitioners: Participants revealed how they were facing distinctive illness-related barriers in gaining recognition of their illness. Their encounters with health professionals were reported as often problematic in ways which both delayed or reduced access to support (to manage the illness required people to gain access to appropriate health expertise which in turn, could affect the likelihood of gaining family and wider social support) and greatly exacerbated emotional pressures. Most participants found doctors saying they could not help, resulting in their feeling abandoned to fight the problem by themselves. They most often encountered oppositional health services responses and some therefore decided to use a private or alternative health services as a way of getting diagnosis or help. There were reiterated experiences of not being listened to by health-care practitioners. This often posed particular problems in the earliest stages of the condition. Nearly all participants, from both white and non-white groups spoke of their illness not being taken seriously by GPs, with individual symptoms being dismissed, perhaps as a 'virus' or as a common cold. Many experienced this as a profound lack of acknowledgement. This was reflected in participants across all ethnic groups wanting health care practitioners to have the time to help the patient feel 'empowered' and 'believed', to increase their sense of inclusion and acknowledgment. Even when bed-bound, participants encountered unsupportive attitudes from health professionals which greatly undermined their chances of wider belief and support. Participants highlighted how lack of access to social care and practical support was exacerbated when health practitioners would not recognise their illness, making a profound impact on their ability to carry out their family caregiving roles, particularly as parents.
	b) By patients themselves: Lack of recognitions could be especially difficult for people from ethnic minority groups in which such illnesses were less commonly identified as self-recognition and belief of the symptoms and experiences was problematic.
	Difficulty obtaining a diagnosis
	Achieving a diagnosis was seen as a crucial milestone for most participants. Where this led to advice from doctors and other health care professionals with particular knowledge of 'CFS/ME', this was almost invariably a positive experience (e.g. one participant commented on his luck in gaining a prompt GP diagnosis, leading to coordinated care and support from his manager, which allowed him to work part-time within his capabilities and to gain sick leave and retirement as the illness progressed'). Participants most often encountered oppositional health services responses and some therefore decided to use a private or alternative health services as a way of getting diagnosis or help, often exacerbating stress, uncertainty and financial pressures. It was also reported that until a diagnosis was gained, social services could not even assess patients' needs in order for them to gain access to social care support. Disagreements over diagnoses and over-attention to psychological symptoms could lead to inappropriate treatments which paradoxically contributed to deterioration in emotional well-being.
	Lack of treatment options within the NHS
	Participants felt that the health-care system should explore useful interventions and suffered from a lack of control over choices of treatment for managing their illness, which they saw as due to both lack of resources in the National Health and social systems and relative lack of recognition or value given to their own experience with illness. Participants desperate for relief of feelings of pain or

Study	De Carvalho Leite 2011[43]
	illness reported finding treatments such as massage, osteopathy, dietary advice and acupuncture helpful, and it caused ongoing frustration that such interventions were not funded by either the NHS or by a private health insurance for 'CFS/ME'.
	Consultation duration
	Some highlighted the limited time for consultation as a barriers to appropriate care provision and another reason for seeking support outside the NHS.
	Stereotypical attitudes as a barrier to care/ Ethnic-group specific lack of understanding
	People from minority ethnic backgrounds reported particular difficulties in accessing health and social care support systems, experiencing more stigmatisation and stereotyped responses that did not fit their health needs. For example reporting not being taken seriously because of ethnicity with all symptoms interpreted as psychiatric in origin.
Limitations and applicability of evidence	Very minor limitations due to the role of the researcher not being explored. No concerns about relevance with patients from diverse social and ethnic backgrounds and various degrees of illness severity and duration being represented in the sample.

Study	Dennison 2010[45]
Aim	To explore in detail adolescent patients' and their parents' experience of both family-focused CBT and psychoeducation for CFS. The study aimed to elicit participants' experiences in their own terms in order to better understand participants' expectations, therapy experiences and views regarding the effectiveness of their treatment.
Intervention details	Family focused CBT 13 x 1-h sessions of CBT every 2 weeks. Treatment protocol adapted from that used in a trial of CBT for CFS in adults (Deale et al. 1997), taking into account the specific needs of this age group. Particular emphasis placed on building a rapport with all members of the family and establishing a collaborative relationship. Involved encouraging the participant to achieve a balance between activity and rest; gradually increasing activities including home, social and school life; establishing a sleep routine; addressing beliefs such as fear regarding the relative benefits of activity and/or exercise, high self-expectations and all-or-nothing thinking; encouraging individuals within the family to express their own views about the illness and agreeing a way forward and paying attention to relapse prevention. The parent providing the majority of the care was supported as the adolescents became more independent. Homework assignments were negotiated with participants at each session. A treatment guide, Self Help for Chronic Fatigue Syndrome: A Guide for Young People (Chalder & Husain, 2002), was given to the family. Therapists sought to maintain neutrality and acted as brokers in the not infrequent adolescent/parent disputes. Delivered by two trained and experienced cognitive behavioural psychotherapists. Duration 6 months. Concurrent medication/care: Close liaison with relevant school teachers and home tutors was initiated from the start of treatment and maintained throughout. Key issues for discussion were: endorsement of the reality of the condition, negotiating a graded return to school and for some reducing the number of subjects taken. In some cases repeat years were negotiated. Anxieties about reintegrating with peer groups were addressed and some adolescents were supported in changing academic institutions altogether. In

Study	Dennison 2010[45]
	both groups the entire family was invited to the first session and the mother accompanied the child to every subsequent session. Other members of the family attended when they could. Psychoeducation 4 sessions over a 6-month period. Content similar to CBT, but mode of delivery was didactic. Involved discussion, information giving and problem solving but specific homework assignments and cognitive restructuring not included. Families were not given a manual. Therapists ensured adherence to protocol by working from a checklist that included the following. (a) Gave the message that untreated CFS in adolescents has a good prognosis.(b) Presented a model of CFS that distinguished predisposing, precipitating and maintaining factors. (c) Introduced the concept of symptom management – that the way we manage our physical symptoms can make a difference to the outcome. Physical illness analogies such as heart disease were used to increase likelihood of engagement. (d) Gave advice on pacing and consistency of activity and rest, in order to break the vicious circle of symptom lead behaviour. (e) Gave advice on sleep management. (f) Conveyed the message that hurt does not equal harm – increased symptoms do not mean more pathology. (g) Advised clients to gradually build up activity over a period of months. Duration 6 months. Concurrent medication/care: Close liaison with relevant school teachers and home tutors was initiated from the start of treatment and maintained throughout. Key issues for discussion were: endorsement of the reality of the condition, negotiating a graded return to school and for some reducing the number of subjects taken. In some cases repeat years were negotiated. Anxieties about reintegrating with peer groups were addressed and some adolescents were supported in changing academic institutions altogether. In both groups the entire family was invited to the first session and the mother accompanied the child to every subsequent session. Other members of the family attended when they could.
Population	Young people and their parents who had participated in a randomised controlled trial comparing family focused CBT with psychoeducation. N=16 young people; all white British; male/female 6/10; mean age (range) 19.9 (16-24; 13-18 at the time of starting therapy) years; n=7 received CBT, n=9 received psychoeducation. N=16 parents; all white British; male/female 2/14; n=9 were involved in CBT, n=7 were involved in psychoeducation
Setting	Telephone based interview, UK
Study design	Qualitative interview study with thematic analysis.
Methods and analysis	Telephone based semi-structured interviews by researchers who had not met the participants, nor been involved in their therapeutic management and who were blinded to the treatment allocation. Interviews consisted of a series of broad open-ended questions and non-directive prompts. Participants were encouraged to talk about the issues they personally considered important and departures were made from the schedule and subjects spontaneously raised by participants were probed further. Interviews typically lasted around 30 minutes (9.5 to 56 minutes). Interviews were tape recorded and transcribed. Thematic analysis conducted by researchers who were blinded to the treatment allocation. An initial coding manual was developed and was subsequently revised to incorporate more data as further transcripts became available. Coding was iterative and the method of

Study	Dennison 2010[45]
	constant comparison was used to ensure that themes were applied sensitively and as indicated by the data. The final coding manual was reviewed by other members of the research team. Researchers were then unblinded to treatment group and themes were examined in the context of treatment group.
Findings	**Physical capacity and access to care**
	A key criticism of the therapy (CBT or psychoeducation) was related to practical aspects. The location of the therapy sessions (South London) was an issue. The travelling and the sessions themselves left the young people feeling drained and struggling to participate fully. Sometimes the effort was perceived to impact on their health over subsequent days. A few interviewees said that the setting was not comfortable or welcoming and that aspects of the environment did not put them at ease.
Limitations and applicability of evidence	No significant methodological limitations noted. No concerns about applicability.

Study	Devendorf 2018[48]
Aim	To investigate factors, other than depression that explain suicidal ideation, including quality of life, loss of functioning, isolation, and hopelessness about prognosis.
Population	Patients who self-identify as having ME/CFS and endorsed suicidal ideation (SI) but did not meet depression criteria; recruited through patient advocacy websites, newsletters, social media and Internet forums. N=29; 79.3% female, 20.7% male. Mean age: 51.48 years old. Mean score for the BDI-PC: 2.38; one participant endorsed active SI (i.e. score of 3), 28 participants endorsed passive SI (i.e. score of 1).
Setting	The study was hosted online, with participants recruited from patient advocacy websites, newsletters, social media and internet forums.
Study design	Mixed-methods design; qualitative analysis of participants' open-ended survey responses from a previous project that examined illness severity, stigma, physician interactions and depression (McManimen *et al*, 2018).
Methods and analysis	After analysing participants' quantitative responses to the Beck Depression Inventory for Primary Care (BDI-PC), the authors qualitatively analysed participants' open-ended responses that followed the previously completed survey. Participants could clarify or expand upon their survey responses through and open-ended format. Analysis was conducted in the following steps: (1) multiple readings of the data; (2) open coding; (3) developing a final code-book; (4) applying the final code-book, while considering the whole context of each response; (5) establishing inter-rater reliability; and (6) finalizing and categorising codes into themes and sub-themes.
Findings	**Lack of trust in healthcare providers**

Study	Devendorf 2018[48]
	Nineteen participants commented on their dissatisfaction with healthcare providers which was likely driven by the disregard for ME/CFS in the medical community. Many encountered disdain, disbelief and a lack of knowledge from their providers. Most encountered doctors who were trained to view ME/CFS as psychiatric, which was dismaying to the participant. Disappointment ensued when doctors vocalized psychological attributions or inferences, with "just exercise" recommendations or prescribing antidepressants to treat depression. Participants became vigilant of these dismissive attitudes and sought treatment elsewhere if possible.
	Lack of access to helpful healthcare providers
	Participants generally lacked access to helpful healthcare providers. Some participants lived in rural areas that lacked access to healthcare altogether.
Limitations and applicability of evidence	Moderate methodological limitations due to the appropriateness of the data collection method, the study being a follow-up to a quantitative study with open-ended online responses. Moderate concerns over applicability due to participants being a subset of a previous quantitative study who were self-identified as ME/CFS (not diagnosed according to accepted criteria) with suicidal ideations but not depression.

Study	Donalek 2009[49]
Aim	To describe the impact of a chronic illness (i.e. CFS) on the ill parent and to embed the experience of the ill parent within the wider family system responses to this chronic parental illness.
Population	Families from the local CFS community in which one biological parent or parent figure (stepparent or parental partner) must have been diagnosed with CFS by a healthcare professional and met the Fukuda et al (1994) criteria. Eight families with a total of 21 members were included. In each family, the ill member's relation to the family unit, [age], (and family members participating) was as follows: (1) husband/father [75] (wife and daughter); (2) separated wife/mother/daughter [38] (mother and daughter); (3) divorced mother [48] (two sons); (4) husband/father [59] (wife and son); (5) divorced mother [60] (two sons); (6) remarried wife/mother [40] (husband and daughter); (7) divorced mother [45] (daughter); and (8) wife/mother [36] (husband).
Setting	United States (Chicago)
Study design	Semi-structured interviews and thematic analysis
Methods and analysis	Participants were recruited from local support groups, an advertisement in the local CFS newsletter, or word of mouth. Parents who expressed interest then approached other family members. All participants were compensated at the rate of $8 per hour in the form of gift certificates. The researcher interviewed the parent together with as many members of the family as possible. A semi-structured interview structure was used, focussing on the history of CFS in the family, member beliefs about the illness, the effect of the illness, family responses and family function. Interviews were preceded by explanation of the research and written informed consent from

Study	Donalek 2009[49]
	adults, written consent for adolescent participation by the parent or guardian, and written assent from adolescents. Participants had to be at least 13 years old. Thematic analysis was used to explore narratives, focussing on identification of the interrelating themes and generalisations within and across cases. After transcription, all interviews were read twice in their entirety. Descriptions of the illness for the parent with CFS and for the family, and unanticipated themes, were identified. Themes were reconteztualized as configurations within individual family members and their individual families/. The researcher met regularly with an expert in family research, with whom analytic processes and tentative findings were reviewed. Thematic analyses were sent to families for review and verification.
Findings	**Barriers relating to diagnosis by a GP, failure to achieve medical legitimacy**
	a) **Lack of knowledge** from the GP: participants stated that sometimes the physician said they simply 'did not know' b) **Inappropriate referral**: participants stated that they were often referred for psychiatric treatment as depressed c) **Lack of belief** from the GP: some participants stated that in their experience the GP implied that the individual's perception of the illness was false Participants said that the above responses from a GP often resulted in humiliation and anger, and meant that individual continued to search for knowledgeable, respectful care. The result of failure to achieve medical legitimacy included difficulty to obtain work modifications or unemployment compensations, as well as trouble explaining their change in health to friends or family members.
Limitations and applicability of evidence	No concerns of methodological limitations. No concerns of applicability.

