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

National Institute for Health and Care Excellence

Draft

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

Appendix 2: Involving adults with severe ME/CFS symptoms in developing a NICE guideline on Myalgic encephalomyelitis/Chronic fatigue syndrome: diagnosis and management

NICE guideline <number>

University of Manchester Centre for Primary Care

November 2020

Draft for Consultation

This guideline was developed by the National Guideline Centre

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

Local commissioners and providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

ISBN

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1 Involving people with severe ME/CFS

An integral part of developing NICE guidelines is the involvement of people with direct experience of the condition and all guideline committees have lay members. The ME/CFS guideline committee has 5 lay members with varying experience of severe ME/CFS either directly or as parents of children and young people who have had periods of severe ME/CFS. However, during the scoping process it was identified there was limited published evidence directly from the perspective of people with severe ME/CFS. For this topic it was considered crucial that the experiences, perspectives and opinions of people with severe ME/CFS inform the guideline and an online questionnaire was conducted with people with severe ME/CFS.

The consultation was commissioned by NICE and carried out by the University of Manchester Centre for Primary Care.

The University of Manchester Centre for Primary Care was awarded the commission after an open tender process. An invitation to tender was sent to the guideline registered stakeholders and posted on the Royal College of Physicians website. Applicants had to submit a written proposal outlining how they met the research brief, submitted bids were shortlisted and shortlisted bidders were then interviewed by telephone. The process was led by the National Guideline Centre (NGC) and overseen by a subgroup from the ME/CFS guideline committee. The subgroup comprised of the ME/CFS guideline chair, vice chair, the NGC guideline lead, two lay members and representation from the NICE Patient and Public Involvement unit. The subgroup shortlisted the bids, interviewed the shortlisted bidders and awarded the tender.

See Section 2 for the report and sections 3 and 4 for how the committee used the report to support their decision making.

2 Report

2.1 Summary

2.1.1 Background

Myalgic encephalomyelitis (ME) and/or chronic fatigue syndrome (CFS) is a poorly understood illness that affects approximately 250,000 people in the UK. It is estimated that around 25% of adults with ME/CFS experience severe symptoms or illness presentation. These people are often housebound or bedbound for long periods, sometimes lasting many years. At the most severe end of the ME/CFS symptom spectrum, patients report fatigue after minimal effort, post-exertional malaise, prominent cognitive deficits, intolerance of light, noise and other stimuli, and a host of other symptoms. This cohort represent the most challenging sub-group within the ME/CFS population. Given the severity of symptoms reported, many of these people find it difficult to access medical and social care.

A new guideline for Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome (ME/CFS): diagnosis and management is currently being developed by the National Institute for Health and Care Excellence (NICE) to inform health and social care practice in England. It is essential that NICE guidelines are informed by the views of those receiving care. This report presents findings from a consultation with people with severe ME/CFS symptoms. The consultation aimed to explore the views and experiences of people with severe ME/CFS symptoms on the following topics identified from the guideline scope: Identification and assessment before diagnosis, diagnosis of ME/CFS, management of ME/CFS, monitoring and review, information, education, and support for people with suspected or diagnosed ME/CFS and their families and carers, and information, education and support for health and social care professionals. The consultation was commissioned by NICE and carried out by the University of Manchester Centre for Primary Care: Professor Aneez Esmail, Dr Keith Geraghty, Dr Charles Adeniji and Dr Stoyan Kurtev.

2.1.2 Methods

The project employs a survey instrument to gauge the views of people with severe ME/CFS, within the context of an exploratory study design encompassing inductive and qualitative methods. Ethical approval for this project was sought and granted from the University of Manchester Research Ethics Committee (*2019-7763-12089*). A series of research questions were derived from an embedded set of research objectives formulated from consultation with the guideline committee and based on the guideline scope. These questions were imputed into an electronic survey that was pilot tested on 10 patients from a convenience sample and then opened nationally to people with severe ME/CFS during November 2019, using social media promotion and advertising via patient organisations. Approximately 1600 persons clicked on the survey link, 343 started the survey, 124 completed all questions and from these we retrieved 60 complete responses, including meeting our inclusion criteria of self-reported severe status and ME/CFS confirmed by a medical professional. We used thematic and narrative methods to analyze and synthesize collected data.

2.1.3 Findings

We identified a clear cohort of people with severe ME/CFS. Almost 2/3^{rds} of the cohort stated their illness started suddenly, the rest reported gradual onset. 90% of respondents are female and the majority of respondents recall an infection as the trigger for their ME/CFS. 97% of participants are unable to work full time or continue in study, most cannot work part-time either. 100% report difficulty attending social events. Approximately half of the participants are unable to walk outside or undertake tasks such as shopping, whilst the other half report difficulties with such activities. Most receive care support from family members, while 1/3rd report having

a funded care assistant. Many participants do not receive funded care support. Most participants receive some form of disability benefit, but many report difficulties and delays accessing such payments. Nearly 2/3^{rds} of the participants report a lack of social care support, other than disability benefits.

Many people with severe ME/CFS report anger and frustration engaging with the medical profession, a significant proportion find getting a diagnosis an arduous task and are reporting that doctors have little knowledge of the illness. Some participants report positive experiences, often building supportive relationships with their general practitioner. Many of the sample reported moving from moderate illness status to severe over the course of the illness. A number of severe patients have tried therapies such as cognitive behavioural therapy (CBT), graded exercise therapies (GET) and variants of pacing therapy (PT). Many have also tried psychotherapy or counselling, physiotherapy and alternative therapies. GET ranked highest for negative responses, followed by CBT and physiotherapy. Responses to CBT and physiotherapy are mixed, whilst pacing receives the largest positive response rank.

Most severe patients take regular medications to control symptoms, often pain killers, sleep aids and anti-depressants, as well as a wide range of other drugs. Severe patients often find it difficult to attend hospital visits and are extremely fearful of hospital in-patient care, even for non-ME/CFS related health complaints, due to a lack of understanding and accommodation of their needs. Despite this, many patients want regular follow-up and monitoring, particularly specialist care, including dealing with symptoms such as pain and postural orthostatic intolerance (POTS). Many of the participants have had ME/CFS for a long time, they follow research and developments in the field, some attempt to communicate these to GPs. The majority appear pragmatic, they know that understanding for the illness is progressing. Most call for more research, particularly biomedical research, and a move away from a focus on psycho-social factors. Most of the cohort report finding it difficult to secure social care and most say they want enhanced support and GP involvement with disability benefit claims and illness management, particularly the use of technologies such as tele-consultations from home. People with severe ME/CFS are generally keen to inform doctors, social workers and carers about their specific needs.

Many people with severe ME/CFS remain unwell for years or decades. Only 8% of our cohort report improving over time. Of the rest, approximately 1/3rd remain stable and 1/3rd continue to deteriorate, whilst others report fluctuations. Many participants experience extremely debilitating symptoms, some remain bedbound and unable to walk, the majority are homebound. Many of the participants report difficulties standing (orthostatic intolerance), aversion to stimuli such as light, noise or enhanced cognitive load. Many of the participants report vulnerability to crashing or deterioration after emotional or physical effort and stress. Participants report that pushing beyond limits, often via participating in graded exercise therapy or physiotherapy, results in some type of negative symptom response that can last from days to months, and many report associated psychological distress with such relapses.

2.1.4 Discussion

High levels of distress, frustration and anger, aimed mostly at the medical profession are reported. ME/CFS is a complex illness that is poorly understood among medical and social care professionals. Participants reported challenges in accessing medical care, such as the need for home-visits. Participants want medical practitioners to receive more training on the illness and its impact on quality of life. Participants want earlier diagnosis and more access to specialist secondary medical care and social care.

Participants at the severe end of the ME/CFS spectrum report little benefit from treatments such as CBT or GET. Many report pacing therapies as their treatment of choice. These findings conflict with evidence from randomized controlled trials but are in line with evidence from patient surveys. However, severe ME/CFS patients are often absent from trials of CBT or GET, and there are very few trials of pacing therapies. The most negative comments and stories

from participants are related to psycho-behavioural treatments, particularly Graded Exercise Therapy. A number of respondents expressed strong views that these treatments are not appropriate and are harmful. Some patients state that CBT helps deal with the psychological stresses that are part of chronic illness, particularly anxiety and depression. Pacing appears to ameliorate symptoms or prevent deterioration, but most severe patients report little improvement in their illness status over the long-term.

Many participants perceive that the medical profession view ME/CFS as a predominantly psychological illness. Many suggest that there is too little focus on existing or new biomedical research on causes and pathogenesis of the illness. Despite their poor health, many participants remain optimistic and are actively engaged in following developments in the field, such as the forthcoming NICE updating of treatment recommendations in the guideline. Involving patients with severe ME/CFS in health care planning is difficult given the limitations the illness imposes on them, thus innovative inclusion methods should be considered or designed to involve this sub-set of ME/CFS patients. Doctors and allied health professionals should adopt a flexible and concordant approach when dealing with these patients. Most people with severe ME/CFS want to form better working relationships with their primary care physician and secondary care specialists.

2.2 Introduction

The prevalence of ME/CFS in the general UK adult population is around 0.5% (NICE, 2007; Nacul et al., 2011), however higher rates of 1-2% are sometimes cited. It is estimated that approximately 25% of people with ME/CFS experience severe symptoms or illness presentation (Strassheim et al., 2018). Severely afflicted patients are often housebound and/or bedbound for large amounts of time and have more intense, diverse and persistent symptomology, including pain, fatigue, malaise after minimal exertion, intolerance to light or noise, and cognitive complaints (Pendergrast et al., 2016). Housebound patients are often socially isolated, are unable to work or continue in education, and may experience anxiety and depression. This group within the wider ME/CFS population represent the most challenging cases of the illness. They are difficult to access from a research perspective. Expert knowledge and careful consideration are needed to engage these patients. In a study of several chronic diseases including cancer, stroke, schizophrenia, and renal failure, patients with ME/CFS have the lowest median quality of life (Falk Hvidberg et al., 2015). Patients with severe ME/CFS report lower functional abilities than patients with Type II diabetes mellitus, congestive heart failure, multiple sclerosis, and end-stage renal disease (Buchwald et al., 1996; Pendergrast et al., 2016).

The guideline will be aimed at supporting health and social care professionals, including those working or providing input into educational and occupational health services, commissioners and people with suspected or diagnosed ME/CFS, their families and carers and the public. Specific consideration will be given to people with severe ME/CFS symptoms.

NICE acknowledge that any involvement from adults with severe ME/CFS symptoms needs to occur within an ethical framework in which the most severely afflicted participants are offered an opportunity to participate in the development of appropriate treatment guidelines for this illness. NICE recognize that this group of participants needs to be afforded an opportunity to provide feedback about the medical and social care they receive in accordance with NICE Patient and Public Involvement Policy.

This project was commissioned by NICE as part of their work to develop a new guideline for Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome (ME/CFS).

2.3 Aim of the project

The aim of this project was to recruit and explore the opinions of people who have severe ME/CFS so that their perspectives informed the development of the new guideline

This project utilises an exploratory study design to engage patients with severe ME/CFS in order to offer the Guideline Committee insights into the needs and perspectives of adults with severe ME/CFS symptoms, including providing high quality data on issues of importance to those severely affected by ME/CFS. The project is specifically tailored to take account of the unique needs of patients with severe ME/CFS. Adults with severe ME/CFS symptoms are an underserved group with symptoms that may result in being confined to their homes, and for some, being bedbound for long periods of time.

2.3.1 Research objectives

The key aspect of the project was to give people with severe ME/CFS the opportunity to provide insight about their perspectives on specific questions and issues identified by the committee based on the guideline scope. The following topics were identified from the guideline scope: Identification and assessment before diagnosis, diagnosis of ME/CFS, management of ME/CFS, monitoring and review, information, education, and support for people with suspected or diagnosed ME/CFS and their families and carers, and information, education and support for health and social care professionals.

2.4 Background

2.4.1 Difficulties getting a diagnosis

Many sufferers anecdotally report problems getting an early diagnosis and appropriate medical care. We conducted a literature search and found scant research on 'diagnosis of ME/CFS', specifically how long it takes patients to get a diagnosis and the process patients go through to get a diagnosis. One study using general practice data shows that ME/CFS patients present to GPs with characteristic symptoms years or decades before receiving a confirmatory diagnosis (Collin et al., 2017). Our review of research studies and patient surveys revealed consistent themes. ME/CFS patients often take years to get a confirmatory diagnosis, physicians are reluctant to diagnose and/or lack confidence in diagnosis and treatment as a result of inadequate training and limited clinical exposure. A GP survey by Bowen et al. finds that 48% of GPs do not feel confident with making a diagnosis of CFS/ME (Bowen et al., 2005). Raine et al. found that UK GPs negatively stereotype ME/CFS patients with having 'undesirable traits' that cause frustration for doctors (Raine, 2004). One Swedish study found that physicians view ME/CFS as a condition below 'disease status' with views that patients are illness-focused, demanding and medicalizing (Asbring and Narvanen, 2003). There are conflicting models of the illness that generate confusion and acrimony for doctors and patients. As a result, despite patients reporting that getting a diagnosis is the single most helpful event for them in managing their condition (Drachler Mde et al., 2009), many sufferers turn to online patient groups for support, disengage with traditional medical care and attempt to manage their condition without medical support.

2.4.2 Difficulties defining and diagnosing severe ME/CFS

There are no clear biomarkers to easily aid a physician in the diagnosis of ME/CFS; often a diagnosis of the condition is made after excluding other possible causes for the patients' fatigue and other symptoms (Komaroff, 2015; Fischer et al., 2014). In addition, different research groups use different diagnostic criteria to assess ME/CFS status (Nacul et al., 2017), thus we observe fluctuating prevalence rates in the literature – and a knock-on impact on diagnosis of ME/CFS at the clinic level (Geraghty and Adeniji, 2019). In an illness that is hard to diagnose

and mimics generalised fatigue, which is a characteristic complaint in many other chronic illnesses or mental health states, such as depression, severe ME/CFS patients might represent the 'clearest' cohort of ME/CFS. However, researchers and clinicians do not have a universally accepted instrument to assess severity. Researchers in this field use a wide range of scales to assess symptoms – the *DePaul Symptom Survey* (Jason et al., 2015) and the *Chalder Fatigue Scale* (Chalder et al., 1993) measure symptom profile and fatigue. Researchers also use quality of life scales, mostly SF-36 to assess functional status and disability levels (Ware et al., 2007), but none of these instruments offer clinicians an accessible or simplistic ME/CFS severity-rating or tool to use in clinical settings.

2.4.3 Lack of focus on severe ME/CFS

Despite almost 25% of all sufferers being classed as severe (Group, 2002), it is estimated that as little as 0.5% of the entire ME/CFS literature base covers 'severe ME/CFS' (Abbot, 2014). Patient charity groups have raised concerns about the neglect of this under-served patient group. A 2002 Chief Medical Officer's Report highlighted this finding and the lack of focus on those patients that are bedbound or housebound "*Severely ill are severely overlooked; just ignored and invisible*" Section 2.3.1 (Group, 2002). Action for M.E.'s 2014 '*M.E. Time to deliver*' patient group survey report found that:

- 96% of respondents with severe M.E. said they had stopped or reduced household tasks
- 95% had stopped or reduced social contact
- 74% require full or part-time care
- 70% were no longer able to leave their home independently.

An international study looked at adults (18 years or over) with ME/CFS who are confined to their homes due to severe symptomatology compared with non-housebound sufferers (Pendergrast et al., 2016). The researchers used the DePaul Symptom Questionnaire to assess ME/CFS symptoms and the SF-36 to measure health impact on physical/mental functioning. Findings indicated that the housebound group (severe sufferers) represented one quarter of the sample and were significantly more impaired with regards to physical functioning, bodily pain, vitality, social functioning, fatigue, post-exertional malaise, sleep, pain, neuro-cognitive, autonomic, neuro-endocrine and immune functioning compared to individuals who were not housebound (Pendergrast et al., 2016). Understanding the differences between housebound and not housebound groups holds implications for doctors and health planners. Important patient characteristics are extracted from the above study and are summarised in Table 1.

Table 1: Characteristics of international cohorts of ME/CFS patients

Key Characteristics	UK Newcastle	US DePaul	EU Norway 1*
No. of Participants	100	216	175
Female v Male	85% f.	84% f.	87% f.
Caucasian vs. other ethnicity	99% c.	98% c.	99% c.
mean age	45	52	43
Receive disability	30%	57%	84%
Currently working *full time or part-time	37.5%	13.5%	10%
University or college Qualifications	50%	75%	50%

1. **Two samples quoted in study (we used 1 sample, both are similar), includes homebound and not.*

Table 1 demonstrates a number of important characteristics of severe ME/CFS sufferers. The majority of sufferers appear to be female, which is in line with epidemiological studies that continually show a higher female ratio. The average age of participants is in the mid-40s. Caucasians appear over-represented in research studies, as are college graduates and professionals. Whilst around one in ten severe sufferers continue in employment in the US or Norway, almost one third of the UK cohort continued to work full-time or part-time. The UK cohort held the lowest level of disability benefits claimed across the three international cohorts, perhaps exemplifying challenges UK sufferers face accessing social care support.

2.5 Study methodology

2.5.1 Survey rationale

Prof. Newton and colleagues at Newcastle University undertook a study to define the prevalence of severe CFS/ME and its clinical characteristics in the North East of England (Strassheim et al., 2018) – from 483 questionnaire packs requested only 63 were returned by patients, showing how difficult it is engage patients with severe ME/CFS in research studies. These patients have very specific needs and difficulties, such as difficulties with cognitive function and extreme fatigue. With this in mind, standard face-to-face interviews are extremely difficult to conduct, requiring home visits that can be difficult for people with severe ME/CFS. In order to reach people with severe ME/CFS in the timeframe of the project, between June 2019 and December 2019, we opted for a survey. It was not feasible to undertake face-to-face interviews with enough ME/CFS patients given their geographical spread, the impact this might have on bedbound patients and the limited resources available to us. We considered tele-interviews with ME/CFS patients but later rejected this option after preliminary feedback from people with ME/CFS that interviews of any length of time, between 15 minutes to 1 hour, would cause considerable fatigue and increase other symptoms. Given our research objectives we opted for an online survey. The benefits of an online survey were two-fold: first, it allows access to a wide number of responders located across England and Wales; second, it could be completed by respondents in their own time, thus minimising the burden on patients with severe ME/CFS.