Study	Haig-Ferguson 2019[65]
Aim	To explore the views of children and young people, their parents, and healthcare professionals of treatment delivered by videoconferencing in a specialist paediatric 'CFS/ME' team
Population	Young people (n=12), aged 9-18 years, who were actively attending video-conferencing (n=6), had been previously attending video-conferencing (n=3) or had declined video-conferencing (n=3). Children and young people (CYP) were eligible if they were 18 or under, receiving treatment (of any sort) within the specialist 'CFS/ME' team (irrespective of whether they had a confirmed diagnosis of 'CFS/ME' or not) and were well-enough to complete an interview as judged by themselves, their parents and the healthcare professional providing the treatment. Mothers of children with ME/CFS (n=6). Parents of eligible children and young people. Health-care professionals from a specialist paediatric 'CFS/ME' service, including psychologist, physiotherapist, occupational therapist and nurse.
Setting	Specialist Paediatric 'CFS/ME' service in the UK

Study	Haig-Ferguson 2019[65]
Study design	Semi structured interviews and one focus group with thematic analysis.
Methods and analysis	The majority of interviews were conducted on an individual basis with either the parent or the CYP, however one parent and CYP were interviewed together as a dyad. Interviews followed a semi-structured interview schedule specifically designed for this study. This included questions about perceptions of treatment via videoconferencing, including the benefits and limitations of video-conferencing use. Interviews lasted between 15 and 35 min. Data collection was an iterative process; initial interviews were used to inform subsequent stages of data collection and analyses. The interview schedule was adapted depending on whether the participant was receiving treatment via videoconferencing, had declined videoconferencing or had never used videoconferencing. The focus group with health-care professionals took place after a team meeting at the hospital site. The group was asked the same questions included in the semi-structured interview schedule. Interviews and focus groups were audio recorded and transcribed verbatim. Transcripts were analysed using thematic analysis. All transcripts were systematically read and re-read to ensure familiarity with the data. Transcripts were then hand-coded using annotation, hand-drawn diagrams and tables in Microsoft Word. Codes were then collated into potential themes, which were reviewed and discussed by the research team. Analysis began while data collection was ongoing in order to explore developing themes. Recruitment continued until researchers were satisfied that they had achieved “thematic exhaustion”.
Findings	**Technical problems of video-conferencing**
	Technical difficulties associated with video-conferencing were considered as a barrier to effective communication with health-care professionals, especially because it could exacerbate the problems in interaction that result from a young persons’ ‘CFS/ME’ symptoms. Those included issues with connection speed, reduced quality of the picture, reduced sound quality sometimes muting the therapist and occasions when video-conferencing would just intermittently stop working, all leading to disruptions to the session. Although technological issues were frustrating, some participants felt that they could be dealt with and almost accepted this as part of the experience. Although the majority of discourse around technological issues was negative, for some participants there were positive experiences of using technology.
	Virtual connection as a barrier/facilitator to effective communication
	Participants talked about communication being negatively affected by a virtual connection, and it seemed that the screen could become a “barrier” to effective communication. That with a virtual connection you “can't tell exactly how people are feeling” . Voices would sound different and subtle emotional ques could be missed. For some, the inability to have direct eye contact via videoconferencing was something that was problematic. Not being able to see the whole person on videoconferencing also made things difficult. Young people, parents and healthcare professionals all talked about how subtle emotional cues may be missed via videoconferencing. The participants talked about how interacting via videoconferencing was inherently different from interacting face-to-face. Some young people felt that the virtual sessions constrained both the content and the depth of what they would discuss. Lack of, or reduced

Study	Haig-Ferguson 2019[65]
	engagement was a potential result. Healthcare professionals wondered whether this potential lack of engagement was because a therapist was not seen as a "real person" when on screen. In contrast some reported that videoconferencing could potentially facilitate more open communication than face to face sessions. Being physically removed from the therapist was seen as a possible reason why young people may find it easier to open up.
	Privacy concerns associated with video-conferencing
	Young people had concerns about confidentiality via videoconferencing, expressing a concern that they would be overheard by other family members when they were at home, which could potentially limit what they felt they could share via videoconferencing. There were also some questions as to how secure the connection would be. Potential confidentiality and security issues arising from using videoconferencing at home were a concern for parents with some reporting it might be invasive of their children's' privacy. For the health professionals privacy was also a concern, though they talked about videoconferencing being "intrusive" for young people or even an invasion of their own privacy.
	Benefits of videoconferencing:
	a) Access to services: Participants felt a benefit of videoconferencing would be that patients who either lived too far away to receive a specialist service or were too unwell to attend hospital appointments, would still be able to access evidence-based therapies. Travel was frequently cited as a potential difficulty in terms of increasing 'CFS/ME' symptoms, therefore the use of videoconferencing was seen in a positive light because it meant that patients would not have to travel long distances to access support.
	b) Convenient and flexible: Participants talked about videoconferencing being beneficial for young people because it was more convenient and flexible, and could "fit around school hours" and for parents especially if they were "struggling to get time off work". There could also be flexibility in terms of appointment times, both in terms of "length of appointment and the right time of day" for the patient. Videoconferencing was easier to fit in to the busy lives of families
	c) Comfort of home Negative view of the hospital environment contrasted with the comfort of home. Hospitals were described as "sterile", "intimidating", "not the most friendly" and "boring", while the home environment was described as "pretty chill", "relaxed" and "very comfortable".
Limitations and applicability of evidence	Very minor methodological limitations due to the role of the researcher not being discussed. No concerns regarding applicability.

Study	Hannon 2012[66]
Aim	To develop an education and training intervention to support practitioners in making an early diagnosis of 'CFS/ME' and supporting patients in the management of their symptoms.
Population	Health practitioners (GPs n=9, practice nurses n=5, 'CFS/ME' specialists n=4), Carers (n=10), patients (n=16), aged 28-71 Patients and carers included n=12 BME (black minority ethnic) group participants.

Study	Hannon 2012[66]
Setting	Patients and carers were recruited through 'CFS/ME' support groups, community groups, specialist 'CFS/ME' services in the NHS. A purposive sample of BME group patients were also recruited from South Asian third sector groups in General Manchester and personal visits to community groups. Practitioners were recruited via a purposive sample of GP Practices and Primary Care Trusts.
Study design	Qualitative interview study
Methods and analysis	Semi-structured interviews were conducted face-to-face using topic guides: patient/carer interview focus included experiences of being diagnosed, support received in primary care; practitioner interviews focused on current practice in the diagnosis and management of patients with ME/CFS, attitudes towards ME/CFS and training and education needs; Specialist 'CFS/ME' practitioner interviews focused on the needs of patients and asked for comments on existing 'CFS/ME' resources. Initially inductive analysis was conducted using thematic analysis in line with modified grounded theory approach, using open coding; a deductive approach was then taken when data fully analysed.
Findings	**Lack of HP knowledge and understanding of ME/CFS**
	Patients described having been given a diagnosis of 'CFS/ME' without any advice on symptom management or support. They described how they had been left to find their own information and persuade the GP to meet their needs. The GP and practice nurse respondents expressed varying degrees of understanding of 'CFS/ME' and some questioned whether 'CFS/ME' was a legitimate illness; they were unaware of the evidence base for this condition or believed the symptoms could be explained by a psychological problem or secondary gains. Those who did recognise it as a legitimate illness were aware that some of their colleagues fail to identify this condition which can lead to inappropriate diagnosis. Some GPs and practice nurses used the label as a last resort and with reluctance due to their own lack of knowledge, but also because making the diagnosis did not lead to obvious treatment. Patients and carers explained how they took information to their GP in an attempt to raise their awareness of the condition. A gap in knowledge was also recognised by 'CFS/ME' specialists who highlighted a training need in primary care
	Lack of clear management pathway
	Some GPs and practice nurses used the label as a last resort and with reluctance because making the diagnosis did not lead to obvious treatment and they believed that there was no cure for 'CFS/ME'.
	Consultation duration
	HPs recognised that a 10 minute consultation with a patient with 'CFS/ME' can be challenging due to the variety and complexity of symptoms. A ten minute consultation was also seen as a potential barrier to diagnosis by 'CFS/ME' specialists as GPs may not be able to gain a complete understanding of the variety of symptoms patients can experience and the impact of those on their life.
	Presence of carers in medical consultations/ support from carers
	Patients and carers described how visiting a GP can be a challenging experience, with patients describing difficulty in remembering or articulating their symptoms and how they would take a carer or family member with them to make sense of the consultation. Patients

Study	Hannon 2012[66]
	and carers described the important role that carers play in the management of the illness, which included support in the home and during a GP consultation.
	Flexibility in medical appointments
	Some patients also highlighted a need for flexibility when making appointments.
	Issues with referral to secondary care and lack of collaboration between health-care services
	Health professionals described difficulties with referral to secondary care due to fragmented services and a lack of collaboration and a number of GPs and practice nurses were unaware of specialist ME/CFS services. Others had referred their patients to the specialist service, but lacked an understanding of what these services can offer patients. Patients were concerned around the long waiting time to attend specialist services and it was also suggested that improved communication between primary care and the specialist service may enable the GP to manage the patient during this period.
Limitations and applicability of evidence	Minor limitations due to the role of the researcher not being discussed, data richness (data occasionally supported by single quotes). No concerns over applicability.

Study	Horton 2010[76]
Aim	To explore the nature of professional 'best practice' in working with people with ME/CFS.
Population	Health care professionals who had been nominated by people with ME/CFS who had taken part in an associated England-wide study of their support needs. N=6; genders not reported. Three participants were from specialist services (medicine, occupational therapy, physiotherapy) and three were from non-specialist services (medicine, occupational health, holistic practice). 36 people with ME/CFS nominated eight HCPs as having provided them with particularly helpful or effective care and six agreed to participate. One HCP was named by six different people with ME/CFS.
Setting	UK (East of England and London)
Study design	Qualitative study using semi-structured interviews.
Methods and analysis	Five interviews were conducted face-to-face ad one by telephone. Semi-structured interviews were based on a topic guide developed to reflect research literature identifying key aspects of service user and HCP experiences of ME/CFS and to deploy a framework of question types (e.g. experience, opinion, feeling). The following topics were covered in interviews: i) general experiences of working with people with ME/CFS; ii) enabling people to access information and resources; iii) recognising and responding to the needs of people with ME/CFS; iv) enabling people to take an active role; and v) experiences of working with people from ethnic minorities, or from manual or routine occupations, or who have a severe condition. Interviews lasted between a half to a full hour and all were audio-recorded.

Study	Horton 2010[76]
	Audio recordings were transcribed in full using English orthography according to an agreed protocol. To maintain anonymity of the participants, transcripts were labelled simply as Health Care Practitioner number 1 to 6. Codes were created from the first two transcripts as a basis for iterative thematic analysis. Themes and sub-themes were identified and developed by the individual researchers and a two-stage process of cross-checking and discussion was used to validate the analysis. Two validation meetings were held in which the main themes were presented to 23 people living with ME/CFS, family carers and ten HCPs. Comments from these groups showed strong accord with the findings of the study.
Findings	**The role of specialist services**
	Specialist HCPs emphasised that there was a need for specialist services to be more 'visible' and to provide education for other HCPs, GPs especially, because there is a lack of knowledge about the condition in the GP population. This was thought to be because GPs lacked frequent exposure to these patients. Specialists had both experience and expertise to be able to support GPs and other HCPs in reaching or confirming a diagnosis, giving advice on appropriate medication, or providing services such as specialist Occupational Therapy. Specialists were involved in supporting people applying for benefits, often trying to help other agencies understand the variability inherent in the condition.
	Lack of knowledge and recognition of ME/CFS
	Specialist HCPs emphasised that there is a lack of knowledge about the condition in the GP population. HCPs described frustration at the lack of recognition or common acknowledgement of the condition by society and its institutions, such as health or benefits agencies, and poor access to resources such as CBT or other psychological services when they were thought to be necessary.
	Lack of experience with or exposure to ME/CFS
	It was acknowledged that reaching a firm diagnosis of ME/CFS can be challenging for GPs working in primary care who have little experience of the condition. Exposure to new presentations of ME/CFS was considered important for improving primary care practice. It enabled HCPs to recognise the condition and develop confidence in their diagnostic skills. Very careful history-taking, listening carefully and patiently to presentation of symptoms, with appropriate investigation were all considered vital elements of practice. Specialist practitioners develop awareness of the wide range of symptoms whether physical or psychological that can be associated with the condition and their significance, through extensive exposure to 'CFS/ME'.
	Role of diagnosis
	Several HCPs saw the lack of any diagnostic test giving conclusive proof of the condition as impacting on practitioners and patients alike. One view was that until such a test is developed the existence of the condition will remain in doubt amongst some medical practitioners and policy-makers. The negative impact of 'no diagnosis', a delayed diagnosis or a mis-diagnosis were clearly acknowledged by participants. Consequences of a delayed diagnosis for improvement and recovery were considered significant, acknowledging that this left patients uncertain and with entrenched and often unhelpful patterns of behaviour. They affirmed that

Study	Horton 2010[76]
	confirmation of diagnosis may represent the end of a long period of uncertainty for a person with 'CFS/ME' and may thus be a significant relief
	Disease severity
	A very small proportion of people seen by specialists HCPs were living with a severe condition and were significantly unwell, confined to home, or bedbound in a darkened room, unable to communicate. This was reported to be extremely challenging even by the specialist HCPs who may have very few helpful suggestions.
	Accommodations/ Tailored care delivery
	Specialist HCPs would visit people with serious condition at home, or if appropriate maintain contact by phone, especially to offer support for the family.
	Acceptance
	Specialist practitioners recognised that for those with long-term illness, changing established patterns can be very hard. Some people continue to fight the idea of 'CFS/ME' and its implications, including actively seeking to engage with health professional services. It may take months before they accept the condition and decide to make positive steps to change their lives by giving up work, reducing working hours, and making significant lifestyle changes.
	Strict NHS therapy acceptance criteria
	Aspects of CBT can be very useful in helping people break counterproductive patterns of thought and behaviour in some cases and specialist HCPs said they often used CBT principles in their practice, especially where unhelpful patterns of thought and behaviour, anxiety or stress were evident. However, NHS HCPs all emphasised how difficult it was for adults with 'CFS/ME' to access formal CBT, despite there being a small proportion of patients who would definitely benefit. Adults with 'CFS/ME' rarely met the strict acceptance criteria set by NHS mental health services for CBT.
	Lack of professional knowledge and referral to specialist services
	Specialist HCPs identified a core minority group of GPs in their region who made referral to their service, but contrasted these GPs with the many who did not understand ME/CFS, and who see it as a psychological rather than a physical condition. They reported whole practices as having decided that ME/CFS did not exist and that many GPs would never make a referral to a specialist service. Participant HCPs reported how some patients told them that their GP openly stated their lack of belief in the existence of ME/CFS. They acknowledged how much pressure some people had had to exert just to get a referral to their service and emphasised that there is a need for specialist services to be more visible and to provide education for other HCPs. Specialists had both experience and expertise to be able to support GPs and other HCPs in reaching or confirming a diagnosis, giving advice on appropriate medication, or providing services such as specialist Occupational Therapy.
	Time constrains in primary care
	All participants emphasised the importance and powerful therapeutic value of listening. Time limits in the primary care system were reported to often constrain patients from recounting their full story.

Study	Horton 2010[76]
Limitations and applicability of evidence	Minor limitations due to the role of the researcher and data richness with some data supported by single quotes No concerns over applicability.
Study	Lin 2009 [89]
Aim	To investigate the prevalence of barriers to healthcare utilisation
Population	Random population sample in Georgia, USA; recruited through a cross-sectional screening survey N=780; mean age (SD; range): 44 (10; 18-59); n=112 with CFS, n=100 classified as CFS but for an exclusionary diagnosis (people who fulfil empiric criteria for CFS but who have an exclusionary diagnosis), n=264 with (ISF) insufficient fatigue (people who have been ill for >6 months but do not fulfil empiric criteria for CFS), n=157 ISF with otherwise exclusionary conditions, n=147 non-fatigued
Setting	
Study design	Cross-sectional population based study with qualitative analysis
Methods and analysis	Data was derived from a healthcare utilisation questionnaire that was part of a one-day clinical assessment. Healthcare utilisation was defined by responses to the question 'During the past year, did you see, talk to, or consult with a healthcare professional about your personal health?' and then 'During the past year, how many times did you see, talk to, or consult with a healthcare professional about your personal health.' Respondents who reported foregoing healthcare were asked to indicate reasons for seeking healthcare and why they did not seek healthcare. Responses were recorded as open-ended text. Participants completed the healthcare Utilisation Questionnaire at home prior to the clinical visit. At the visit, study coordinator reviewed the responses to assure the understanding of questions and logic of skip pattern and worked with subjects to rectify omissions and errors if necessary. All text (verbatim) responses were analysed with SPSS Text Analysis for surveys 2.0. Emerging categories were extracted by combined methods: 1) a semantic network approach based on Wordnet; and 2) 'term inclusion' that creates 'categories using lexical series algorithms'. After automatic extractions, manual review was done by a statistician and a CFS research clinician, for each category to reduce the misclassification of theme categories automatically extracted via the software through term, pattern, and contextual qualifier. If a potential misclassification was observed by the first manual reviewer, the second reviewer would consolidate the discrepancies with the first reviewer. The categories of text responses were exported as dichotomous variables into Microsoft Excel format and imported to SAS Version 9.1 for subsequent data analyses.
Findings	Accessibility
	a) Physical constraints were identified, such as family and work responsibilities that interfered with seeking help, geographical location (not enough providers in the area), difficulty obtaining transportation to the providers' office, difficulty obtaining a timely appointment to see a provider, and inconvenient office hours.