2.5.2 Questionnaire development

Following discussions with the guideline committee and a review of relevant literature, we formulated a survey questionnaire with a series of questions that covered our main research objectives (page 8). These objectives aligned with the guideline scope and the committee's identified areas of special interest for patients with severe ME/CFS (Appendix 1). We opted for a series of predominantly semi-structured questions to allow respondents to elaborate on their experiences of care, diagnosis and management. Each question was specifically structured to allow respondents to provide their responses with the minimum of effort in terms of cognitive load or time-effort. The questionnaire could be completed by the patient, with the help of a care assistant or family member if needed – thus it allowed the patient to complete the questionnaire in their own time. This, we believed, would cause the minimum of stress and would allow for the best possible results. *SurveySelect* software (2019 TM) was used to administer the survey. Table 2 provides an overview of the link between scoping areas identified by the guideline committee and our research objective areas of interest and key areas of focus within our survey instrument.

Table 2: Overview of research areas, objectives and linked details attended to in survey

Scoping Area	Research Objective: Exploring	Explored in Questionnaire with patients with severe ME/CFS
Identification and assessment before diagnosis	*1. Participants' views on illness identification and assessment before diagnosis*	Their experience of: • Initial illness ○ Being believed • Initial illness and impact on life (including family, friends, school, college, university, work) • Initial contact with a health and social care professional about symptoms • What worked well • What didn't work well
Diagnosis of ME/CFS	*2. Participants' experiences of diagnosis of ME/CFS*	Their experience of: • Continuing illness and severe ME/CFS • Continuing illness and impact on life (including family, friends, work, college, university) • Contact with health and social care professionals to get a diagnosis, approach taken • Time to get a diagnosis • What worked well • What didn't work well

Management of ME/CFS	*3. Participants' experiences of management of ME/CFS*	Their experience of:
		• Interventions (benefits and harms)
		  ○ For ME/CFS and symptomatic relief
		  ○ Outcomes: benefits and harms
		  ○ If offered interventions have not been taken up, why
		• Contact with health and social care professionals and services
		  ○ Are your basic needs met?
		  ○ Co-ordination of care
		  ○ Referral to specialists
		  ○ Hospitalisation
		  ○ Involvement in decision making
		  ▪ Feelings of control and choice
		  ○ Access to services
		  ▪ Access to appointments and getting to appointments (distance to clinics)
		  ▪ Home visits
		  ▪ Support services (mobility aids)
		• What worked well

		○ Experience of recovery if appropriate ○ Experience of reintegration if appropriate (for example, work, friendship groups) • What didn't work well ○ Experience of relapse
Monitoring and review	*4. Participants' experiences of monitoring and review of ME/CFS*	Their experience of: • Continuing care • Follow up Who does this? Information about prognosis or future planning
Information, education, and support for people with suspected or diagnosed ME/CFS and their families and carers	*5. Participants' experiences of information, education, and support for ME/CFS as well their families and carers*	Their experience of: • Accessing information, education and support ○ What was useful and what wasn't ○ Information and support networks
Information, education and support for health and social care professionals.	*6. Participants' views on Information, education and support for health and social care professionals.*	Their experience of: • Knowledge of the health and social care professionals ○ Where do you think they get information from • Health and social care professionals' attitude to ME/CFS • Do they have the ability to provide support and what has been useful

2.6 Sample selection

The respondents involved in this survey were recruited in two phases, a pilot test phase and an open survey phase. To ensure confidentiality, respondents were given questionnaire questions with no names or signature input requirements.

2.6.1 Pilot test phase participant recruitment

In this first phase we invited a select number (n=10) of people with severe ME/CFS to participate. This group were drawn from a mix of direct contacts between Dr. Geraghty and a number of patients and contacts with a number of patient advocacy organizations, asking them to select a small number of their members to trial our survey (*a convenience sample*). This group were given access to the online survey and were encouraged to give feedback on the survey and the process of completing it. Our aim was to test the survey, to ascertain if it was viable, to see if patients with severe ME/CFS had any specific problems or concerns

completing the questions. Feedback received proved valuable insights into how respondents might experience survey completion.

2.6.2 Main purposeful recruitment

Given the short time-frame available to our team to conduct this project (between June and December 2019) we opted for a *purposeful sampling* strategy. Our survey was advertised via social media (using Twitter and University of Manchester website). Given the scope of NICE guidelines, we restricted our survey to patients living in England and Wales. Patient advocacy and charity organizations were also contacted and asked to advertise our survey to their online platforms. This dual approach of open-survey and targeting of charity groups, helped widen coverage of our survey to members of ME/CFS patient representative groups and non-members. To take part in the survey participants had to meet the following inclusion criteria:

1. Have a confirmed diagnosis of ME/CFS from either a GP or NHS specialist.
2. Be adults age 18 or over residing in England or Wales.
3. Self-identify as suffering from 'severe ME/CFS'.
4. Consent via signing of a consent form & reading of a participant information sheet.

2.6.3 Target sample

Purposive samples are commonly used for of non-probabilistic sampling and their size typically relies on the concept of "*saturation*," or the point at which no new information or themes are observed in the data. Guest et al. suggest saturation occurs within the first twelve interviews (Guest et al., 2006), however other qualitative methodologists suggest 20+ respondents to establish credible findings (Hagaman and Wutich, 2017). We opted for a survey methodology over interviews and thus aimed for higher numbers of respondents, circa 50 complete responses to garner a credible sample, before beginning data analysis.

2.7 Research ethics and confidentiality

Formal ethical approval for this project was sought and granted from the University of Manchester Research Ethics Committee (*2019-7763-12089*). Given the nature of the project – a commissioned project not recruiting patients from the NHS, NHS ethical approval was not required. Our project involved a range of ethical considerations. Our team highlighted the need for ensuring respondent confidentiality and awareness of the specific needs of patients with severe ME/CFS as important ethical considerations. In undertaking this project, all members of the research team adhered to the core principles of research ethics outlines in the Belmont Report (1979):

1. Respect for research participants, their health status and confidentiality.
2. Beneficence, awareness of participants circumstances and limitations and efforts to minimize distress in the interview process.
3. Justice, fairly and accurately representing the feedback given by participants.

2.7.1 Disclosure and informed consent

All potential participants were asked to sign a Consent Form in order to begin the survey (Appendix 2). In addition, each participant received a detailed Participant Information Sheet (PIS) (Appendix 3) that we attached to the beginning of the survey and respondents had to positively click that they had read this before proceeding to answer survey questions. This PIS was downloadable as a PDF for participants to retain. We were particularly concerned that

completing the survey might be an onerous and exhausting task for people with severe ME/CFS, thus we gave detailed instructions that the survey could be completing over different days and we gave instructions for responders to get help if needed and not to endure symptom flare. Participants were encouraged to contact a member of our research team if they have any prior questions or concerns, or problems, completing the survey. We received many emails, discussed in our findings section.

2.8 Data analysis

2.8.1 Data collection and synthesis

Data processing entailed data collection via survey responses, data cleaning to exclude ineligible participants, thematic analysis of responses, data coding, analysis and interpretation. A database of responses was extracted from our *SurveySelect* programme and exported to Microsoft Excel. Both Excel and Microsoft Word were used to tabulate data and undertake analysis. We utilised a mix of *Thematic Content & Narrative Analysis* to arrive at meaningful interpretations of the collected data (Glaser and Strauss, 2017). Our aim was to draw out recurrent themes (frequent response or patterns), whilst allowing for individual narratives to also emerge, that accurately and fairly represented the views of patients with severe ME/CFS. The process of data synthesis and interpretation involved:

- Two researchers undertook data collection and collation.
- Responses from questionnaires were collated into a project file by exporting a dataset from *SurveySelect* tool to MS Excel.
- Each researcher read over responses allocated to them.
- Text responses to key questions or series of questions were categorised as relevant to our specific research objectives. Themes were identified and coded applying Ryan and Bernard's (2003) repetition approach to identify themes (Ryan and Bernard, 2000).
- A senior member of the research team with expertise in qualitative methods reviewed completed data outputs to assess consistency and the quality of analysis.
- Both data sheets were merged into a single report using headlines to cover the main themes to emerge from the overall dataset (creating a coherent narrative that includes quotes from respondents to support reported themes).
- All members of the research team approved the data entries in our report.

2.9 Findings

Participant characteristics and classification

Approximately 1600 persons clicked on our survey link and opened the survey. From these 343 started the survey, 124 completed, 219 did not complete, 60 self-reported clearly as severe, 27 self-reported moderate-to-severe, 33 self-reported as moderate-to-mild and 4 had no confirmed diagnosis. For the purposes of our analysis we decided to take only those 60 that had severe illness status with a confirmed diagnosis of ME/CFS. Respondents' ages spanned 19 years old to 80 years old, with a mean age of 50 and SD = 13.4 years (Figure 1). The majority of the respondents were female (50/60), 9 were male and 1 classified themselves as non-binary.

Participant responses

In this section, we present participant responses with reference to identified themes and sub-themes. We include direct quotations from participant responses to expand on our summarised themes and to contextualise the meaning behind these themes. We use participant code identifier numbering to differentiate respondents.

2.9.1 Participants' views on illness identification and assessment before diagnosis (including current status)

Illness onset

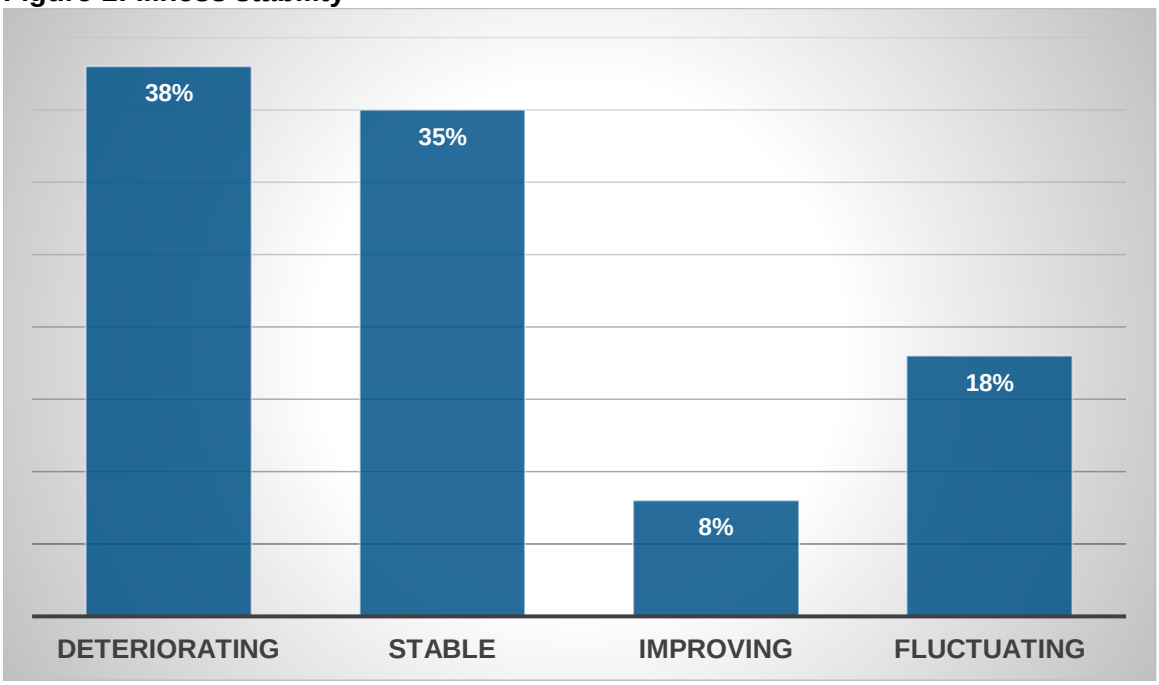
Almost two thirds of respondents indicated that the illness started suddenly (38/60), while the rest report the illness had a gradual onset of worsening symptoms (22). Many respondents report a singular infection event, such as glandular fever, as the trigger, and gradual worsening of their condition in the subsequent months and years.

Illness stability/progression

We asked early on in our survey questionnaire whether patients felt their illness was stable and whether they had periods of remission or improvement (we ask a similar question in Q39 but include symptom fluctuations after the treatment section – it is reported below in Section 4 with similar results as reported here).

38% of respondents stated their illness had generally gotten worse over time (Figure 1). 35% remain stable (moderate-to-severe) over time, 18% tend to fluctuate. Only 8% report generally improving over time.

Figure 1: Illness stability



The proportion of self-reported fluctuating condition also increases with decreasing severity of the illness, just like the self-reported improving condition. This can be due to the fact that participants experience ill health without any periods of relief, meaning that their condition cannot fluctuate between bad and better, while with decreasing severity it is easier for the condition to fluctuate between bad and better.

Education or work status with illness

- 58 out of 60 respondents said their ME/CFS is preventing them from continuing in work or study.
- 3 said they could continue to work but on a reduced level (partially).
- 1 respondent gave a 'no' answer and 1 gave a 'nondescript' answer.

Social event participation

- 59 out of 60 respondents said they were unable to attend social events.
- 1 stated that they are partially impeded.
- Social isolation is a key indicator of severe status.

Outside activities (walking or shopping)

- Half of respondents (30) report that they are not able at all to go outside for any activities.
- The other half (30) report that they are only able to do so partially for limited periods, often minutes only.

Support from family members

Three quarters of the respondents (44) state that they receive support from family members, while a quarter (15) state that they do not receive such support, either because the family are unable or unwilling to provide it.

Support from a care assistant

One third (19) of the respondents state they have a care assistant, typically provided to them, but in some cases paid for by them. 1/3rd (17) state they don't have a care assistant, but typically would like to have one if it could be provided. Around 1/3rd (21) state that their carer is one or multiple family members. 1 reports being on a waiting list for a carer, 1 has had a carer in the past and 1 can't find a suitable person to provide care because of too many special requirements.

2.9.2 Participants' experience of diagnosis of ME/CFS

Time to first diagnosis

We found large variability in the time it took to get diagnosed, ranging from 2 months to 21 years. The mean value excluding extreme cases of over 10 years, is 24 months (SD=22.6 months). There are 3 extreme cases (11 years, 11 years and 21 years).

Getting a diagnosis: GP, specialist or other

The majority of respondents indicated that their diagnosis was given by a medical professional:

- GP (23),
- Specialist (13) and
- ME/CSF clinic (8)
- Consultant (7)
- Other: neurologist 3, paediatric specialist 3, immunologist 2, rheumatologist 1.

Experiences of getting diagnosed

About a third of respondents indicated that they were reasonably satisfied with the process of getting ME/CFS diagnosed (23).

1577773 "*most doctors haven't heard of myalgic encephalomyelitis. they certainly haven't been trained to know the tests to diagnose it. I was lucky I found one*."

The most frequent complaint among others related to the process taking too long (25) and not feeling believed by doctors (14). 8 indicated that they had to suggest the diagnosis to the GP or specialist, while 5 indicated that they had to get the diagnosis privately. 7 indicated that they were diagnosed initially with depression, 1 with anaemia, 1 with anxiety and 1 with hypothyroidism.

*Our numbers do not add up to 60 because most respondents had multiple complaints.

1560014 "*I was made to feel it was somehow my fault I was still ill; At that time we were told that you couldn't have ME if you had underactive thyroid."*

1574885 "*He seemed dismissive about anything that fell outside of the strict boundaries he had regarding cfs/me."*

1577409 "*My then GP was very nice, she said she didn't believe in ME but that in my case she was prepared to diagnose ME*."

1577978 "*NHS was worse than useless. Left me without a correct diagnosis for 2 years. As a result I had to keep working full time and got gradually worse and worse. They accused me of being depressed which was ironic as that was the only symptom I didn't have. In the end I had to see a private physician, who was the first doctor who actually listened to me*."

Many respondents said that getting a diagnosis gave them a sense of relief and legitimacy.

1578853 "*Good to be validated. The dx of ME as it was called back then seemed to legitimise me in the eyes of doctors! Myalgic encephalomyelitis sounded serious to them*..."

Others talked about the practicalities of a diagnosis, for example making claims for benefits or private insurance claims to support them whilst unwell.

1579148 "*I paid for a specialist diagnosis as I needed this to make an insurance claim*."

Factors that patients felt helped in getting a diagnosis

The main factor is the positive attitude from the GP or specialist setting the diagnosis. 14 respondents mentioned the GP being informed and educated as an important factor, 11 indicated the importance of the GP being supportive and listening to their concerns.

1582572 "*Being able to see a GP who had significant knowledge about the illness. Many doctors had failed to spot it in the months/years before then despite me being seriously ill*."

The second major factor was the patient's own efforts – doing research and asking questions of medical professionals (16), including perseverance in trying to persuade the doctor that this is the right diagnosis. Secondary factors were paying to get a diagnosis privately (7) and having clear symptoms (7). 2 respondents mention having a family history of the illness as a facilitating factor, and 1 mention being a child as a facilitating factor, since this draws more sympathy from the doctors and makes them put more effort in the investigations.

1574735 "*Going to the doctor many times to complain that I couldn't function, although this wasn't a positive thing because it went on for three years and was very upsetting because they were very rude to me. They got fed up with me and the nurse would sulk and be angry when I went to see her for the blood tests that the ME clinic asked for, for the referral….Having a local ME service with a GP who knew the diagnostic criteria for ME was helpful because it meant I could get a diagnosis*."

Factors that delayed diagnosis

A quarter of the respondents said there were no factors that delayed their diagnosis. The main factor indicated in delays (about half of the sample) is uninformed GP or specialist (32). Secondary factors are ambiguous symptoms (5) and NHS waiting times (5). Some respondents complained about not being believed as a factor (3) and the lack of clarity in the diagnostic criteria (3). The lack of an ME/CFS specialist locally is also mentioned (2) as well as the lack of remote support for patients who are unable to travel for investigations (2). Other patients mention the lack of availability of private specialists and their own denial of the illness as factors. A typical story,

1582331 "*If I had been taken seriously the first few times I saw a GP I could have been diagnosed years earlier, and may not be so ill now. The waits between appointments delayed my diagnosis massively…It took me a very long time to meet a GP who suggested it, and he was not confident in his knowledge of it at all. Even now when I see a different GP they know very little and sometimes misunderstand basic parts of it very often*."

Physician acceptance of ME/CFS diagnosis and support of patient

52 respondents said their doctor agreed with their diagnosis, while only 8 said that their doctor did not agree. Less than half (25/60) said their GP was supportive and a little over half (34) said their GP was unsupportive of their diagnosis and illness. 4 respondents said that they had to change their GP. Patients report changing GPs either purposefully or because of life circumstances and having different experiences with them.