Study	Horton 2010[76]
	b) Financial concerns about cost, insurance company co-payment, and that insurance would not cover the care received were identified.
	Knowledge, attitudes & beliefs
	The primary knowledge barrier consisted of both those with the illness and healthcare professionals overlooking a fatiguing illness due to a lack of knowledge about such illnesses. Attitudinal barriers included subjects' thinking that the problem was 'no big deal' or would 'get better on its own' and that individuals needed an excuse or a better reason to see a healthcare professional. Personal barriers (minimization of illness and lack of family support) and fear (fear of stigmatisation and confronting the problem) were additional beliefs held by study subjects.
	Healthcare system barriers
	a) Trust and confidence in the healthcare system: Subjects indicated that trust and confidence in healthcare professionals impacted their decision not to seek healthcare consultation: a doctor may not do enough to find out what is making them sick; the treatment did not make them feel better; a healthcare professional will require more tests without reviewing previous test results; belief that doctors did not believe in the diagnosis of CFS; the subjects felt rejected by healthcare professionals or that healthcare professionals might minimise their illness.
	b) Structural/system barriers: A lack of referral system and insensitivity to patient needs were reported. Subjects sometimes self-diagnosed their symptoms or illness and considered them as consequences of lack of exercise, overweight, aging, hormone imbalance, depression, pre-menopause, menopause and intermittent pain. As a consequence of foregoing healthcare and self-diagnosis, subjects self-treated themselves. One of the commonly used self-treatments of their symptoms or illness was using over-the-counter medications to treat their 'comes and goes' pain.
Limitations and applicability of evidence	Serious limitations due to risk of selection bias as the sample was originally recruited for a different study and selection criteria were unclear; the role of the researcher; data analysis with data collection method and analysis not being transparent, implicating our ability to assess data richness and whether findings are well grounded in the data. Moderate concerns over applicability due to the majority of the sample consisting of people without CFS; paper still included as 62% of sample consisted of people with 'CFS-like illnesses' i.e. suspected of having CFS at the time of clinical evaluation, but themes also emerging from data of non-fatigued individuals.

Study	Marks 2016[94]
Aim	To explore HCPs experiences of working with children and adolescents with 'CFS/ME' so as to develop an understanding of the process relating to how they understand the condition.

Study	Marks 2016[94]
Population	Paediatricians, physiotherapists and clinical psychologists, working in two NHS organisations in the UK: a hospital outpatient paediatric service and a specialist centre providing inpatient and outpatient care for young people with 'CFS/ME'. All had a minimum 3 years' experience of working with ≥ 3 young people with 'CFS/ME'. Consistent with theoretical sampling, participants were selected on the basis of how they informed and validated emerging theory. (n=10; 3 male, 7 female; 5 specialists: inpatient and outpatient care, 5 non-specialists: hospital based-outpatient care)
Setting	Hospital outpatient paediatric service and a specialist centre providing inpatient and outpatient care for young people with 'CFS/ME'
Study design	Qualitative interview study
Methods and analysis	Semi-structured interviews were conducted, using a semi-structured interview schedule developed by the research team. This focused on how participants referred to and understood 'CFS/ME', exploring thoughts about aetiology, maintaining factors and effective recovery. Following data analysis, the schedule was modified and focussed on the emerging theory. The audio-recorded interviews were conducted by the primary researcher and varied between 28 and 83 minutes. Interviews were transcribed and analysed consecutively by the primary researcher and transcripts were simultaneously analysed by two of the researchers. Concepts were constantly compared within and between transcripts and grouped together into categories. Axial coding was used to explore the relationship between categories. The theory was refined through selective coding where a core category emerged and a provisional model is proposed outlining how concepts produce particular beliefs which generate certain actions and consequences.
Findings	**HCPs' belief in ME/CFS**
	One participant shared how their belief in the existence of ME/CFS facilitated engagement and granted access to appropriate care; another suggested that past clinical experience biased HCPs towards one perspective (e.g. focussing on psychosocial aspects at the expense of physiological factors). Another participant stated that their understanding of ME/CFS fluctuated while working with an individual, suggesting that beliefs are modified and illustrating the reflexivity of the proposed cycle.
	Choice of label/diagnosis
	The choice of label given to a young person influenced subsequent intervention. The experience of receiving a diagnosis, and the explanation around it, was pivotal in families' acceptance of the diagnosis and label and the recovery process as it either facilitated engagement or provided a barrier to treatment. The pathway to recovery varied as a consequence of the label give. For example, the HCP who referred to ME/CFS as 'last straw syndrome' felt that this label guided interventions exploring the impact of stress on the body. Similarly, the participant who felt that a child could receive a diagnosis of either chronic pain or ME/CFS highlighted that different specialist teams would be involved, and rehabilitative treatment would differ in each case.
Limitations and applicability of evidence	Minor limitations due to recruitment skewing towards HCPs with positive attitudes towards ME/CFS as participants were recruited on the basis of how they informed and validate emerging theory.

Study	Marks 2016[94]
	No concerns over applicability

Study	Parslow 2017[109]
Aim	To explore the views of health professionals who work in specialist paediatric 'CFS/ME' services in England and have regular contact with children with 'CFS/ME' and identify outcomes that are clinically important.
Population	Health professionals treating children <19 years old were recruited via a purposive sample of specialist 'CFS/ME' paediatric services within the NHS (four largest specialist services were recruited, based on the following UK regions: South West, London, East of England and the North East; all health professionals in the study worked in a multidisciplinary team. n=15; male/female: 5/10; with 2 month to 25 years of experience in paediatric ME/CFS; including a range of clinical disciplines
Setting	Paediatric ME/CFS services, NHS England
Study design	Qualitative focus groups and interview study
Methods and analysis	Two focus groups (comprising 5 participants in one and 4 in the other), a paired interview, two individual face-to-face interviews and two telephone interviews took place at the participants' place of work or over the telephone and lasted between 43 and 61 minutes (median 52 minutes). One author facilitated the focus groups and conducted all interviews, using a flexible topic guide developed following discussions with all authors to enable participants to talk about their views and to raise issues of importance and provide consistency. This covered: 1) the service context within which the professionals worked; 2) current use of PROMs and 3) views about the aspects of health that are important in their assessment of outcomes and shared decision making with children with 'CFS/ME'. Analysis, led by the author was conducted alongside data collection, to enable data gathered earlier to inform subsequent data collection. Data were transcribed verbatim and checked for accuracy and analysed thematically incorporating a mixture of deductive and inductive coding, to enable development of both anticipated and emergent themes. Initial coding was undertaken and other members of the research team read and independently coded a subset of the data. The coding framework was refined with new codes added and existing codes merged or split. Through this process broader categories and higher-level recurring themes were developed, data were examined for disconfirming evidence and finally a narrative summary of the findings was written.
Findings	**Nature of ME/CFS**
	All health professionals talked about the complexity of paediatric 'CFS/ME' and the impact across multiple aspects of health. They described the difficulty of treating children with 'CFS/ME' due to variability and fluctuation of the **condition** and environmental barriers preventing children from returning to normal; and described a number of coping strategies were employed to help children cope with the condition. They talked about the complexity of the condition with symptoms varying between children; circularity was also described as a feature of the condition; children experience a 'boom and bust' pattern with increasing symptom severity following activity which can lead to a downward spiral of reduced activity.

Study	Parslow 2017[109]
	Low mood
	Health professionals described the circularity of low mood as maintenance factor preventing improvement in 'CFS/ME'. Children can have low mood due to symptoms and a lack of participation (to school, leisure activities and social life) and can then become more vigilant to symptoms. This can then lower their thresholds for participation, further lowering their mood in a negative cycle.
	Flexibility and tailored treatment approach
	Flexible strategies were required to treat the variable severity of symptoms and functional ability of individual children. Considering the individual functional level and priorities of children when setting treatment goals was highlighted. Health professionals described how they could be working with an athletic child one minute and then a child who only wants to see their friends the next. They described how in some cases children appeared to improving in terms of function whilst symptoms remained the same.
	Attitudes and support from social environment
	Health professionals identified external environmental factors that can act as a barrier to children with 'CFS/ME' returning to normality. These included understanding, attitudes and support from others (friends, school and family). Due to a lack of understanding from the community, children with 'CFS/ME' can be faced with negative attitudes and comments. All health professionals reported the profound impact 'CFS/ME' has on the family. They felt this could affect the ability of families to follow clinical advice. It was reported that family dynamics, family tension or other external stresses could impact their ability to follow clinical advice.
	Collaboration of health professionals with schools
	Working with schools was reported to be a core part of treatment for all services involved in the study; educating schools, correcting unrealistic expectations and formulating reduced timetables
Limitations and applicability of evidence	Very minor limitations due to the role of the researcher not being discussed. No concerns over applicability

Study	Picariello 2017[112]
Aim	To explore the experiences of patients with CFS who undertook CBT at a specialist service for CFS.
Intervention details	Face-to-face CBT from experienced therapists, guided by a standardised CBT manual and with regular clinical supervision. Sessions were typically fortnightly, with up to 15 sessions, depending on progress and agreement between the client and therapist. Participants were offered follow up sessions at 3, 6 and 12 months after the end of treatment.
Population	Patients who had finished CBT or were in the follow up stage, recruited consecutively. Participants were excluded if they did not have a diagnosis of CFS.

Study	Picariello 2017[112]
	N=13; male/female 2/11; age range 18-24 (n=1), 25-34 (n=7), 35-44 (n=2), 45-54 (n=2), 55-64 (n=1).
Setting	Recruited from a specialist outpatient unit, UK.
Study design	Semi-structured interviews with thematic analysis.
Methods and analysis	Semi-structured interviews either face-to-face or by telephone. Interviews were digitally recorded and transcribed. Transcripts were analysed using inductive thematic analysis. This included extracting initial codes, incorporating emergent codes into broader themes and development of a coding manual. Grounded theory techniques were also used: constant comparison, generating a storyline and diagramming. Data coded separately by two authors, discrepancies discussed and themes modified accordingly.
Findings	**Motivation and illness-dependent capacity (CBT-specific)**
	Participants recognised that in order to benefit from CBT, one must be ready to invest effort in it and motivation must come from within. However, the ability to invest effort might depend on illness severity and personal circumstances at the time of therapy. Some participants felt that starting CBT was more suitable at a time when symptoms were less severe. Participants found self-monitoring tasks useful, but at the same time found some tasks tedious or difficult to fit in to their routine.
	Beliefs and attitudes towards treatment (CBT-specific)
	An important facilitator of engagement with therapy was prior beliefs and attitudes towards CBT. Patients reported that the ability to be open and receptive towards CBT helped them to engage in therapy. Many participants also reported that their acceptance of psychological explanations was crucial in the process of engagement.
	Diagnostic process and unhelpful health care professionals
	Many participants reported difficulty with the process of obtaining a diagnosis. Some were misdiagnosed with other illnesses, which seemed to contribute to a feeling of frustration and disillusionment with the health care system. One participant felt that the battle to get diagnosed, and the lack of recognition and poor communication from health care professionals, could alienate patients from CBT. Another participant said that getting diagnosed and referred to the clinic was the first step towards improvement, but that the lengthy process of obtaining a diagnosis can potentially act as a barrier to CBT uptake.
	Stigma
	A major subtheme that emerged in the study was related to the stigma associated with mental health and psychological treatments. Many participants perceived that their illness did not belong to the realm of mental health problems. Another participant reported 'feeling stigmatised… the psychiatric hospital was somewhere where people went when they were seriously ill… I felt very ashamed'.
	Communication
	Many participants also reported difficulties communicating their experiences to health care professionals and relatives or friends. Many participants valued building a relationship with the therapist and reported a preference for face-to-face consultations. Some participants found face-to-face sessions to be more personal and felt that they were able to be more forthcoming.

Study	Picariello 2017[112]
Limitations and applicability of evidence	Moderate methodological limitations due to recruitment strategy (only participants who had completed treatment), unclear relationship between researcher and participants. No concerns regarding applicability.

Study	van der Vaart 2019[149]
Aim	To identify factors experienced by mental health care practitioners and managers influencing the implementation process of Internet-based cognitive behavioural therapy (ICBT) for chronic pain and CFS in mental health care.
Intervention details	The implementation of ICBT programs was part of a National implementation project to improve care for patients with medically unexplained somatic symptoms, called Master your Symptoms. Leiden University and Radboud UMC were responsible for implementing their own developed and evidence-based ICBT program but during half-yearly meetings with all project partners the strategy and progress was discussed. The implementation process included: finding agreement with managers with respect to the use of the treatment, treatment capacity; instruction of therapists; therapist training and supervision; monthly contact with therapists of each centre to discuss progress and possible threats, such as reorganizations or changes in procedures of routine clinical care that may hamper the project; and PR actions to notify possible referrers of the treatment options. The ICBT programs for CFS and chronic pain made use of the same digital platform and are build up in a highly comparable manner. Both programs start with a face-to-face intake, to assess whether the ICBT is indicated. For CFS this was when patients met CDC criteria (revised, 2003 criteria) for CFS or idiopathic chronic fatigue (Worm-Smeitink et al., 2019), both stating that patients should have severe and ongoing fatigue that leads to impairment in daily functioning and is not explained by a medical or psychological condition. Co-morbidity was allowed when this could not explain the presence of severe fatigue. ICBT was offered to all these patients. Therapists decided whether ICBT was suitable. The intake was also used to explain the treatment and the online program and (for chronic pain) to set personal treatment goals. Thereafter, patients continued to work via the online platform, on which they could access the six treatment modules that together form the complete online CBT. Examples for CFS are: 'Getting started and goal setting', 'Regulate sleep-wake cycle', 'Gradually increasing my activity'. The content of both programs included psycho-education, assignments and diary registrations. Master your Fatigue also included video's with patient examples. Patients are guided by the same therapist they had their intake session with. They received therapist feedback weekly or fortnightly in a secured e-mail box in the program. Therapists were trained in a 1.5 day training. The training for CFS included using ICBT in stepped care. This was because the ICBT was implemented as a first step of stepped care, in which patients who were still severely fatigued or impaired after ICBT would be offered additional face-to-face CBT.
Population	Therapists and team managers from 12 mental health care clinics were recruited via purposive sampling. All clinics were participating in an implementation program and had been using 'Master your Pain' and/ or 'Mater your fatigue' during 2 to 4 years.