2.9.3 Participants' experience management and treatment of ME/CFS

Prescribed medications/drugs

In question 19, we asked if patients had been prescribed any drugs by their doctor or a specialist, specifically for their ME/CFS or related symptoms. To our surprise, given there are no recommended drug treatments for ME/CFS, only 7 out of 60 respondents said 'no' to drug prescriptions for their ME/CFS symptoms. Some gave a yes answer without details, but the majority gave long lists of drugs taken, often spanning many years, even decades (see quotes below). We were initially going to list the drugs mentioned but this became too complex given lists were often long and patients talked about drugs currently taken and drugs taken in the past, thus we decided to record the drug classes most often mentioned by respondents. These are:

Table 3: Drugs taken to treat illness/symptoms

Most Mentioned Medications	Lesser Mentioned Medications
• **Pain Medications –** often amitriptyline, Pregabalin, Gabapentin, codeine, lyrica, NSAIDs and others	• Migraine – Sumatriptan • Anti-virals – acyclovir • Proton Pump Inhibitor – Omeprazole

- **Sleep Medications** – Zopiclone and others
- **Anti-depressants** – often not named
- **Anxiety (also muscle spasm) – Diazepam**
- **Steroids – hydrocortisone**
- **Vitamin supplements – most Vit B12, Mg, Vit C**
- Anti-histamine – cetirizine
- Beta-blocker – propranolol
- Postural Orthostatic Intolerance meds (POTS) - Pyridostigmine
- Mast Cell Activation meds (MCAS) - Ketotifen

Some typical patient comments about drugs taken,

1560312 "*So many over decades. My medical drugs are an archaeological document of fads in treatment1. Antidepressants of different types2. Antivirals -valtrex, amantidine3. Pain - codeine, lyrica, 4. Experimental - ivig, kutapressin, magnesium injections, b125. Spasms -baclofen6. Antibiotics7. Steroids, Prednisone, hydrocortisone*."

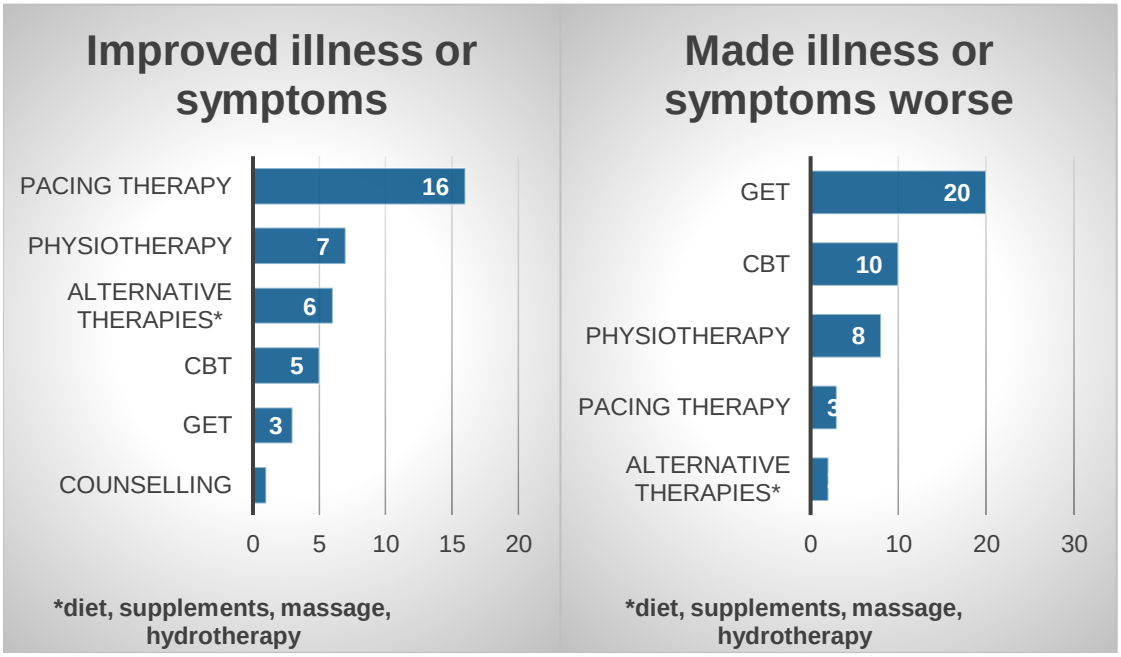
1585039 "*Amitriptyline alleviates headaches; Baclofen reduces muscle spasm; Clonazepam reduces muscle spasm; Gabapentin reduces shooting, stabbing and gnawing breakthrough pain; Hydrocortisone made a big difference in my energy levels since the day I started taking it. Lanzaprazole - helps the nausea; Nimidopine- marked improvement in cognitive function:- ability to word-find, improvement in vocabulary and structuring sentences. Been on it for 10 years; Pizotifen helps to control the migraines; Sumatriptan tablets/nasal spray/IM injection works to a degree*."

Interventions: treatments and responses

We asked in questions 21 and 22, whether participants had undertaken any specific treatment or been prescribed a treatment for their ME/CFS and whether such treatments made things better, worse or had no change. We specifically listed CBT, GET and Pacing, as these are the three most common treatments reported in the literature, but we asked respondents to list any other treatments if they had tried something other than the above. Respondents gave a lot of information across both questions, so in our analysis we had to combine answers across both questions.

Results were mixed. Overall, respondents mostly gave negative or neutral responses. We detail these below (Figure 3). The therapies respondents most often tried were CBT, GET, Pacing Therapy (either self-directed or guided by a health professional), physiotherapy, psychotherapy, counselling, and alternative medicine or therapies. It is important to note that a significant number of respondents stated that they had not tried CBT, GET or other therapies, or that these made no difference if tried. 23 respondents said they either did not try the therapy recommended, or it made no difference. In table 3 below we list what therapies improved symptoms most often or made symptoms worse most often, as reported by the number of participants. We can observe an inverse relationship, that correlates, between both sides (improved or worsened).

Figure 2:



Number of people reporting

Cognitive behavioural therapy (CBT)

Overall, responses about CBT and symptoms changes were slightly negative to neutral, 30 respondents out of a cohort of 60 said they had tried CBT (50%), and of these, 10 respondents stated it made things worse, whilst 5 stated it helped and 15 stated it had no impact of neutral change.

1579580 "*CBT helped with my depression. The loss of my previous life has been difficult to come to terms with*".

1586506 "CBT made me worse since I was taught to view my illness as a false belief, and therefore repeatedly ignored post-exertional malaise until it developed into permanent worsening of my symptoms."

1560014 "*I dragged myself to CBT sessions because I was assure(d) it would make me better…They made me permanently more ill*."

Graded Exercise therapy

GET in all forms generates the most negative responses. 26 respondents said they had tried GET in Q21 and in Q22 20 participants reported it made them feel worse, 3 stated it helped or improved symptoms and the rest had neutral change. The remainder of the 60 cohort had not tried GET.

1560312 "*The early type was to increase activity regardless if how one functioned. I never recovered back to the activity level I had when I started The 2nd type of GET was to increase on when stabilised but this never worked as the disease got worse the more I did*."

1579580 "*GET was given by a physio who was sent from Stockport. They were really supportive and very knowledgeable regarding ME so exercise was very gentle. I understood that I needed to move my legs and arms to prevent muscle wastage*."

1582572 "*The GET was unhelpful and reduced my overall level of activity*."

1586506 "*GET made me worse every time I tried it - and I kept trying it throughout my twenties*."

Physiotherapy

Responses about physiotherapy were mixed, 8 respondents stated that it made them worse, whilst 7 reported it helped. Respondent 1575763 who had reported some benefit using CBT for anxiety tried physio with profoundly negative comments:

> "*I saw a physio at my local NHS centre. I had gone from my bed, to my wheelchair to the appointment. At the appointment she looked me in the face, repeatedly telling me 'ME is all in the mind, you're making it up' whilst instructing me to attempt to do arm push-ups on the arm rests of the wheelchair. This was both physically and emotionally damaging. I have lost all faith in medical professionals*."

Respondent 157563's loss of faith in health professionals following a bad experience is not an uncommon reported event. Participants that experience a distressing experience may mistrust health professionals and often disengage from all formal treatments.

Respondent 1585039 reports moving between two types of physiotherapy for their very severe ME/CFS. Their experience exemplifies how subtle changes in approach bring about differing results and how understanding of ME/CFS is essential for a good relationship between therapist and patient,

> "*I was bed bound and the emphasis was solely on sitting me out in a chair. This approach exacerbated the ME. My physiotherapy was then taken over by a neurophysiotherapist who worked with MS and Parkinson's patients. She did passive and then active assisted exercises to put all the joints through their range of movement. She also did chest physio which improved the oxygen levels in my body. If I was very fatigued she would do massage. She came to the house three times per week for eight years and over time I progressed to walking with a frame. Setbacks were frequent, often due to my response to external noise as well as infection etc. After each set back she would have to start again with the passive exercises and then build up again. A lot of the work was on muscle memory. The physio was sympathetically done and without it I would not have been able to make the progress I have*."

1574735 recounts a similar experience,

> "*I was given physiotherapy exercises to do by the ME/CFS clinic but these caused me to crash for a month, so once I recovered I saw a non-specialist physiotherapist at my university who pared down the exercises to make them more efficient, gentle and manageable for me. These help with core strength, joint mobility and muscle stiffness which I find beneficial in reducing musculoskeletal pains that result from my limited mobility, but it does not have any impact on my ME symptoms. I have to be extremely careful with it because I can only do a tiny but of very gentle physiotherapy each day before it makes me feel really unwell*."