Study	van der Vaart 2019[149]
	Therapists: n=14, mean age (SD): 41.9 (9); male/female: 4/10; sample included health care psychologists (n=5), clinical psychologists (n=2), one psychotherapist, MSc Psychologists (n=6). Team managers: n=4, mean age (SD): 51.8 (11.2); male/female: 2/2
Setting	12 mental health care clinics in the Netherlands
Study design	Qualitative; Semi-structured interviews.
Methods and analysis	Semi-structured interviews took place either face-to-face, at the health clinic or at the university, or via telephone or lasted approximately 30 min (median: 32 min range 21-56 min) The interview guide covered the five domains of the Consolidated Framework for Implementation Research (CFIR), covering five domains: (1) the implemented intervention, (2) individual characteristics of the users, (3) the inner setting of implementation, (4) the outer setting, and (5) the implementation process. The interviewee was first invited to reflect about his or her experience with the implementation in general, after which further questions was prompted to ensure that facilitators and barriers regarding all domains of the CFIR were covered. The interviews were audiotaped and transcribed verbatim. Analysis of the interviews took place in three steps. First, two authors (RV and YB) independently categorized fragments within the interviews and placed them within one of the five CFIR domains. Discrepancies in choice of domain were discussed by the two researchers until consensus was reached. As CFIR is based on research in medical settings and the current study focused on the mental health care setting, the second step in the analysis used an inductive approach to bottom up identify themes within the five main domains. This way, specific factors related to ICBT use in mental health care practice could be distilled. One of the authors (YB) created a coding scheme in which the themes that had come up in a subset of three interviews were divided in the five levels of the CFIR model. This coding scheme was checked by a second author (RV) before it was used to code all other interviews. During the second phase of coding, themes could be combined and any new themes that emerged could be added, resulting in the definitive subdivision in themes. Finally, all themes were divided into either facilitators or barriers.
Findings	**Individual characteristics of therapists**
	Regarding individual characteristics that influenced implementation, respondents mentioned both determinants among therapists and among their patients. The attitude of the therapist is key, which is often expressed in a feeling of confidence and trust in the ICBT, and also confidence in therapist's own skills and working with a strict protocol. Also, the ability to use the ICBTs in a flexible manner was frequently mentioned. Skills to tailor the ICBT to the needs of each individual patient are a prerequisite in order to use the program beneficially. For example, therapists who mentioned they still saw their patients face-to-face from time to time, or who skipped certain assignments if they did not seem appropriate, valued the ICBTs a lot more. This also relates to the self-efficacy that therapists report. Feeling in control of the program and the treatment process was essential. Clear and positive communication about the program towards patients was perceived as very beneficial, also increasing the motivation of patients to work with the program.
	Patient attributes
	a) **Co-morbidity and symptoms:** Barriers that related to patients often involved the presence of comorbidity, according to the respondents. Patients with chronic pain or fatigue regularly experience other psychological problems, such as PTSD,

Study	van der Vaart 2019[149]
	depression, or personality disorders. Respondents indicated to expect that ICBT would not be enough to help these patients effectively and would therefore not start an online therapy. It was also reported that patients often struggle with a low level of energy and concentration, which was described as a 'low load capacity', which made it difficult for some to read the texts in the programs or to even sit behind a computer.
	b) **Attitude:** the attitude regarding online therapy among patients could be a barrier. Some patients did not want to start with ICBT at all, because they lacked trust, felt hesitance to take responsibility and/or had no interest in computers. Other patients did start, but had problems staying engaged. It was also mentioned that the ICBTs seemed to be particularly useful for a specific subgroup within the patient population, according to some respondents. This subgroup was described as being younger, of the male gender, intelligent, and with an existing interest in computers.
Limitations and applicability of evidence	Very minor limitations due to the role of the researcher not being discussed Serious concerns over applicability due to the research not being limited to the implementation of ICBT for 'CFS' but also for 'Chronic pain' and not always being possible to distinguish whether reported barriers and facilitators were applicable to ICBT for CFS, chronic pain or both.

Study	Ward 2008[151]
Aim	To explore users' views and perceptions of their experiences of counselling, in particular what they found useful and what they found unhelpful or negative.
Intervention details	Any type of counselling intervention delivered by a counsellor, therapist, or clinical psychologist. Length of counselling ranged from eight weeks to one year and included both NHS and private settings. From the material, authors concluded that participants had experienced CBT, person-centred, psychodynamic and integrative/eclectic approaches to counselling.
Population	People who had received a formal diagnosis of ME from a medical practitioner and who had experienced any type of counselling intervention recruited through advertisements in the newsletters of the ME Association and the Action for ME user group. N=25; male/female 4/21; age mean (SD, range) 44 (11, 23-65) years; illness duration (range) 2-19 years.
Setting	Telephone based interviews, UK
Study design	Unstructured interviews
Methods and analysis	The interview began with a general introduction and the direction was determined by the interviewee, with the interviewer prompting and encouraging. Participants were offered to be interviewed over a number of sessions if this was helpful, but this was not necessary for any participants. Interviews lasted 20-90 minutes, were digitally recorded and transcribed.

Study	Ward 2008[151]
	Interview transcripts were analysed using thematic analysis by the authors following grounded theory principles and the resulting thematic structures were compared and discussed until the final thematic structure was derived.
Findings	**Physical impact of attending therapy (physical capacity)**
	One negative issue mentioned by several participants related to the physical impact of the counselling on someone with severe ME. For example, they described the difficulty of making their way to and from the session each week, and the strain of keeping up a session of 50 minutes.
Limitations and applicability of evidence	Moderate methodological limitations due to recruitment strategy (ME charities; more likely to be patients who did not recover), research design (unclear interventions, based on participant recall) and data analysis (insufficient data presented to support all findings). Minor concerns regarding applicability due to unclear interventions.

Study	Webb 2011[155]
Aim	Study: To examine factors associated with time taken to access specialist services and explore the issues experience by parents prior to assessment in a specialist service. Interview: To explore the barriers to accessing healthcare experienced by parents of children with 'CFS/ME'.
Population	Parents of children with 'CFS/ME' under 16 years of age with a confirmed diagnosis of 'CFS/ME', attending assessment or follow-up at the Bath Specialist paediatric 'CFS/ME' service, based at the Royal National Hospital for Rheumatic Diseases (RNHRD) by the specialist 'CFS/ME' clinician between November and December 2010. Parents (mothers and one step-father) of N=9 children (including one parent couple); 5 female children; mean age (SD) 11.9 (4.3); mild/moderate illness severity n=4, severe n=3
Setting	Specialist services
Study design	Mixed methods study design involving semi-structured interviews
Methods and analysis	Semi-structured interviews were conducted at the RNHRD and lasted 30-40 minutes. Interview content was initially based on a review of literature and then amended with advice from the Association of Young People with ME (AYME). Interviews were digitally recorded and transcribed verbatim. Each interview tape was listened to and transcripts read several times to develop a sense of the content. Data was analysed manually using content analysis after categorisation into main sub-headings. Thematic analysis was conducted with themes identified in a semi-deductive manner where codes were identified from adult 'CFS/ME' literature and compared with themes that emerged from the data. This included salient ideas, concerns and perceptions from different interviews being grouped together to form meaningful themes.

Study	Webb 2011[155]
	Ideas emerging from the data were grouped into a thematic framework including Global Themes, Sub-themes, codes and sub-codes. Themes were identified and compared by two independent researchers and interviews were revisited by a third researcher for final coding. Data validation was achieved by feeding the themes back to AYME and clinicians to ascertain whether they considered the themes to reflect the reality of parents' experiences.
Findings	**Lack of health professional knowledge**
	Parents felt both GPs and paediatricians lacked knowledge of 'CFS/ME', were unsure how to make a diagnosis and didn't understand the referral process or how to access practical support. They felt that GPs in particular knew little about the condition or the recommended guidelines when ME/CFS was suspected or diagnosed. This led to a delay in diagnosis and to the parent having to inform the GP about the specialist service and referral criteria. Parents felt they were dismissed by GPs as worrying over normal childhood illnesses and weren't signposted to the practical support they were entitled to.
	Communication problems
	a) **Doctor communication problems:** Parents reported that GPs and in one case a Child Psychiatrist, delegitimised their child's experience, were patronising, didn't listen to them and dismissed their concerns. They also failed to ask questions and empower their child to talk; nor did they express empathy. Parents reported having to attend the GP surgery on many occasions to convey the seriousness of the problem; they felt they were patronised and made to feel inadequate as parents. They felt that lack of empathy was expressed both in the verbal communication with doctors and their facial expressions and body language. They felt unable to ask questions and approach the GP because they felt dismissed. Parents sometimes found their GPs and paediatricians' attempts to give information (even if they knew something about the condition) were not always helpful or were not given in a way they could understand it or put it into practice.
	b) **Parent communication problems:** Parents struggled to communicate an illness that wasn't visible as well as having difficulty communicating a problem that their child, and not themselves, were experiencing. They reported that their children found it hard to put their experiences into words and that it was difficult answering more probing questions in front of the child
Limitations and applicability of evidence	Very minor limitations due to the role of the researcher not being discussed. No concerns over applicability

Study (& subsidiary paper)	Whitehead 2006[157] (Study 1); Whitehead 2006[156] (Study 2)
Aim	Study 1: To explore how people with chronic fatigue syndrome/myalgic encephalomyelitis ('CFS/ME') describe and interpret their illness experience.

Study (& subsidiary paper)	Whitehead 2006[157] (Study 1); Whitehead 2006[156] (Study 2)
	Study 2: To further illuminate the reconstruction of identity in 'CFS/ME' with an emphasis on the experiences that facilitate this and to explore a possible trajectory. Research question: 'What does the experience of 'CFS/ME' mean to people who are experiencing this state of being-in-the-world and their families?'
Population	17 British people with ME/CFS Ages ranged from 13 to 63 years. 6 men, 11 women. Time since diagnosis ranged from 1 to 8 years. Time between start of symptoms and the interviews ranged from 2 to 40 years. Time between the start of symptoms and diagnosis ranged between 6 months and 32 years, with the majority of the group gaining a diagnosis within 2 years of the onset of symptoms (n=10), a further three within 10 years and four over 10 years. Family circumstances ranged from those with children at home, older children living away, geographically dispersed families and those in retirement.
Setting	UK
Study design	Longitudinal qualitative study involving up to three in-depth interviews and analysis using narrative topologies.
Methods and analysis	Study 1: Up to three interviews were conducted with each person to help to build up rust. Participants were asked to start their narrative by describing the onset of symptoms and describe their illness experience up to the present day. People were recruited from a number settings, an ME/CFS clinic at a local hospital, a local ME/CFS support group and through a snowballing approach to recruit people with ME/CFS who neither attended a ME/CFS clinic nor a support group. Analysis was interpretative in orientation and the researcher's preunderstandings were acknowledged and reflected upon with the aim of achieving a fusion of horizons/ The analysis did not seek to assimilate the material into a prearranged framework and was not entered into to seek an objective valid truth. No set method of analysis was adhered to rather general principles used. Each narrative was analysed individually to identify events in that transcript. An emerging framework was created by analysis alongside the next transcript narrative, with the aim of producing both narrative and paradigmatic thematic analysis. The key analysis steps involved reading and immersion, identification of stories, identification of topics, summarising stories and sequences, constructing a representation of the narrative as a whole, followed by micro-analysis of specific events and processes. Study 2: In-depth interviews were conducted mainly in participant's own homes with follow-up interviews conducted over a two and a half year period. All interviews were tape-recorded and transcribed verbatim. The interview schedule was unstructured with minimal probes throughout the interview, starting with one question; 'can you describe the onset of symptoms?' Verbatim transcriptions of the interview were sent back to participants to review the content and accuracy. Analysis began by identifying key words and concepts that emerged. Themes were created based on segments of data and drawing from conceptual literature until a decision to leave the hermeneutic circle of analysis was made. Codes were mostly descriptive at first, developing into interpretive themes through in-depth reflection.
Findings	**Unsupportive GPs**

Study (& subsidiary paper)	Whitehead 2006[157] (Study 1); Whitehead 2006[156] (Study 2)
	Half of the participants felt that their GPs were not supportive and this set them back. Experiences of unsupportive GPs often led to self-doubt and withdrawal from services.
	Lack of diagnosis
	Around half of the participants said they did not receive a diagnosis or referral to secondary care when visiting the GP in the first 6 months of onset of symptoms. These participants remained without a diagnosis, despite further investigation and repeat visits to the GP. This group instead used books, media publicity and complementary/alternative medicine to help interpret their symptoms and then support the diagnostic label. People waited until they had collected 'proof' from a number of sources before approaching the GP with a possible diagnosis. All eight of this group 'forced' the issue of a diagnosis of ME/CFS by presenting the GP with a self-made diagnosis supported by the evidence they had acquired to back these assertions, a process that took most several years. The use of alternative therapies by participants was widespread and was linked to a lack of access to specialist care. Everyone in the group had tried a form of complementary/alternative medicine, with diets the most common form of alternative treatment.
Limitations and applicability of evidence	No concerns of methodological limitations. No concerns of applicability.

Study	Williams 2016[159]
Aim	To explore the impact of physical dependency on well-being for adults with ME/CFS.
Population	Adults with ME/CFS who are physically dependent on other people for help in daily life. N=10; 9 female, 1 male. Mean age: 45.5 years old (range 25-60 years). Participants included people with mild, moderate and severe ME/CFS. Participants were self-selected as they responded to a mass invitation via their support group coordinator. Inclusion criteria were: (1) aged between 18 and 60 years; (2) diagnosis of ME/CFS by a registered GP for a minimum of 3 years; and (3) to live with at least one other person or require help from others.
Setting	Participants were recruited from Southern England.
Study design	An exploratory qualitative methodology was used in order to capture variability in experiences and emotions. Thematic analysis was used to provide rich and detailed accounts. An inductive approach was taken and themes were identified at the semantic level. The researcher adopted a realist epistemological perspective, meaning that it was assumed participants' experiences were true. The findings were conceptualised as themes that were found within the experience of being physically dependent on other people.

Study	Williams 2016[159]
Methods and analysis	Data were collected from semi-structured telephone interviews. Each interview was recorded using a telephone-recording device and Dictaphone. These were transcribed verbatim using Express Scribe transcription software. Participants were provided with an information sheet, a consent form and a summary of the research findings. The participant sample was obtained by contacting ME/CFS support groups that advertised their services on the website of 'Action for ME'. Questions were informed by Spradley's guidance (1979), previous literature and from three people with ME/CFS who were asked to express their thoughts regarding the research topic. Each interview was 45 minutes in duration, followed by a formal debrief reminding participants of the aims of the research. After conducting 10 interviews, saturation was reached The following steps were followed to produce thematic analysis: (1) immersion in the data; (2) generate initial codes that identify features of the data; (3) sorting codes into potential themes; (4) reviewing the themes at the level of coded data extracts and considering the validity of themes in relation to the data set; and (5) defining and naming the themes and sub-themes.
Findings	**Invisibility of the illness**
	ME/CFS was described as an 'invisible illness', with sufferers sometimes looking healthy to those around them but feeling incredibly unwell. Participants linked this to difficulty in being recognised as needing help, and not feeling able to ask for help. A lack of understanding due to the invisibility of the condition was reported to generate reluctance in asking for help.
	Communication problems
	Participants spoke of the frequent problems they face with trying to communicate with others about the condition and their needs, as other people struggled to understand why they required help. Participants felt that communicating their needs was difficult because of how they felt about themselves, their low self-esteem and loss of self-worth playing a role in hindering their ability to communicate. Due to these problems with communicating the nature of the condition, some participants described attempts to go for long periods of time without asking for help.
	Seeking help limited by exhaustion of the task
	Participants expressed that the task of explaining to someone how, when and why they need help could be exhausting. Individuals often had to weigh up their energy resources in order to determine whether asking for help was the best course of action.
Limitations and applicability of evidence	Minor concerns over methodological limitations due to selection bias: participants were self-selected as they responded to a mass invitation via their support group coordinator. Minor concerns of applicability due to focus of research on physical dependency on others.

Appendix E GRADE-CERQual tables

Summary of evidence: Barriers and facilitators to the diagnosis of ME/CFS in adults

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	Design	Finding	Criteria	Rating	Overall assessment of confidence
Lack of health-professional knowledge and medical legitimacy					
9 (9 studies reported by 10 papers)	Semi-structured interviews and thematic analysis (4 studies); semi-structured interviews and grounded theory analysis (2 studies); focused interview and constant comparative method (1 study);	Lack of medical legitimacy, limited health professional knowledge and understanding of ME/CFS and insufficient medical training were reported both from a patient's and clinician's perspective; and meant that health professionals struggled or were unwilling to make a diagnosis, while patients and carers had to seek a diagnosis from multiple doctors or adopt a proactive role.	Limitations	Very minor methodological limitations	HIGH
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
	focus groups & written qualitative response questionnaire and qualitative analysis (1 study); focus groups and grounded theory analysis (1 study)				

Seven studies with very minor to minor issues; Limitations due to the potential influence of the researcher on the findings not being discussed (Bayliss 2014; Chew-Graham 2008; Clarke 1999 & 2000; Gilje 2008; Hannon 2012; Horton 2010; McCue 2004), due to concerns over data richness with some findings supported by limited quotes in three studies (Chew-Graham 2008; Hannon 2012; Horton 2010).

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Nature of diagnosis					
7	Semi-structured interviews and thematic analysis (3 studies); semi-structured interview and study-developed analytic framework (1 study); focused interview and cross-case analysis (1 study); focus group and thematic analysis (1 study);	The lack of a diagnostic test or sufficient diagnostic criteria causes doubt among health care professionals and complicates the diagnosis of ME/CFS which is essentially done by exclusion of different conditions through multiple medical tests and medical appointments, as reported by both patients and health care professionals.	Limitations	Minor methodological limitations	HIGH
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
	semi-structured interview and grounded theory analysis (1 study)				

Six studies with very minor to minor issues; methodological limitations due to the potential influence of the researcher on the findings not being discussed in four studies (Bayliss 2014; Clarke 2000; Devendorf 2019; Gilje 2008; Hannon 2012; Horton 2010), due to concerns over data richness with some findings supported by limited quotes (Devendorf 2019; Hannon 2012; Horton 2010).

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
Focus on physical symptoms					
1	Semi-structured interviews and open explorative	Both HPs and BME patients were reported to focus on physical symptoms during medical consultations by each other, with the HPs reporting that patients tend not to seek medical advice for symptoms other than physical and	Limitations	Very minor methodological limitations	MODERATE
			Coherence	No concerns about coherence	

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
	thematic coding using components of grounded theory	patients feeling discouraged to discuss non-specific symptoms.	Relevance	Moderate concerns about relevance	
			Adequacy	No concerns about adequacy	

One study with very minor issues; methodological limitations in the contributing study due to the potential influence of the researcher on the findings not being discussed (Bayliss 2014); moderate concerns over relevance due to the population of the contributing study being relevant to black minority ethnic groups and of potentially limited applicability to ME/CFS patients of other ethnic groups.

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
Referral to specialist services					
4	Semi-structured interviews and thematic analysis (3 studies);	ME/CFS patients, GPs and ME/CFS specialists reported that referral to specialist services or secondary care facilitates the diagnosis, providing access to experts that can confirm the diagnosis and support GPs and HPs who may lack the confidence to do so alone.	Limitations	Very minor methodological limitations	HIGH
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
	focus group and written response questionnaires and qualitative analysis (1 study)		Adequacy	No concerns about adequacy	

Two studies with very minor to minor issues; methodological limitations due to the role of the researcher not being discussed in two studies (Glje 2008; Horton 2010) and minor concerns over data richness with findings mostly supported by single quotes in one study (Horton 2010).

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
Complicated journey to specialist services					
4	Semi-structured interviews and thematic	The journey to specialist services, which are likely to facilitate the diagnosis, is complicated by long waiting times, misdiagnoses, numerous tests and medical appointments as well as the limited availability of those services or GPs lack of awareness of them.	Limitations	Very minor methodological limitations	HIGH
			Coherence	No concerns about coherence	

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
	analysis (3 studies); focus group interviews and grounded theory analysis (1 study)		Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

One study with minor issues; methodological limitations due to the role of the researcher not being discussed and minor concerns over data analysis with findings mostly supported by single quotes in one study (Horton 2010).

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Diagnostic overlap (co-morbidities & misdiagnosis)					
5	Semi-structured interviews and thematic	Conditions with symptomatic overlap and co-morbid conditions were reported to complicate the diagnosis, often leading to unnecessary referrals and misdiagnosis, with ME/CFS patients and health professionals mentioning	Limitations	Minor methodological limitations	MODERATE
			Coherence	No concerns about coherence	

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
	analysis (2 studies); focused interviews and constant comparative method and cross-case analysis (1 study); semi-structured interviews and grounded theory analysis (2 studies)	multiple sclerosis and psychiatric disorders including depression.	Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	

Four studies with very minor to serious issues; methodological limitations due to the role of the researcher not being discussed in four studies (Clarke 2000; Devendorf 2019; Lovell 1999; McCue 2004), due to concerns over data richness in two studies due to findings mostly supported by single quotes in one study (Devendorf 2019) and limited information in one study (Lovell 1999) and due to concerns over the lack of detail on the data collection method in one study (Lovell 1999); minor concerns about adequacy due to concerns over data richness associated with two studies.

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Lack of definitive treatment					
2	Semi-structured interviews and thematic analysis (1 study); Semi-structured interviews and grounded theory analysis (1 study)	GPs and practice nurses described how the lack of a clear management pathway and cure for ME/CFS caused reluctance to make a diagnosis, with it even being viewed as harmful.	Limitations	Minor methodological limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Moderate concerns about adequacy	

One study with minor issues; methodological limitations due to the potential influence of the researcher on the findings not being discussed and concerns over data analysis with findings mostly supported by single quotes in one study (Hannon 2012); moderate concerns about adequacy the finding supported by relatively limited information from two studies.

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Heterogeneity of ME/CFS					
3	Semi-structured interviews and thematic analysis (2 studies); Focused interviews and constant comparative method (1 study)	There is great variability with ME/CFS both on an individual level with symptoms fluctuating from time to time but also from patient to patient and within one's lifespan with developmental differences in the illness experience, as reported by ME/CFS patients and health care professionals.	Limitations	Minor methodological limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance	
			Adequacy	Minor concerns about adequacy	

Three studies with very minor to minor issues; methodological limitations to the role of the researcher not being discussed in three studies (Clarke 2000; Devendorf 2019; Horton 2010) and minor concerns over data analysis due to data richness with findings mostly supported by single quotes in two studies (Devendorf 2019; Horton 2010); minor concerns over relevance with the reported between and within patient variability not being explicitly linked to the diagnosis but deduced to be complicating the diagnosis within the context of the present review; minor concerns about adequacy due to concerns about data richness at the individual study level associated with two studies (Devendorf 2019; Horton 2010).

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Invisibility of ME/CFS					
1	Semi-structured interviews and thematic analysis (1 study)	Physicians and patients raised the invisibility of ME/CFS which could not be demonstrated within the context of medical consultations or diagnostic tests, hindering the diagnosis.	Limitations	Minor methodological limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Very minor concerns about relevance	
			Adequacy	Minor concerns about adequacy	

One study with minor issues; methodological limitations due to concerns over data richness with some findings supported by limited quotes (Chew-Graham 2008); very minor concerns about relevance, the sample of the study consisting of people that had been previously recruited in a RCT (Chew-Graham 2008); minor concerns about adequacy with minor concerns about the richness of the information supporting the theme in the contributing study.

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Language barriers					

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
1	Semi-structured interviews and open explorative thematic coding using components of grounded theory	Not speaking English acts as a barrier to the diagnosis and management of ME/CFS, with patients not being able to adequately describe their symptoms or understand their GP during consultations	Limitations	Very minor methodological limitations	LOW
			Coherence	No concerns about coherence	
			Relevance	Serious concerns about relevance	
			Adequacy	Minor concerns about adequacy	

One study with very minor issues; methodological limitations in the contributing study due to the potential influence of the researcher on the findings not being discussed (Bayliss 2014); serious concerns about relevance, the finding being of limited applicability to ME/CFS patients outside black minority ethnic groups; minor concerns about adequacy with information emerging from one study.

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
BME cultural beliefs					
1	Semi-structured interviews and open explorative thematic coding using components of grounded theory	BME people may sometimes turn to religion or spiritual healers rather than primary care when experiencing fatigue, relying on religion and prayer to manage their symptoms and not seeking medical advice, which can result in a delay or lack of diagnosis.	Limitations	Very minor methodological limitations	LOW
			Coherence	No concerns about coherence	
			Relevance	Serious concerns about relevance	
			Adequacy	Minor concerns about adequacy	

One study with very minor issues; methodological limitations in the contributing study due to the potential influence of the researcher on the findings not being discussed (Bayliss 2014); serious concerns about relevance, the finding being of limited applicability to ME/CFS patients outside black minority ethnic groups; minor concerns about adequacy with information emerging from one study.

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
BME community attitudes towards some health issues					

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
1	Semi-structured interviews and open explorative thematic coding using components of grounded theory	The expectation to fulfil certain roles within the family or community as well as the lack of acknowledgment of tiredness and fatigue as symptoms requiring medical assistance may lead people to ignore symptoms of ME/CFS and can be a barrier to the diagnosis and management of ME/CFS in BME communities,	Limitations	Very minor methodological limitations	LOW
			Coherence	No concerns about coherence	
			Relevance	Serious concerns about relevance	
			Adequacy	Minor concerns about adequacy	

One study with very minor issues; methodological limitations in the contributing study due to the potential influence of the researcher on the findings not being discussed (Bayliss 2014); serious concerns about relevance, the finding being of limited applicability to ME/CFS patients outside black minority ethnic groups; minor concerns about adequacy with information emerging from one study.

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
Racism and stereotyping by health-care professionals					

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
1	Semi-structured interviews and open explorative thematic coding using components of grounded theory	The stereotypical beliefs of some health professionals towards people from BME groups may act as a barrier to the diagnosis while BME peoples' awareness of those beliefs and fears of being given stigmatising labels by their community can act as a motivator to avoid the diagnosis of ME/CFS.	Limitations	Very minor methodological limitations	LOW
			Coherence	No concerns about coherence	
			Relevance	Serious concerns about relevance	
			Adequacy	Minor concerns about adequacy	

One study with very minor issues; methodological limitations in the contributing study due to the potential influence of the researcher on the findings not being discussed (Bayliss 2014); serious concerns about relevance, the finding being of limited applicability to ME/CFS patients outside black minority ethnic groups; minor concerns about adequacy with information emerging from one study.

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Inconsistencies between health professionals					

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
2	Semi-structured interviews and thematic analysis; Focused interviews and cross-case analysis	Lack of consensus in the case definitions used by health care professionals, as well as in what they regarded as the cause of the symptoms patients presented with, could impact the diagnosis given to patients as reported by patients and physicians.	Limitations	Minor methodological limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	

Two studies with very minor and minor issues; methodological limitations due to the role of the researcher not being discussed in both studies (Clarke 2000; Devendorf 2019) and minor concerns over data analysis in one study with finding mostly supported by single quotes (Devendrof 2019); minor concerns over adequacy with relatively sufficient information from two studies supporting the theme.

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Consultation duration					

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
1	Semi-structured interviews and grounded theory analysis	Health professionals emphasised how challenging it can be to establish an understanding of symptoms within 10 minute consultation appointments.	Limitations	Minor methodological limitations	LOW
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Serious concerns about adequacy	

One study with minor issues; methodological limitations due to the role of the researcher not being discussed and concerns over data analysis with some findings supported by single quotes (Hannon 2012); serious concerns about adequacy, the theme supported by limited information from one study.

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
Continuity of care					
2	Semi-structured interviews	Establishing an ongoing relationship with their physician was seen as important for the diagnosis of ME/CFS by	Limitations	Minor methodological limitations	MODERATE

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
	and thematic analysis (1 study); Semi-structured interviews and open explorative thematic coding using components of grounded theory (1 study)	patients, while lack of continuity of care was considered to impede the diagnosis.	Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance	
			Adequacy	Moderate concerns about adequacy	

Two studies with very minor to minor issues; methodological limitations due to the potential influence of the researcher on the findings not being discussed in one study (Bayliss 2014) and due to concerns over data richness with some findings in one study supported by limited quotes (Chew-Graham 2008); minor concerns about relevance, the sample of one study contributing to this finding being limited to black minority ethnic group patients (Bayliss 2014) and the sample of the other study consisting of people that had been previously recruited in a RCT (Chew-Graham 2008); moderate concerns about adequacy with relatively limited data from two studies illustrating the finding.

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Good health professional practice					
1	Semi-structured interviews and thematic analysis	Attention to symptom presentation and rigorous history-taking were viewed as vital elements of practice by health care professionals.	Limitations	Minor methodological limitations	LOW
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Serious concerns about adequacy	

One study with minor issues; methodological limitations due to the role of the researcher not being discussed and concerns over data analysis with some themes supported by single quotes (Horton 2010); serious concerns over adequacy due to theme emerging from limited information in one study.

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Exposure to presentations of ME/CFS					

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
1	Semi-structured interviews and thematic analysis	Sufficient exposure to various presentations of ME/CFS was reported to enable practitioners to identify the condition and build confidence in their diagnostic skills.	Limitations	Minor methodological limitations	LOW
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Serious concerns about adequacy	

One study with minor issues; methodological limitations due to the role of the researcher not being discussed and concerns over data analysis with some themes supported by single quotes (Horton 2010); serious concerns over adequacy due to theme emerging from limited information in one study.