Pacing Therapy

Respondents rated Pacing Therapy as most useful in terms of stabilizing or improving symptoms – 16 reporting improvement, while only 3 reported becoming worse using pacing. We note here that respondents tried different forms of pacing therapies – Adaptive Pacing Therapy (APT) similar to that used in clinical trials such as the PACE Trial, self-directed pacing and other variants.

1576479 "*Pacing is a good strategy- stay within energy envelope and very occasionally bounce the boundaries to see if underlying health has improved enough to do*

more. I got back to normal activity levels doing this, though how my underlying health improved is a mystery. Any treatment with an emphasis on increasing activity to a schedule reveals that the therapist fundamentally misunderstands the nature of ME."

1574735 "*I have been visiting NHS ME/CFS clinics 2-3 times a year since my diagnosis, who give me advice on pacing. I find pacing helpful to minimize flare-ups, longer-term worsening and reduce the frequency and intensity of crashes, but it has not led to any improvement in symptoms overall*."

Some patients noted the difference between pacing and GET.

1579730 "*The pacing course encouraged increasing activity, which for me wasn't appropriate. I deteriorated to bedbound within 18 months of diagnosis." Pacing requires staying within limits and gentle testing of boundaries, whereas GET requires pushing past limits and increasing activity steadily*."

Counselling and alternative therapies

Many patients reported that they had tried counselling. Responses were generally mixed for counselling, some found it of benefit, while others reported no change. For example:

1578170 "Counselling helped me deal with some of the frustration and loss involved with having a chronic illness but it did not improve my symptoms. In fact, sometimes the cognitive effort of counselling sometimes left me feeling very unwell physically for several days after an appointment."

The types of alternative therapies most often mentioned were massage therapy, hydrotherapy, dietary changes, including supplements, and meditation/yoga. Results were generally mixed to neutral, having overall positive to neutral impact on symptoms.

Treatment refusal

In question 23, we asked patients if they had ever refused a treatment and why. 35 respondents out of 60 said they had refused treatment or would again if treatment were offered (22 never refused and the rest stated non-applicable). Common reasons given for not trying were 'being too ill' or deeming the treatment 'inappropriate'. Unsurprisingly, severe patients are often too unwell to attend out-patient treatments such as CBT or GET. Respondent 1577539 writes, "*GET…assessed as too ill for it. I couldn't even have got to the appointments often enough*." The same patient did try physiotherapy privately and found it of some help.

Specialist treatments: in-hospital care and outpatient

In question 24, we asked if patients ever had any other specialist treatment, with a list of examples such as tube-feeding or IV fluids, treatments one might expect patients to potentially experience at the more severe end of the ME/CFS spectrum. 46/60 said no. From those who gave answers the following treatments were ranked:

- Tube Feeding (or variants of feeding support)
- IV Fluids
- Speech Therapy

*we suspect if we listed more examples, respondents may have added more items to their responses.

In-hospital stays

28 respondents said they had no hospital in-stays, 32 recorded at least one hospital in-stay, mostly for non-ME/CFS related health complaints, cancer treatment, surgery, infections and investigations.

A number of respondents reported being anxious or fearful of needing to go into hospital, expressing the view that hospital staff would not understand their ME/CFS and needs. Respondent 1580186 writes,

> "*No - its my biggest fear. If I had a non-terminal illness (I would chose to die rather than cope with undergoing something like chemo for instance, I could never cope with it) that was very painful, I have no idea how I would cope with a hospital admission - people around me drains me within minutes*."

1582572 "*I have avoided all in-patient stays including checking myself out*."

1575763 "*I do not feel safe in hospital. I avoid A&E and hospital at all cost. My illness is treated poorly*."

1560312 "*Only 1 hospital stat as hospitals are dangerous places for PWME (people with ME)."*

*In Section 5-6 below we review doctors' knowledge of ME/CFS.

2.9.4 Contact with health and social care professionals and services

GP home visits

We asked respondents whether their GP visits them at home if they are unable to attend a GP surgery. 30 patients said yes, their GP visits them at home, 28 said no, they can't get a home visit and 2 said they hadn't asked for a visit. It was surprising that almost 50% of participants could not get a home visit given their severe status, often being homebound. We also detected a worrying trend – in the group that answered 'yes', a fair number said that it was becoming increasingly difficult to get a home visit and GPs were very reluctant to offer this service:

1575763 "*They did in the past but currently do not*."

1578170 "*No. The one time I insisted on a home visit, and the doctor very reluctantly agreed, I heard her muttering expletives down the phone - in German!!"*

1579197 "*Yes now but I was once told by one of the GPs at the surgery we don't make home visits to people with M.*E."

1578559 "*Reluctantly. They fight it every time despite me being so housebound. Because I *could* force myself there, despite the toll it would take, they insist that I do unless I cannot get up from the bed at all*."

Special accommodations for patients attending GP or hospital appointments

Again, results are mixed. However, GPs appear to be more accommodating than hospital care/specialists. GPs allow phone consultations, use of email and home-visits, whereas these appear to be absent in specialist care. 26 respondents state that they had not been offered any special arrangement or accommodation whilst attending their GP or hospital care. 30 patients said they had been offered some accommodation.

1560411 "*My GP will visit at home if requested. I no longer attend specialist hospital appointments as they, in their own words, tell me there is nothing they can offer*."

Patient control and choice

We asked in question 32, if patients make choices about the types of care they receive or take. Respondents answered this question from different perspectives – some talking about medical

care, others about access to social care, and others about their personal funds that allow them to pay for certain treatments. The majority said they were involved or had choices, but then added that there are no real choices to make, given there are few available treatments. A selection of responses:

1560014 "*I make decisions about my care…To be quite honest, one size does not fit all. What is suitable for some illnesses is not suitable for me*."

1583136 "*There is no care - there is no choice. I feel that I am seen as a heart-sink patient*."

1578559 "*I make all the decisions about my care with family support, but there are few options to choose from*."

1586506 "*Since my family is comfortably off, I am able to make my own choices. However, there is almost no suitable care available for patients with M.E. even if you are able to pay*."

Taking patients' views on board in treatment

In question 33, we asked patients whether doctors consult them and take their views on board during treatment. Results were mixed. We coded 'yes' for patient's views mostly taken on board, 'no', for mostly not, and 'mixed' for mixed responses: we had 20 no, 19 yes, 9 mixed and the rest non-applicable. Many answers did include mixed experiences. One example of a positive response reveals that good relationships with open communication and patient participation are key:

1580063 "*To be fair, some do. I had an excellent gynaecologist who also seemed quite familiar with ME. We considered a hysterectomy at one point as I suffered excessive bleeding. He was able to discuss how ME affects recovery and it definitely factored in his advice to me. My ME consultants have been kind, supportive and very helpful. They treat the relationship as a partnership. I am lucky that I have been able to afford choice in going private*."

More negative responses centre around dismissive doctors, not feeling listened to and a lack of physician knowledge.

1583769 "*They have often said over the years that are constrained by NICE Guidelines. One particular GP in the surgery will consult me and be willing to listen and the Community Neuro Rehab Team also do, to some extent*."

Many respondents talk about trying to educate their GP or specialist about the condition.

1578864 "*They mainly like to impose their views on me. I try to educate them, most know I know more of ME than they do however do not like to admit it*."

1584124 "*Yes but those I have encountered have less knowledge about ME than I do. We are 'lucky' to get one who actually thinks we are ill*."

2.9.5 Participants' experiences of monitoring and review of ME/CFS

GP or specialist monitoring and review of patients

We asked respondents if their ME/CFS is regularly monitored by either a GP or hospital specialist. 41 respondents said 'no' they did not have regular GP monitoring, 13 said 'yes' they did, and the rest said either not applicable or did not give an answer. From those who did give an answer of 'yes', the main method for GP follow-up was a home visit or telephone consultation. 11 said they had specialist monitoring (these 11 include those who gave a yes to GP follow-

up), again mostly via hospital visits or tele-consultation. The rest of the cohort had no specialist follow-up or gave a non-applicable answer. Typical patient comments include:

1586506 "*No. Any doctor visit makes me ill (even a home visit), so it is only worthwhile for a specific purpose*."

1584124 "*GP comes once every 3 months. This is very good by ME standards BUT in context of how ill we actually are, this is pathetic. I have not had any specialist person in many years*."

1583136 "*No, I see the gp only for problems caused by the ME, such as Reynaud's or meds reviews once a year*."

In a separate question (Q45) we asked patients whether or not they felt their illness receives 'adequate ongoing medical support'. Results were even worse than medical monitoring above. 55 respondents said no or disagreed, while only 5 said yes or agreed.

Some patients commented that given GPs have so little to offer they don't often ask for help.

1574885 "*No - although some of that is down to me, I have anxiety around doctor appointments and I am able to manage it alone, and as I have not been offered anything that would improve my health situation previously I see no point in regularly attending doctors appointments when I am not really well enough for it*."

1569304 "*No although I understand GPs are limited in what they know about the illness (as they obviously need to have knowledge of a wide range of illnesses) and by what they can offer."*

Patient improvement or deterioration

We asked respondents about their illness stability after treatment in question 39. Therefore, we feel Section 4 'ongoing experiences after diagnosis and treatment' is the best place to report our findings.

Many respondents report long periods of gradual small improvement followed by relapse and "crashing down" after some health-related event and failing to recover after that. A little less than half (26) patients report that their condition is relatively stable and about the same number (25) that it is slowly deteriorating. The majority of those in the stable category classify themselves as very severe and state that the reason why their condition does not change is because it can hardly get any worse, i.e., they are stuck at the upper end of the scale. About a quarter of the respondents (13) report fluctuations in their condition, which can be small-scale (on the scale of individual days or even within a day) or larger-scale (on the scale of months), with 1 reporting seasonal fluctuations – feeling better in the summer. Slow improvement is reported by only 5 respondents (8%) and another 2 report slow improvement from a very severe to a severe but manageable condition. Another common theme is the reporting of singular or multiple "sharp crash" events, typically due to illness, accident or similar events with significant impact on health. 9 respondents report sharp crashes punctuating the overall trend, which can be stable or slowly deteriorating, and some report fluctuations besides the overall trend. The numbers do not add up to 60 as respondents typically report more than one type of event.

2.9.6 Participants' experiences of information, education and support for people with suspected or diagnosed ME/CFS and their families and carers

Information and educational material available about the illness

We asked in question 47, whether respondents felt there is enough information or educational material available relating to the illness. 48 of the 60 said 'no', 11 said 'yes' and the remainder were undecided or gave no answer. The majority of respondents stated clearly that there was either no information on the illness provided to them from the NHS or health professionals, or that any information available was deeply flawed. Respondents blamed a focus on the psychology of ME/CFS and psychological treatments such as CBT and GET. Even for the few patients that said there was adequate information available, they often said this came from charity groups or international sources, not the NHS. Many respondents said they got information from charity groups. Here is a sample of typical responses:

1582572 "*It feels there is quite a lot of information out there, but much of it is inaccurate or unhelpful and the crucial information is not being got across to those who need it. Information on things like PEM and aerobic capacity does not seem to be understood properly even by some 'experts''.*"

1580063 *"I think the information is unclear, the advice is either incorrect or misleading. The assumption that most patients improve in time is unfounded. This makes it impossible for the patient to adjust and handle practical matters like finances, relationships with employers and family and friends. This has a hugely detrimental effect in the long term*."

1578343 "*No. The lack of funding for research into the condition and the pyscho-somatic model of treatment is more detrimental to informed education than it is helpful (in my opinion)*."

1561885 "*absolutely not. There is far too much information focusing on the physiological side of things and non explaining the true reality*."

1578170 "*There is lots of information if you look online often provided by ME charities or voluntary organisations. However, the information available through the NHS is insufficient and frequently incorrect*."

How accessible is information and educations material about ME/CFS and sources?

The majority of participants stated that where information of educational materials existed, these were accessible. The most frequent sources used were:

- Online materials and sources
- Via charities, either on or offline
- Via social media and patient forums

*NHS sources were almost never mentioned.

Peer support: membership of an ME/CFS patient group

Most respondents said they belonged to such a group (only 12 respondents out of 60 were not a member of a support group). The 25% ME Group and the ME Association were the two charities mentioned most, however many respondents mentioned being part of online support groups, such as Facebook or local ME/CFS groups.

Support from a social worker/social services

Nearly two thirds of the respondents (38) stated that they do not have any social care support, with few saying that they are paying for care privately and a couple saying that it is currently being arranged. About one third (21) said that they have social carer, but 6 of them complained that the service provided is inadequate and only 2 report being very satisfied with the service.

*As we noted in Section 1 'Support from Care Assistant,' many patients are cared for by family members.

Many respondents report a battle to access social care and a lack of awareness of the illness among social workers.

1584124 "*I had an assessment some years ago. Refused funded care. ME team supported me but had no success. No social worker. Probably I am too ill for a long talk with one even if offered and I doubt their training on ME amount to anything at all*."

1585039 "*Had support from social services. It was exhausting, stressful. They failed to do what they agreed to and were disorganised & inaccurate care plans etc*."

1580186 "*No - I choose to pay out of my PIP for my carers - I don't want to have to go through regular social services assessments and cope with the fear of the service being withdrawn for lack of Government funding*."

1577409 "*Local social services don't involve clients in writing or developing care plans so they bear little relevance to the support needed*."

Types of social support accessed

6 report receiving household aids for bathroom, kitchen and bed. 6 report receiving part-time personal and domestic care by a care assistant and 1 reports receiving full-time care. Individual respondents report receiving hydrotherapy, psychological therapy and nutritional support.

Use of mobility scooter

Nearly two thirds (38) report having or using an electric or manual wheelchair. 12 report having a scooter. 10 report having no aids and 4 report having other types of aids – walking sticks, bed lever, stairlift.

Social care payments/benefits received

In question 36, we asked respondents whether they had received any government disability or sickness benefits. The majority, 56 respondents, stated they had. 2 stated they had not, *1 of those who gave a yes answer said they were currently "too ill" to apply, whilst 2 gave non-descript answers. It was not possible to accurately collate what benefits were received given some respondents answered with a 'yes', whilst others gave details. Of those who provided details we note that Disability Living Allowance (DLA), Personal Independence Payment (PIP), Employment Support Allowance (ESA) or some combination of these, such as ESA and DLA. A fair number of respondents reported stress dealing with applications for benefits.

1580063 "*ESA. I applied for DLA and was refused,but was granted Incapacity Benefit. I was later transferred to ESA. I should be entitled to at least some element of PIP, but I simply haven't got the capacity to cope with yet another form and more hassle*."

1583814 "*No, they stopped my disability it's in appeal*."

Barriers and difficulties in accessing social care

The most common complaint (18) is that the process is too difficult. Respondents use expressions like “gruelling and punishing”, “awful”, “interrogation”, “stressful”, “accused of lying”, “nightmare”, “major fight”, “bullied”, “harassed”, “treated like criminal”, “cruel campaign”, “physically, cognitively and emotionally exhausting”, “a lot of stressful form filling”, “total nightmare”. 12 respondents complain that the process has had negative impact on their health. 11 have complaints about the assessment process, stating that the assessors did not document objectively their condition. 13 stated that they had some difficulties with accessing care and benefits, but that it worked out for them in the end. 20 respondents state that they received the benefits only after going through an appeal process. Minority groups of respondents stated that they were denied benefits (5), they had to give up trying to get them (3), the GP did not support their claim (4) and that they did not even want to try (1).

*Only 5 out of 60 stated that they did not encounter problems in the process.

1582331 “*Yes, many.*

> *Universal Credit: I have to turn in fit notes every few weeks until a Work Capability Assessment is done. It has been over a year and I still have not had one. I have to get a phone appointment with my doctor (can only manage about 1x a month), ask for a fit note, get someone else to pick up the fit note for me, register it on the online account (very hard for me), then get someone else to bring it to the job centre for me. Every 3 weeks. It is the biggest cause of PEM for me at the moment, and I can't even manage it as often as they want me to. There's been times I put the date in wrong by one day on the online account, managed to get someone to take it in for me, then had it refused because of it and sent back to me again because the job centre people won't edit the date on my claim. I've had threats of being sanctioned during time periods I was so ill I was not able to use a computer to turn one in. I've had times I couldn't afford my internet bill, so couldn't register the fit note - there is no way I can get to a library to do it there. Countless issues like that.*

> *Social Care: I had a family worker from the council, who didn't believe in ME/CFS. 2 charity workers made a referral to social care for me as she wasn't helping at all, my first two were denied because I had involvement from another council service. Because of the wait times involved with every aspect of my care right now, my social workers haven't been able to do much before they change again. Because of this I have the manager of the team helping me all the time, but she is very busy, and I've gone through 3 others in the past few months. I am constantly having to go through the situation over and over every time they change, which is very hard for me*.”

Patient suggestions about what doctors and care or social support workers can do to support them

We asked respondents in question 46, what more they feel doctors or care support workers could do to assist those living with ME/CFS. We had a range of informative answers, some very detailed. Below we list a summary of the common themes within these answers:

- More empathy, understanding and respect to patient and the illness.
- More and better training of doctors and allied health profession – information booklets, training courses, severe patient case studies.
- More flexibility – especially with appointments.
- Home visits & use of technology such as tele-consults.
- More support – especially home social support and social care benefits.

- More follow up – particularly specialist review and management of symptoms, specifically POTs.
- More detail and coverage within the NICE guidelines.

2.9.7 Participants' views on of information, education and support for health and social care professionals

Doctors' knowledge of ME/CFS

We asked respondents whether or not their primary care doctor or hospital specialist had knowledge of ME/CFS. Results were predominantly poor. We coded answers Y for positive knowledge, N for lacking knowledge and M for mixed results, such as different doctors both having knowledge and lacking knowledge. Results were N=34, Y=10, M=16.

1556935 "*I have generally had to educate any doctors I've been involved with*."

1560014 "*Absolutely not. The advice I always got was try harder, put more effort in. Exercise*!"

1568000 "*No, all GPs I have ever seen know of it but don't know anything about it. The specialist I saw followed the NICE guidelines, believed it was caused by deconditioning and GET was not harmful. Which I now know is not true. I was also told to take a multivitamin and that out of all the alt therapies the lightning process was the most promising. Which seems ridiculous knowing what I now know*."

More positive accounts include:

1580063 "*My specialist is very knowledgeable and experienced in managing ME. I see him privately outside the NHS*."

1580186 "*GP - pretty good. M.E. clinic O.T - very good*."

Typical mixed (M) account:

1576475 "*Hospital specialist very knowledgeable but Primary Care useless & not well informed*."