Table 8: Summary of evidence: Barriers and facilitators to the diagnosis of ME/CFS in young people

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Lack of health-professional knowledge and understanding					

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
2	Semi-structured interviews and thematic analysis (1 study); semi-structured interviews and grounded theory analysis (1 study)	Mothers of adolescents with ME/CFS reported the lack of knowledge of both GPs and paediatricians about the condition, while a lack of an empirical understanding of the condition was acknowledged by health care professionals.	Limitations	Minor methodological limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance	
			Adequacy	Minor concerns about adequacy	

Two studies with minor issues; methodological limitation due to the role of the researcher not being discussed and concerns over data richness with findings mostly supported by single quotes in one study (Beasant 2014) and due to concerns over recruitment skewing towards HCPs with positive attitudes towards ME/CFS in one study, as participants were recruited on the basis of how they informed and validate emerging theory (Marks 2016); minor concerns about relevance since the theme was reported

mainly as a barrier to accessing ME/CFS specialist services in one of the studies but is inferred to inevitably impact the diagnosis which was also reported to be uncertain prior to accessing the specialist service; minor concerns about adequacy with the theme supported by two studies and issues with data richness in one study

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Nature of diagnosis					
2	Semi-structured interviews and thematic analysis (1 study); semi-structured interviews and grounded theory analysis (1 study)	Mothers of adolescent patients reported how the non-specificity of symptoms and repeated tests conducted to rule out other illnesses complicated and delayed the diagnosis, while HCPs emphasised how the absence of a diagnostic test complicates the diagnosis.	Limitations	Minor methodological limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance	
			Adequacy	Minor concerns about adequacy	

Two studies with minor issues; methodological limitation due to the role of the researcher not being discussed and concerns over data richness with findings mostly supported by single quotes in one study (Beasant 2014) and due to concerns over recruitment skewing towards HCPs with positive attitudes towards ME/CFS in one study, ,as participants were recruited on the basis of how they informed and validate emerging theory (Marks 2016); minor concerns about relevance since the theme was reported

mainly as a barrier to accessing ME/CFS specialist services in one of the studies but is inferred to inevitably impact the diagnosis which was also reported to be uncertain prior to accessing the specialist service; minor concerns about adequacy with the theme supported by two studies and issues with data richness in one study

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Referral to specialist services					
1	Semi-structured interviews and thematic analysis	Referral to specialist services gave adolescents with ME/CFS and their families access to a team of experts that enabled the diagnosis which had previously been uncertain.	Limitations	Minor methodological limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	

One study with minor issues; methodological limitation due to the role of the researcher not being discussed and concerns over data richness with findings mostly supported by single quotes (Beasant 2014); minor concerns about adequacy due to the theme emerging from one study.

Study design and sample size			Quality assessment		
Number of studies contributing to the finding	**Design**	**Finding**	**Criteria**	**Rating**	**Overall assessment of confidence**
Complicated journey to specialist services					

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
1	Semi-structured interviews and thematic analysis	Mothers of adolescents with ME/CFS described a long journey to specialist services involving numerous tests and interactions with multiple professionals, that was complicated by co-morbid conditions and the time needed for the funding required to access services. .	Limitations	Minor methodological limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance	
			Adequacy	Minor concerns about adequacy	

One study with minor issues; methodological limitation due to the role of the researcher not being discussed and concerns over data richness with findings mostly supported by single quotes (Beasant 2014); minor concerns about relevance related to the applicability of the evidence to the phenomenon of interest, with most factors cited to complicate access to specialist services being extrapolated as barriers to diagnosis since the diagnosis was reported to result from referral to specialist services and to be uncertain prior to that; minor concerns about adequacy due to the theme emerging from one study.

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
Co-morbidities					
1	Semi-structured interviews	Mothers of adolescents with ME/CFS reported that co-morbid conditions introduced complexity to the process of diagnosis or masked ME/CFS.	Limitations	Minor methodological limitations	LOW

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
	and thematic analysis		Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Serious concerns about adequacy	

One study with minor issues; methodological limitation due to the role of the researcher not being discussed and concerns over data richness with findings mostly supported by single quotes (Beasant 2014); Serious concerns about adequacy with the finding supported by very limited information from one study.

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
Inconsistencies between health professionals					
1	Semi-structured interviews and grounded theory analysis	There were differences in the conceptualisation of the illness and the terminology used between health-care professionals working with children and adolescents The aetiological beliefs of HCPs were reported to influence the label HCPs chose to give to patients.	Limitations	Minor methodological limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	

Study design and sample size		Finding	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
			Adequacy	Minor concerns about adequacy	

One study with minor issues; methodological limitations due to concerns over participant recruitment skewing towards HCPs with positive attitudes towards ME/CFS, as participants were recruited on the basis of how they informed and validated emerging theory (Marks 2016); minor concerns about adequacy due to the finding supported by one study but emerging from a wealth of information.

Table 9: Summary of evidence for barriers and facilitators to care in adults

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
Lack of health professional knowledge and medical legitimacy					
12	Semi-structured interviews (10 studies, one of which included focused groups); longitudinal study with multiple in-depth interviews (1 study)	The general lack of health professional knowledge, disbelief and unsupportive attitudes patients encountered constitute a barrier to care, leading to diagnostic delay, limited, incorrect or no management advice, can hinder access to specialist services and treatments and lead patients to disengage from health services.	Limitations	Minor limitations	HIGH
			Coherence	Very minor concerns about coherence	
			Relevance	Very minor concerns about relevance	
			Adequacy	No concerns about adequacy	

Nine studies with very minor to moderate issues: Overall minor concerns over methodological limitations due to the role of the researcher not being explored in 7 studies (Arrol 2008; Bayliss 2014; Chew-Graham 2011; De Carvalho Leite 2011; Hannon 2012; Horton 2010; Picariello 2017), one study being a follow-up of a previous study involving open-ended questionnaire responses implicating our ability to assess risk of bias in the data collection method (Devendorf 2018), potential selection bias due to the recruitment strategy of one study (were only patients who had completed treatment were selected) (Picariello 2017) and 2/8 interviews being discarded in one study (Arrol 2008), issues with data richness in two studies (Chew-graham 2008; Hannon 2012) and some data supported by single quotes in one study (Horton 2010); very minor concerns about coherence with some participants in one study reporting positive experiences with healthcare professionals (Broughton 2017); very minor concerns over relevance due to patients in one study being self-identified as having ME/CFS (Devendorf 2018), GPs of one study largely caring for black-minority ethnic group people.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Lack of diagnosis					
5	Semi-structured interviews (4 studies, one of which included focused groups); longitudinal study with multiple in-depth interviews (one study)	The negative implications of a lack of a ME/CFS diagnosis on patients' access to appropriate treatment and support, their relationship with health care providers, improvement and 'recovery' were acknowledged by both patients and health-care professionals.	Limitations	Minor limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Very minor concerns about relevance	
			Adequacy	No concerns about adequacy	

Four studies with very minor to moderate issues; overall minor limitations due to the role of the researcher not being discussed (Arrol 2008; De Carvalho Leite 2011; Horton 2010; Picariello 2017) potential selection bias as 2/8 interviews were discarded in one study (Arrol 2008) and only participants who had completed treatment being selected in one study (Picariello 2017), some data supported by single quotes (Horton 2010); very minor concerns about relevance due to the population of one study not being limited to the adult age stratum (Whitehead 2006).

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Referral to specialist services					
7	Semi-structured interviews (5 studies); open-ended questionnaires (1 study); longitudinal study with multiple in-depth interviews (1 study)	Specialist services can benefit patients in terms of diagnosis, advice and symptom management but the general lack of or delayed referral due to a lack of medical knowledge, fragmented healthcare services or the lengthy diagnostic procedures associated with ME/CFS presents a barrier to care, often leading to self-diagnosis and the use of alternative or complementary therapies.	Limitations	Moderate limitations	LOW
			Coherence	No concerns about coherence	
			Relevance	Very minor concerns about relevance	
			Adequacy	No concerns about adequacy	

One study with very minor issues, two studies with minor issues and one study with serious issues; methodological limitations due to the role of the researcher not being discussed in four studies (Bayliss 2016, Hannon 2012, Horton 2010, Lin 2009), some data supported by single quotes in two studies (Hannon 2012; Horton 2010), selection bias and lack of transparency in the data analysis in one study (Lin 2009); very minor concerns about relevance associated with two studies, due to the population of one study not being limited to the adult age stratum (Whitehead 2006) and the sample of one study consisting of people previously recruited in a RCT (Chew-Graham 2010)

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Time constrains in primary care					
4	Semi-structured interviews (4	Time limited consultations in the health-care system present a barrier to the provision of appropriate care, impeding health professionals' understanding of patients' symptoms and	Limitations	Minor limitations	MODERATE
			Coherence	No concerns about coherence	

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
	studies, one of which included focus groups)	preventing patients from benefiting from consultations, often leading them to seek support outside the NHS.	Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	

Four studies with minor issues; limitations due to the role of the researcher not being discussed (Bayliss 2016; De Carvalho Leite 2011; Hannon 2012; Horton 2010) and some data supported by single quotes (Hannon 2012; Horton 2010); minor concerns about adequacy with limited information to support the theme in two studies (De Carvalho Leite 2011; Horton 2010) but sufficient information emerging from two studies (Bayliss 2016; De Carvalho Leite 2011).

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
The nature of ME/CFS					
3	Semi-structured interviews (3 studies)	The nature of ME/CFS in terms of its uncertain aetiology, its complicated diagnostic process, its non-specific symptoms and the absence of cure made the role of health professionals in managing patients difficult, while the invisibility of the illness often meant patients' need for help remained unrecognised and made them reluctant to ask for help	Limitations	Moderate limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Very minor concerns about relevance	
			Adequacy	No concerns about adequacy	

Two studies with minor issues; methodological limitations due to potential selection bias in two studies (Arrol 2008; Williams 2016) and the role of the researcher not being discussed in one study (Arrol 2008); very minor concerns about relevance due to the sample of one study consisting of people previously recruited in a RCT (Chew-Graham 2010)

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Lack of cure and clear management pathway					
2	Semi-structured interviews (2 studies)	Lack of cure and clear management pathway for ME/CFS caused health-professionals' reluctance to make a diagnosis and impeded their management of patients.	Limitations	Minor limitations	LOW
			Coherence	No concerns about coherence	
			Relevance	Very minor concerns about relevance	
			Adequacy	Moderate concerns about adequacy	

One study with minor issues: methodological limitations due to the role of the researcher not being explored and lack of data richness with data supported by single quotes (Hannon 2012); very minor concerns about relevance due to the sample of one study consisting of people previously recruited in a RCT (Chew-Graham 2010); moderate concerns about adequacy with information supporting the theme emerging from two studies and concerns over data richness associated with one study (Hannon 2012)

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Accessibility of treatment options in primary care					
3	Semi-structured interviews (3 studies, one of which included focus group discussions)	Patients lack access to helpful treatment options for managing ME/CFS due to the unavailability of those in primary care or due to the strict acceptance criteria often involved.	Limitations	Minor limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	

Three studies with very minor and minor issues; overall minor methodological limitations due to the role of the researcher not being discussed (Arrol 2008, De Carvalho Leite 2011, Horton 2010), potential risk of selection bias in one study (Arrol 2008) and issues with data richness in one study (Horton 2010); no concerns about coherence; minor concerns about adequacy with the idea of accessibility to certain treatments being implicated by their strict acceptance criteria only emerging from limited information from one study.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Unworkable treatment models					
1	Semi-structured interviews	Patients may experience difficulty implementing certain treatment models into their life	Limitations	Very minor limitations	VERY LOW
			Coherence	Minor concerns about coherence	
			Relevance	Moderate concerns about relevance	
			Adequacy	Serious concerns about adequacy	

One study (Chew-Graham 2011) with minor issues: very minor methodological limitations due to the impact of the researcher on the findings not being explored; minor concerns about coherence, the theme supported only by part of the participants in the study; moderate concerns over relevance due to the finding emerging from one study where the sample consisted of patients previously recruited in a RCT and who had received a 'pragmatic rehabilitation ' intervention and may thus not be relevant to other treatment models; serious concerns over adequacy with very limited information to support the theme

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Realistic goal setting					
1			Limitations	No limitations	MODERATE

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
	Semi-structured interviews (1 study)	Realistic goal setting towards management rather than cure was seen as vital for treatment success.	Coherence	Very minor concerns about coherence	
			Relevance	Minor concerns about relevance	
			Adequacy	Minor concerns about adequacy	

One study (Broughton 2017) with no particular methodological limitations identified; very minor concerns about coherence, the theme being supported by some patients in the study but not all but with no oppositional views reported; minor concerns about relevance due to the finding emerging from one study which excluded severely affected patients; minor concerns about adequacy the theme emerging from one study supported by relatively rich information

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Patients' acceptance of ME/CFS					
4	Semi-structured interviews (4 studies)	The importance of acceptance of the diagnosis of ME/CFS and its implications for one's life, although challenging, was reported to be crucial in engaging with treatment and health services and obtaining the most benefit from them by both patients and ME/CFS specialists.	Limitations	Moderate limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Very minor concerns about relevance	
			Adequacy	No concerns about adequacy	

Three studies with very minor to moderate issues; moderate methodological limitations due to the recruitment strategy in one study (with selection of participants who had completed treatment) (Picariello 2017), some data supported by single quotes in one study (Horton 2010) and the role of the researcher not being discussed in three studies

(Chew-Graham 2011; Horton 2010; Picariello 2017); very minor concerns about relevance over one study due to the sample of one study consisting of people previously recruited in a RCT (Chew-Graham 2011) that did not lower the confidence rating further.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Patient's personal circumstances & availability					
3	Semi-structured interviews (3 studies)	Attending medical appointments and benefiting from treatment can depend on being able to invest time and effort in the treatment which is influenced by patients' personal circumstances at the time including their work commitments and symptom severity.	Limitations	Minor limitations	HIGH
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

One study with moderate issues; potential bias in the recruitment strategy and unclear relationship between the researcher and participants (Picariello 2017) but no limitations to lower the confidence rating in 2/3 studies and no concerns over any other domain of quality assessment.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Symptom or illness severity					
5	Semi-structured interviews (4 studies); unstructured interviews (1 study)	Symptom and illness severity can influence patients' ability to articulate their problems and ask for help, their physical capacity to attend medical appointments or keep up with the length of intervention sessions and can limit the extent to which health professionals can provide helpful suggestions; while the experience of co-morbidities and symptoms	Limitations	Moderate limitations	LOW
			Coherence	Very minor concerns about coherence	
			Relevance	No concerns about relevance	

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
		including cognitive difficulties may limit the effectiveness of interventions for some patients.	Adequacy	Moderate concerns about adequacy	

Four studies with very minor to moderate limitations; overall moderate methodological limitations due to the role of the researcher not being explored in three studies (Horton 2010; van der Vaart 2019; Ward 2008), potential selection bias in one study, where participants were self-selected through their support group coordinator (Williams 2016), concerns over data analysis, with insufficient data presented to support all findings in one study (Ward 2008); very minor concerns about coherence with different aspects of severity reported to influence care between different groups of patients and between patients and health-care professionals but views not being contradictory; moderate concerns about adequacy with the information supporting the theme in four out of the five contributing studies being limited (Horton 2010; van der Vaart 2019; Ward 2008; Williams 2016).

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	Design		Criteria	Rating	Overall assessment of confidence
Practical accessibility of care					
3	Semi-structured interviews (1 study) open-ended text questionnaires (2 studies)	The geographical location of healthcare providers, transportation links as well as the availability of appointments can implicate patients' ability to attend health care services and have access to healthcare.	Limitations	Serious limitations	VERY LOW
			Coherence	No concerns about coherence	
			Relevance	Moderate concerns about relevance	
			Adequacy	Minor concerns about adequacy	

Two studies with moderate and serious limitations: Limitations due to the data collection method of one study, it being a follow-up to a quantitative study with open-ended online responses implicating our ability to assess risk of bias in the data collection method (Devendorf 2018) and due to selection bias with the sample of the other study originally recruited for a different study and selection criteria being unclear, the role of the researcher not being discussed and lack of transparency over the data collection and analysis method not allowing us to assess data richness and whether findings are well grounded in the data (Lin 2009); moderate concerns about relevance due to the

majority of the sample of one study consisting of people suspected of having ME/CFS at the time of data collection but did not actually have ME/CFS (Lin 2009) and the sample of one study consisting of people who were self-identified as having ME/CFS and had suicidal ideations (Devendorf 2018); minor concerns about adequacy due to concerns over data richness in two studies (Devendorf 2018; Lin 2009) but with sufficient information supporting the theme in the other contributing study (Broughton 2017)

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Flexibility in medical care appointments					
3	Semi-structured interviews (3 studies	Flexibility in the frequency and mode of medical appointments can help overcome barriers of practical accessibility and symptom severity that implicate treatment attendance.	Limitations	Very minor limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	

Two studies with minor limitations that did not lower the confidence rating with no limitations in the third study that provided the most information for this theme; limitations due to the role of the researcher not being discussed and lack of data richness (Hannon 2012; Horton 2010); minor concerns about adequacy with the information supporting the theme in two studies being very limited (Hannon 2012; Horton 2010) but with rich information emerging from the third study (Broughton 2017).

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Relationship with health-care professional					
4	Semi-structured	Absence of an established and on-going relationship with a health care professional (GP, family physician or therapist delivering care) influenced the management of patients,	Limitations	Minor limitations	MODERATE
			Coherence	No concerns about coherence	

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
	interviews (4 studies	implicating their ability to demonstrate their symptoms and gain a diagnosis, communicate their experiences and their engagement to primary care.	Relevance	Very minor concerns about relevance	
			Adequacy	Very minor concerns about adequacy	

Four studies with very minor to moderate limitations; overall minor methodological limitations due to potential selection bias the recruitment strategy in one study (with selection of participants who had completed treatment) (Picariello 2017) and the role of the researcher not being discussed in three studies (Bayliss 2014; Bayliss 2016; Picariello 2017), some issues with data richness in one study (Chew-Graham 2008); very minor concerns about relevance with participants in one study consisting of people previously recruited in a RCT (Chew-Graham 2008) and participants in one study being limited to black-minority ethnic groups (Bayliss 2014); very minor concerns about adequacy due to concerns over the richness of data supporting the theme in one study (Chew-Graham 2008) but sufficient information overall.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Patients' beliefs & attitudes towards ME/CFS and treatment					
6	Semi-structured interviews (5 studies); open-ended questionnaires (1 study)	Pre-existing beliefs about the illness and the treatment offered can influence patients' decision to seek medical advice for their symptoms and treatment acceptance or engagement.	Limitations	Moderate limitations	VERY LOW
			Coherence	No concerns about coherence	
			Relevance	Serious concerns about relevance	
			Adequacy	No concerns about adequacy	

Five studies with very minor to serious issues; methodological limitations due to selection bias in two studies (Lin 2009; Picariello 2017), the role of the researcher not being examined in five studies (Bayliss 2014; Chew-Graham 2011; Lin 2009; Picariello 2017; van der Vaart 2019) and lack of transparency in the data analysis of one study (Lin

2009), serious concerns about relevance associated with four studies due the majority of the sample in one study consisting of people who were suspected of having ME/CFS at the time of data collection but did not actually have ME/CFS (Lin 2009), the population of one study being limited to black minority ethnic groups (Bayliss 2014), the population of one study consisting of people who had been recruited in a RCT(Chew-Graham 2011) and one study not being limited to the implementation of ICBT for 'CFS' but also for 'Chronic pain' and not always being possible to distinguish whether reported barriers and facilitators were applicable to ICBT for CFS, chronic pain or both.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Personal attributes & motivation					
4	Semi-structured interviews (4 studies)	Patient attributes such as being proactive, determined and positive can facilitate treatment access and their motivation to engage in and benefit from treatment even in the face of challenges.	Limitations	Minor limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Very minor concerns about relevance	
			Adequacy	Very minor concerns about adequacy	

Two studies with minor to moderate issues; minor methodological limitations due to potential selection bias the recruitment strategy of one study and the relationship between the researcher and participants not being explored (Picariello 2017) minor issues with data richness in one study (Chew-Graham 2008), very minor concerns about relevance due the sample of one study consisting of people recruited in a RCT (Chew-Graham 2008), very minor concerns about adequacy due to concerns over data richness in one study (Chew-Graham 2008).

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Individual characteristics of the therapist					
1		Individual characteristic of the therapists such as their attitude towards treatment, the ability to flexibly tailor the intervention	Limitations	Very minor limitations	VERY LOW

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
	Semi-structured interviews	to the needs of the individual and to effectively communicate with them were seen as important factors influencing the implementation of interventions.	Coherence	No concerns about coherence	
			Relevance	Serious concerns about relevance	
			Adequacy	Minor concerns about adequacy	

One study with minor methodological limitations due to the role of the researcher not being explored (van der Vaart 2019); serious concerns over relevance, the information reported being of potentially limited applicability to ICBT and the research not being limited to the implementation of ICBT for 'CFS' but also for 'Chronic pain' meaning it was not always possible to distinguish whether reported barriers and facilitators were applicable to ICBT for CFS, chronic pain or both; minor concerns about adequacy with the theme supported by limited quotes

Table 10: Summary of evidence for barriers and facilitators to care in Children and young people

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Health professionals' knowledge and attitudes					
3	Semi-structured interviews (2 studies)	HCP knowledge and attitudes towards ME/CFS can influence the support they provide, with a lack of knowledge and unsupportive attitudes acting as a barrier to the diagnosis or referral to services that can provide care and with professionals with experience in ME/CFS facilitating access to appropriate care.	Limitations	Minor limitations	MODERATE
			Coherence	Minor concerns about coherence	
			Relevance	Very minor concerns about relevance	
			Adequacy	No concerns about adequacy	

Three studies with minor issues: methodological limitations due to the role of the researcher not being discussed in one study (Webb 2011) and the recruitment strategy of one study where participants were recruited on the basis of how they informed and validated emerging theory (Marks 2016); minor concerns about coherence the information

supporting the theme emerging only from a small number of people in the sample of one study (Webb 2011); very minor concerns over relevance with the sample of the study contributing the least information to the theme not being limited to the stratum of children and young people (Whitehead 2006).

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Referral to specialist services					
2	Semi-structured interviews (2 studies)	Specialist services gave young people and their families access to information, treatment and support that enabled symptom management and improvement while a lack of referral to specialist services presented a barrier to the diagnosis and management of ME/CFS and led patients to alternative therapies.	Limitations	Minor limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	Minor concerns about relevance	
			Adequacy	No concerns about adequacy	

Two studies with minor issues: minor methodological limitations due to the role of the researcher not being discussed and minor issues with data richness in one study (Beasant 2014); minor concerns about relevance due to the population of one study not being limited to the children and young people stratum (Whitehead 2006) and that of one study consisting of people recruited in a feasibility RCT (Beasant 2014).

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Acceptance and adaptation of ME/CFS					
1	Semi-structured interviews	Young people or their families may experience difficulty adapting their everyday life to medical care strategies and to the implications of ME/CFS.	Limitations	Minor limitations	VERYLOW
			Coherence	No concerns about coherence	
			Relevance	Very minor concerns about relevance	

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
			Adequacy	Serious concerns about adequacy	

One study with minor issues: minor methodological limitations due to the role of the researcher not being discussed and some findings supported by single quotes (Beasant 2014); very minor concerns over relevance (due to the sample that had been previously recruited in a feasibility RCT); serious concerns over adequacy with limited information from one study supporting the theme.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Diagnosis of ME/CFS and its communication across settings					
2	Semi-structured interviews and thematic and comparative analysis (1 study); semi-structured interviews and grounded theory analysis (1 study)	The diagnostic label given to people with ME/CFS will influence the intervention that follows and sharing the diagnosis with the school setting is crucial in receiving support, while the explanation given around it can influence treatment engagement.	Limitations	Minor limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	

Two studies with very minor to minor issues: methodological limitations due to potential selection bias in the recruitment strategy of one study as participants were recruited on the basis of how they informed and validated emerging theory (Marks 2016) and the potential influence of the researcher on the findings not being discussed (Brigden

2020); minor concerns over data richness with the information from one study and being mainly based on the authors' interpretation of what was reported by the health professionals in the study rather than by the actual information reported by participants (Marks 2016) but no similar concerns in the other contributing study.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Nature of ME/CFS					
1	Focus groups and semi-structured interviews with thematic analysis	The great variability and fluctuation of ME/CFS symptoms can greatly complicate management in children while the circularity of low mood characterising the illness can be a barrier to improvement.	Limitations	Very minor limitations	MODERATE
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Minor concerns about adequacy	

One study with minor issues: methodological limitations due to the role of the researcher not being explored Parslow 2017); minor concerns about the adequacy of information supporting the theme emerging from one study.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Practical accessibility					
2	Semi-structured interviews (1 study) semi structured interviews	The location of therapy or health services as well as the everyday commitments of young people and their parents can negatively impact patients' health and their ability to fully engage in therapy while the flexibility of videoconferencing could overcome the barriers to care posed by the distance of	Limitations	Very minor limitations	HIGH
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
	and focus groups (1 study)	healthcare services, the family's availability and symptom severity.	Adequacy	No concerns about adequacy	

One study with very minor methodological limitations due the role of the researcher not being discussed (Haig-Ferguson 2019)

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Technical problems as a barrier to care					
1	Semi-structured interviews and focus groups	Technical difficulties associated with video-conferencing can impede effective communication with health-care professionals	Limitations	Very minor limitations	LOW
			Coherence	Minor concerns about coherence	
			Relevance	Moderate concerns about relevance	
			Adequacy	No concerns about adequacy	

One study with very minor methodological limitations due to the role of the researcher not being discussed (Haig-Ferguson 2019) but also minor concerns about coherence due to participants in the study expressing conflicting views on the extent to which technical problems act as a barrier to care but the majority of participants agreeing that they do; serious concerns over relevance due to the theme being particularly relevant and of limited applicability to people with ME/CFS who are to receive care via videoconferencing.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Virtual care					
1	Semi-structured interviews and focus groups	Despite the benefits that can be provided by a virtual connection with health professionals, communication can be compromised compared to face-to-face interactions with emotional cues being missed, the content and depth of discussions being limited.	Limitations	Very minor limitations	MODERATE
			Coherence	Minor concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

One study with very minor methodological limitations due to the role of the researcher not being discussed (Haig-Ferguson 2019); minor concerns about coherence due to participants in the study expressing conflicting views regarding whether a virtual connection positively or negatively influences communication but the majority of participants reporting on the potential negative implication involved.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Child-centred care					
2	Focus groups and Semi-structured interviews with thematic analysis (1 study); semi-structured interviews	Children can benefit from treatment that is tailored to their individual functional needs and priorities and the involvement of children with their care to facilitate this is crucial.	Limitations	Very minor limitations	HIGH
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
	with thematic and comparative analysis (1 study)				

Two studies with very minor issues: methodological limitations due to the role of the researcher not being explored (Brigden 2020; Parslow 2017)

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Ongoing communication across schools, families and health-care professionals					
2	Focus groups and Semi-structured interviews with thematic analysis (1 study); Semi-structured interviews with thematic and comparative analysis (1 study)	There is often a lack of sufficient or direct communication between schools, families and health-care professionals, implicating the care of children with ME/CFS and the importance of such an ongoing communication across settings is acknowledged by all parties.	Limitations	Very minor limitations	HIGH
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

Two studies with very minor issues: methodological limitations due to the role of the researcher not being explored (Brigden 2020; Parslow 2017)

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Lack of social support					
1	Focus groups and Semi-structured interviews with thematic analysis	Negative attitudes from the social environment can act as a barrier to improvement implicating the family's ability to follow clinical advice.	Limitations	Very minor limitations	VERY LOW
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	Serious concerns about adequacy	

One study with minor issues: methodological limitations due to the role of the researcher not being explored Parslow 2017); serious concerns about the adequacy of information supporting the theme.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Communication barrier					
1	Semi-structured interviews	Both children and their parents may have difficulty communicating their experiences with health-care professionals.	Limitations	Very minor limitations	LOW
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
			Adequacy	Serious concerns about adequacy	

One study with very minor issues: methodological limitations due to the role of the researcher not being explored Webb 2011); serious concerns about the adequacy of information supporting the theme

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Limited capacity to self-manage and need for support					
1	Semi-structured interviews and thematic and comparative analysis (1 study)	Children cannot manage their condition independently across the home, school and clinical setting and rely on adults for support with management, communication, understanding and self-regulation.	Limitations	Very minor limitations	HIGH
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

One study with very minor issues; very minor concerns over methodological limitations due to the potential influence of the researcher on the findings not being discussed (Brigden 2020) that were too minor to lower the confidence rating .

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Integrated/shared care					
1	Semi-structured interviews and thematic and comparative analysis (1 study)	Clinicians, parents as well as teachers have a distinct role in the diagnosis and care of children with ME/CFS and the involvement and communication of all three is crucial to maximise the quality of the care received.	Limitations	Very minor limitations	HIGH
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

One study with very minor issues; very minor concerns over methodological limitations due to the potential influence of the researcher on the findings not being discussed (Brigden 2020) that were too minor to lower the confidence rating.

Study design and sample size		Findings	Quality assessment		
Number of studies contributing to the finding	**Design**		**Criteria**	**Rating**	**Overall assessment of confidence**
Accommodations in the school setting					
1	Semi-structured interviews and thematic and comparative analysis (1 study)	Health professionals, teachers and parents raised the importance of a management plan that involves the school setting, the responsibility of teachers in day-to-day management and of accommodations at school to support the care of children with ME/CFS.	Limitations	Very minor limitations	HIGH
			Coherence	No concerns about coherence	
			Relevance	No concerns about relevance	
			Adequacy	No concerns about adequacy	

One study with very minor issues; very minor concerns over methodological limitations due to the potential influence of the researcher on the findings not being discussed (Brigden 2020) that were too minor to lower the confidence rating.

Appendix F Excluded studies

Table 11: Studies excluded from the qualitative review for barriers and facilitators to the diagnosis

Reference	Reason for exclusion
Aikman 1995[1]	Unable to obtain paper
Anderson 2012[6]	Incorrect study design (non-PICO systematic review)
Anderson 2014[5]	No relevant themes
Antcliff 2018[7]	No relevant themes
Asbring 2001[9]	Incorrect population: included CFS patients but majority had fibromyalgia diagnosis and results were not analysed separately
Asbring 2002[11]	Incorrect population: mixed CFS and fibromyalgia patients
Asbring 2004[10]	Incorrect population: mixed CFS and fibromyalgia patients
Ashby 2006[12]	No relevant themes
Ax 1997[15]	No relevant themes
Ax 1998[14]	No relevant themes
Bayliss 2014[16]	Incorrect study design (non-PICO systematic review)
Bayliss 2016[17]	No relevant themes
Bazelmans 2005[19]	Incorrect study design: questionnaire; no extractable themes
Bennett 2007[23]	No extractable themes; analysis focused on the identification of symptoms experienced by patients.
Brady 2016[24]	Incorrect population: mixed population of people with ME/CFS and type 1 and 2 diabetes
Bridgen 2018[25]	No relevant themes
Brigden 2020[26]	No relevant themes
Broadbent 2020[27]	No relevant themes
Brooks 2012[28]	Incorrect study design: included interviews but findings are based on questionnaire i.e. cross-sectional data with no qualitative analysis; no relevant themes
Bulow 2003[30]	Incorrect population: interviews of patients with CFS or a related diagnosis in which fatigue was a significant part of their suffering
Caplan 2001[31]	Incorrect study design: patient story
Chernow 2008[33]	Unable to obtain paper
Cheshire 2020[34]	No relevant themes
Chew-Graham 2011[35]	No relevant themes
Clements 1997[40]	No relevant themes
Costello 1998[41]	Unable to obtain paper
Davison 1997[42]	Incorrect study design: article
De Carvalho 2011[43]	No relevant themes
Dennison 2010[45]	No relevant themes
Devendorf 2017[47]	No relevant themes
Devendorf, 2018[48]	No relevant themes
Drachler 2009[50]	Incorrect study design (non-PICO systematic review)
Edwards 2007[51]	No relevant themes
Everett 2002[52]	No relevant themes
Fisher 2013[54]	No relevant themes

Reference	Reason for exclusion
Fowler 2005[55]	No relevant themes; incorrect population: inadequate definition (children experiencing 'disabling fatigue' classified as CFS).
Friedberg 1998[57]	Unable to obtain paper
Friedberg 2016[56]	Incorrect population: majority diagnosed with unexplained chronic fatigue, not CFS; no relevant themes
Gan 2010[58]	Incorrect population: caregivers of people with acquired brain injury
Gotts 2016[61]	No relevant themes
Gray 2003[62]	No relevant themes
Guise 2007[64]	No relevant themes
Guise 2010[63]	No relevant themes
Hareide 2011[67]	No relevant themes
Harris 2016[69]	Incorrect study design (non-PICO systematic review)
Harris 2017[70]	No relevant themes
Higginson 2008[72]	Incorrect population: not ME/CFS
Horrocks 2015[73]	Unable to obtain paper
Hart 2000[71]	No relevant themes
Horton-Salway 2002[74]	Incorrect study design: article
Horton-Salway 2004[75]	Incorrect study design: article
Jason 2015[77]	Incorrect study design: article
Jelbert 2010[78]	No relevant themes
Jensen 2001[79]	Unable to obtain paper
Keech 2015[80]	No relevant themes; study employed qualitative methods to devise a self-reported psychometric measure for fatigue
Kendrick 2016[81]	Incorrect study design: questionnaire measures
Kisely 2002[82]	Incorrect study design: evaluation of web-based information
Larun 2007[84]	Incorrect study design (non-PICO systematic review)
Larun 2011[83]	No relevant themes
Lee 2000[85]	Unable to obtain paper
Lee 2001[86]	Incorrect population: insufficient definition of CFS, patients described to have chronic fatigue and weakness
Levine 1997[87]	Analysis does not meet protocol: quantitative analysis and no extractable themes.
Lian 2016[88]	No relevant themes
Littrel 2012[91]	Unable to obtain paper
Lingard 2014[90]	No relevant themes
Lombaard 2005[92]	No relevant themes
McDermott 2011[97]	No relevant themes
McInnis 2015[98]	Incorrect population: included CFS patients but majority had fibromyalgia diagnosis rather than CFS and results were not analysed separately
Mihelicova[99]	No relevant themes
Missen 2012[100]	No relevant themes
Moore 2000[101]	Incorrect study design: combination of quantitative and qualitative methodology with results from statistical and thematic analysis not reported separately and no extractable themes.
Njolstad 2019[103]	No relevant themes
Ong 2005[105]	No relevant themes

Reference	Reason for exclusion
Parslow 2015[106]	No relevant themes
Parslow 2017[108]	Incorrect study design (non-PICO systematic review)
Parslow 2017[109]	No relevant themes
Pemberton 2014[111]	No relevant themes
Pemberton 2014[110]	No relevant themes
Picariello 2017[112]	No relevant themes
Pinxsterhuis 2015[115]	Incorrect study design (non-PICO systematic review)
Pinxsterhuis 2015[114]	No relevant themes
Prins 2000[116]	Analysis does not meet protocol: qualitative responses used to support quantitative questionnaire analysis; no extractable themes
Raine 2004[117]	Incorrect population: GPs perceptions of CFS and irritable bowel syndrome; no relevant themes
Ray 1995[119]	Incorrect study design: questionnaires and quantitative analysis
Ray 1998[118]	No relevant themes
Reme 2013[120]	No relevant themes
Reynolds 2006[122]	Incorrect study design: qualitative analysis of three narratives: o relevant themes
Reynolds 2008[123]	No relevant themes
Reynolds 2010[121]	Incorrect population: self-reported ME/CFS that was not confirmed; no relevant themes
Richards 1998[125]	Incorrect study design: questionnaires and no qualitative analysis to allow the extraction of themes
Richards 2002[124]	No relevant themes
Ryckeghem 2017[127]	No relevant themes
Schoofs[130]	Incorrect population: mixed ME/CFS and fibromyalgia population
Sidi-Ali-Mebarek 2009[131]	Thesis; unable to obtain paper
Snell[132]	Incorrect study design: Qualitative case study of two patients with no extractable themes
Soderlund 2000[134]	No relevant themes
Soderlund 2005[133]	No relevant themes
Son 2015[135]	No relevant themes
Stenhoff, 2015[136]	No relevant themes
Stormorken 2015[137]	No relevant themes
Sturge-Jacobs 2002[139]	Incorrect population: people with Fibromyalgia
Sunnquist 2017[140]	Incorrect study design: quantitatively reported survey
Swoboda 2006[141]	Incorrect population: mixed population of self-identified people with CFS, multiple chemical sensitivities and Gulf War Syndrome
Taylor 2017[142]	No relevant themes
Tevens 2004[144]	Incorrect population: women with fibromyalgia and CFS
Theorell 1999[145]	Incorrect study design: reports questionnaire results quantitatively only
Travers 2008[146]	No relevant themes
Tuck 1998[147]	No relevant themes
Tuck 2000[148]	Incorrect study design: questionnaires and no qualitative analysis to allow the extraction of themes
Velleman 2016[150]	No relevant themes

Reference	Reason for exclusion
Ward 2008[151]	No relevant themes
Ware 1993[152]	No relevant themes
Ware 1998[153]	No relevant themes
Ware 1999[154]	No relevant themes
Whitehead 2006[156]	No relevant themes
Whitehead 2006[157]	No relevant themes
Williams 2016[159]	No relevant themes
Wilson 2011[160]	Incorrect population: experiencing chronic fatigue due to other long-tern condition
Winger 2014[161]	No relevant themes

Table 12: Studies identified but not included in the qualitative review for barriers and facilitators to the diagnosis due to saturation being reached

Reference
Anderson 1997[4]
Ax 2002[13]
Arrol 2008[8]
Beaulieu 2000[22]
Donalek 2009[49]
Pinikahana 2002[113]
Olson 2015[104]

Table 13: Studies excluded from the qualitative review for barriers and facilitators to care

Reference	Reason for exclusion
Aikman 1995[1]	Unable to obtain paper
Alameda Cuesta 2019[2]	Incorrect population: mixed population of ME/CFS, Fibromyalgia and multiple chemical sensitivity; only 3/9 had ME/CFS and findings were not reported separately
Anderson 2012[6]	Systematic review: references checked for inclusion
Anderson 2014[5]	No relevant themes
Antcliff 2018[7]	No relevant themes
Asbring 2001[9]	Incorrect population: included CFS patients but majority had fibromyalgia diagnosis and results were not analysed separately
Asbring 2002[11]	Incorrect population: mixed CFS and fibromyalgia patients
Asbring 2004[10]	Incorrect population: mixed CFS and fibromyalgia patients
Ashby 2006[12]	No relevant themes
Ax 1998[14]	No relevant themes
Ax 2002[13]	No relevant themes
Bayliss 2014[16]	Systematic review: references checked for inclusion
Bazelmans 2004[20]	Incorrect study design: quantitative questionnaire
Bazelmans 2005[19]	Incorrect study design: questionnaire; no extractable themes
Bennett 2007[23]	No extractable themes; analysis focused on the identification of symptoms experienced by patients.
Brady 2016[24]	Incorrect population: mixed population of people with ME/CFS and type 1 and 2 diabetes

Reference	Reason for exclusion
Bridgen 2018[25]	No relevant themes
Brooks 2012[28]	Incorrect study design: included interviews but findings are based on questionnaire i.e. cross-sectional data with no qualitative analysis; no relevant themes
Bulow 2003[30]	Incorrect population: interviews of patients with CFS or a related diagnosis in which fatigue was a significant part of their suffering
Caplan 2001[31]	Incorrect study design: narrative article
Catchpole 2019[32]	No relevant themes
Chernow 2008[33]	Thesis, unable to obtain paper
Clements 1997[40]	No relevant themes
Costello 1998[41]	Unable to obtain paper
Davison 1997[42]	Incorrect study design: article
Devendorf 2019[46]	No relevant themes
Devendorf 2017 [47]	No relevant themes
Drachler 2009[50]	Systematic review: references checked for inclusion
Edwards 2007[51]	No relevant themes
Everett 2002[52]	No relevant themes
Fisher 2013[54]	No relevant themes
Fowler 2005[55]	No relevant themes; incorrect population: inadequate definition (children experiencing 'disabling fatigue' classified as CFS).
Friendberg 1998[57]	Unable to obtain paper
Friedberg 2016[56]	Incorrect population: majority diagnosed with unexplained chronic fatigue, not CFS; no relevant themes
Gan 2010[58]	Incorrect population: caregivers of people with acquired brain injury
Gotts 2016[61]	No relevant themes
Gray 2003[62]	No relevant themes
Guise 2007[64]	No relevant themes
Guise 2010[63]	No relevant themes
Hareide 2011[67]	No relevant themes
Harland 2019[68]	No relevant themes
Harris 2016[69]	Systematic review: references checked for inclusion
Harris 2017[70]	No relevant themes
Hart 2000[71]	No relevant themes
Higginson 2008[72]	Incorrect population: not ME/CFS
Horrocks 2015[73]	Book chapter; not available
Horton-Salway 2002[74]	Incorrect study design: article
Horton-Salway 2004[75]	Incorrect study design: article
Jason 2015[77]	Incorrect study design: article
Jelbert 2010[78]	No relevant themes
Jensen 2001[79]	Unable to obtain paper
Keech 2015[80]	No relevant themes; study employed qualitative methods to devise a self-reported psychometric measure for fatigue
Kendrick 2016[81]	Incorrect study design: questionnaire measures
Kisely 2002[82]	Incorrect study design: evaluation of web-based information
Larun 2007[84]	Systematic review: references checked for inclusion
Larun 2011 [83]	No relevant themes
Lee 2000 [85]	Unable to obtain paper

Reference	Reason for exclusion
Lee 2001[86]	Incorrect population: insufficient definition of CFS, patients described to have chronic fatigue and weakness
Levine 1997[87]	Analysis does not meet protocol: quantitative analysis and no extractable themes.
Lian 2016[88]	No relevant themes
Lingard 2014[90]	No relevant themes
Littrel 2012[91]	Unable to obtain paper
Lombaard 2005[92]	No relevant themes
Lovell 1999[93]	No relevant themes
McCue 2004[95]	No relevant themes
McDermott 2011[97]	No relevant themes
McInnis 2015[98]	Incorrect population: included CFS patients but majority had fibromyalgia diagnosis rather than CFS and results were not analysed separately
Mihelicova[99]	No relevant themes
Missen 2012[100]	No relevant themes
Moore 2000[101]	Incorrect study design: combination of quantitative and qualitative methodology with results from statistical and thematic analysis not reported separately and no extractable themes.
Njolstad 2019[103]	No relevant themes
Ong 2005[105]	No relevant themes
Parslow 2015[106]	No relevant themes
Parslow 2017[108]	Systematic review: references checked for inclusion
Parslow 2018[107]	No relevant themes
Pemberton 2014[111]	No relevant themes
Pemberton 2014[110]	No relevant themes
Pinxsterhuis 2015[115]	Systematic review: references checked for inclusion
Pinxsterhuis 2015[114]	No relevant themes
Prins 2000[116]	Analysis does not meet protocol: qualitative responses used to support quantitative questionnaire analysis; no extractable themes
Ray 1995[119]	Incorrect study design: questionnaires and quantitative analysis
Ray 1998[118]	No relevant themes
Reme 2013[120]	No relevant themes
Reynolds 2006[122]	Incorrect study design: qualitative analysis of three narratives: o relevant themes
Reynolds 2008[123]	No relevant themes
Reynolds 2010[121]	Incorrect population: self-reported ME/CFS that was not confirmed; no relevant themes
Richards 1998[125]	Incorrect study design: questionnaires and no qualitative analysis to allow the extraction of themes
Richards 2002[124]	No relevant themes
Sachs 2001[128]	Incorrect study design: no thematic analysis
Saltzstein 1998[129]	Incorrect study design: findings reported quantitatively
Schoofs[130]	Incorrect population: mixed ME/CFS and fibromyalgia population
Sidi-Ali-Mebarek 2009[131]	Thesis; unable to obtain paper.
Snell[132]	Incorrect study design: Qualitative case study of two patients with no extractable themes

Reference	Reason for exclusion
Soderlund 2000[134]	No relevant themes
Soderlund 2005[133]	No relevant themes
Son 2015[135]	No relevant themes
Stenhoff, 2015[136]	No relevant themes
Stormorken 2015[137]	No relevant themes
Strassheim 2019[138]	Partially incorrect design: involves synthesis of single sentence responses into themes; themes already captured by included studies; partially incorrect population: includes 10/33 participants with ME/CFS
Sturge-Jacobs 2002[139]	Incorrect population: people with Fibromyalgia
Sunnquist 2017[140]	Incorrect study design: quantitatively reported survey
Swoboda 2006[141]	Incorrect population: mixed population of self-identified people with CFS, multiple chemical sensitivities and Gulf War Syndrome
Taylor 2017[142]	No relevant themes
Tevens 2004[144]	Incorrect population: women with fibromyalgia and CFS
Theorell 1999[145]	Incorrect study design: reports questionnaire results quantitatively only
Travers 2008[146]	No relevant themes
Tuck 1998[147]	No relevant themes
Tuck 2000[148]	Incorrect study design: questionnaires and no qualitative analysis to allow the extraction of themes
Velleman 2016[150]	No relevant themes
Ware 1993[152]	No relevant themes
Ware 1998[153]	No relevant themes
Ware 1999[154]	No relevant themes
Wilson 2011[160]	Incorrect population: experiencing chronic fatigue due to other long-tern condition
Winger 2014[161]	No relevant themes

Table 14: Studies identified but not included in the qualitative review barriers and facilitators to care due to saturation being reached

Reference
Ali 2019[3]
Anderson 1997[4]
Ax 1997[15]
Beaulieu 2000[22]
Broadbent 2020[27]
Clarke 1999[38]
Clarke 2000[39]
Devendorf 2019[46]
Geraghty 2019[59]
Gilje 2008[60]
Pinikahana 2002[113]
Raine 2004[117]
Rowe 2020[126]
Ryckeghem 2017[127]

Reference
Taylor 2005[143]
Wilde 2020[158]
Woodward 1995[162]

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