Awareness and understanding among health professionals

We asked respondents for their suggestions about what could be done to improve raising awareness of the illness among health and social care professionals. Most gave expansive

answers to this question, writing full paragraphs in the answer. The key themes to emerge from our analysis are:

- More and better training of doctors and allied health profession – information booklets, training courses, severe patient case studies.
- A focus on ME/CFS as a physical disease rather than on CFS which is associated with a psychological syndrome
- Widening the focus of debate away from focus on CBT and GET treatments – viewed as stigmatizing and harmful
- Update NICE guidelines to reflect their experiences
- Improving doctors' attitudes and empathy with severe patients.

Most respondents asked for more training and education of doctors, starting at medical school and extending into GP level training, to view the illness as a serious debilitating illness, similar to diseases such as multiple sclerosis.

1578560 "*As I said before CCG's need to commit to GP awareness and education. This has to be a priority, especially with the lack of specialist services. As part of my role as a patient rep working with the NHS patients cite poor GP care as their main concern. They describe falling into a black hole of lack of care. I know exactly what they mean. I don't go to my GP about new or worsening ME symptoms, there is no point*."

1578864 "*I feel in medical school students should go out and visit those who are amongst the worst cases of ME and see how real it is prior to teaching them how to deal with it*."

1582331 "*I really want doctors to be taught more about ME/CFS. There are still doctors who think it isn't real, or believe patients are mentally ill or hypochondriacs. I am aware not an awful lot about this disease is known yet, but the knowledge of even the most basic parts of it is very lacking in health and social care professionals considering how severe and how common it can be. More of my social workers have known about it than my GPs. Which is not the way it should be at all. My social workers have done more for my health than a GP has in 10 years. I am massively grateful of course, but it should not be this way at all*."

Some respondents recounted they had tried to inform their GPs, offering leaflets or booklets, however GPs were often dismissive. Changing GP attitudes via awareness training was also highlighted as a priority, such as visiting severe patients at home, interacting with charity groups and reviewing the latest research, particularly on the biology of ME/CFS and its impact on participants.

Professional empathy and respect for patients

We asked whether respondents felt they had been treated with respect and empathy/understanding by health and social care professions in question 57. Their answers were informative. Results were mixed. We coded answers 'yes' for mostly, 'no' for mostly not, and 'm' for mixed, meaning that different professionals are seen acted differently (y and n). 13 respondents gave an affirmative answer that they had been treated with respect and empathy, 20 respondents said no, whilst 20 said their experience was mixed (y and n) and 7 said it was not applicable.

<u>Poor</u>

1577409 "*No. Lack of belief in ME has meant GPS are rude and behave badly if I raise ME treatment or symptoms. I now won't go to the GP on my own, after I was shouted at a few times*."

1579810 "*No. I have been treated with contempt by the NHS. My previous GP hardly deigned to talk to me*."

1579825 "*I have had many many bad experiences where I have been dismissed, belittled, made to feel I am at fault for not being able to understand/communicate with the doctor, irrational for being upset, responsible for becoming and staying ill, making up symptoms or trying to get attention, had my needs and experiences with drugs, especially withdrawal, dismissed etc*."

Mixed

1580863 "*Doctors and hospital consultants are the worse can be very dismissive and sometimes plain arrogant and rude. Nurses vary, I have had really nice kind caring ones and others not so.*"

1577978 "*Last time I went my GP was one of the good ones and he was excellent. A nurse practitioner however said oh we don' get much ME these days, I don't think people get that anymore! Implying it was a 1980's fad*."

1583769 "*Some just dismiss ME as insignificant others are respectful and understanding. Things have improved over the years. From my experience it's now 50/50*."

Good

1578864 "*Yes…I have also had in my home during an emergency The Acute Care team who treated me wonderfully. Three times they came and each time I was treated with dignity and respect*."

Patients' free comments: additional information

In our last question, 59, we asked respondents if there was any other relevant information they wished to share not covered in other questions. We allowed respondents space to detail anything they felt was relevant. In total, 46 respondents gave feedback in this question, while 14 opted not to. 10 of the 46 gave feedback on the process of data collection itself, the majority talked about how taxing and exhausting it is to complete a survey like ours with severe ME/CFS. Others thanked us and NICE for undertaking this study,

1578559 "*Thank you for taking an interest in our condition and the often poor quality of life for patients because of the lack of appropriate care*."

The remaining 36 gave substantive feedback. 24 respondents complained about the poor quality of care they received from the NHS and GP services and gave a range of recommendations to improve things. These were on the common themes we identified throughout our survey – training of doctors, sympathy and understanding, accommodation of special needs, such as quiet rooms in GP practices, help with or reduction of paperwork, not pushing for more exercise (GET), equality of care with e.g., MS and Parkinson's. For instance,

1575763 "*In my 19yrs of living with ME, most of these years with severe ME, I have never had a care plan. I have face much medical abuse, neglect and gaslighting. I have very little support and no action for my ME. I have lost nearly 20 years of my life and had no help, that is a sobering thought. We live in a first world country yet I am constantly left to fight for the same level of medical care others receive because of ignorance, misunderstanding and poor guidelines. The government has not funded biomedical research since 2012, yet other countries are thriving with it. We have one of the best health systems in the world yet I do*

not feel safe to go to hospital because of how I am treated because of my illness. This must change. We need support. Drs are bound by guidelines. They must change. Education and Reid needed and mostly, patients need help." (complete answer)

10 respondents gave advice for improvements in the research on ME, mainly the suggestion to refocus attention away from psychological and psychiatric research to biological causes and mechanisms.

1574735 "*I really think it is extremely important that the current biopsychosocial model of ME (on which CBT and GET but also the form of pacing currently taught in ME clinics) is completely done away with. It isn't helpful and it causes so much harm to patients, and misunderstanding among medical professionals which negatively impacts our care in a serious way which can lead to neglect, mistreatment, inappropriate advice, worsening of our condition, isolation, loss of benefits, preventable mental health problems (trauma), and suicides. We really need to do away with all of the unnecessary suffering caused by this outdated and unscientific model. Medical education is a priority, as is updating the ME clinics so they are staffed by medical professionals who actually understand the biological nature of the illness, the latest biomedical research, and the best approaches to clinical management of symptoms e.g. through pharmaceuticals and appropriate pacing/physiotherapy, not the kind that is currently used. These for me are top priorities, because we can't go on as we have been for decades. There has been too much unnecessary suffering already.*" (complete answer)

A few respondents mentioned the need to improve NICE guidelines, for example respondent 1579730 – "*NICE guidelines need to acknowledge [that] CBT/GET are not adequate and are potentially dangerous to patients. The focus should be on supportive and pragmatic care."* 3 respondents expressed complaint with the benefits system of support for the patients, reinstating the points made in question 38. 2 respondents make an explicit request that patients should be believed by the doctors.

*Our numbers do not add up to 36 because in a few cases participant responses cover two coded categories.

2.9.8 Summary of salient findings

Table 4: Points from each scoping areas

	Salient Summary Points
Section 1 *Patient Characteristics*	• The majority of respondents are female and our full cohort had ages from 19-80, with more than half between 30-60 years old. • Over half of severe patients report that their illness started suddenly after some infection. • Around 1/3rd of severe patients report deterioration of the condition over time, another 1/3rd report fluctuations, whilst just 8% report improvement. • The majority of severe ME/CFS patients are unable to work or study, are homebound and do not participate in social events, or walk outside for anything more than very short distances.

	• Most severe ME/CFS patients are cared for by family members or a care assistant.
Section 2 *Diagnosis*	• Most participants experience delays in getting a confirmatory diagnosis, with time to first diagnosis averaging 2 years but spanning anything from 2 months to 21 years in extreme cases. • Most participants are diagnosed by a GP or hospital-based specialist or at an ME/CFS clinic. • Approximately 1/3rd of respondents indicate that they are reasonably satisfied with the process of getting ME/CFS diagnosed, but approximately 2/3rds report being unsatisfied. The most common complaint is delay in diagnosis or not being believed. • Many respondents state that getting a diagnosis is positive and offers them legitimacy and access to social support. • GP or specialist awareness of ME/CFS is rated as the most important factor in speedy diagnosis of delay in diagnosis. • Around half of GPs remain uninformed and skeptical of the illness and many patients report feeling unsupported, a small number change GPs because of this, others limit their interactions with doctors.
Section 3 *Treatment & Management*	• A significant number of patients with severe status are too ill to try recommended therapies. • Many respondents have tried multiple therapies – CBT, GET, Pacing, Physio, and alternative approaches. • Results are generally negative for CBT, GET and Physio for the majority of respondents, however a small percentage do find some elements of CBT, GET and Physio useful, particularly when they are tailored to their individual needs. • Medical professionals sometimes give assurances to patients that they will improve if they follow CBT or GET, yet this does not often happen and may cause distress to the patient if they fail to improve or worsen in any way, they may also lose faith in health professionals. • Many participants reported losing faith in medical professionals after a bad or distressing experience and going off to try alternative approaches. Health professionals need to treat ME/CFS with understanding and maintain open and respectful communication. Where health practitioners express anger or frustration with patients, trust is often lost and the therapeutic relationship also. • Pacing, whether self-directed or supported by a professional, appears to help a higher percentage of patients, but not all respondents. • Almost half of all severe participants struggle to get a GP home-visit and the trend seems to be increasing. • Many severe patients find going to hospital a distressing experience, or they avoid hospital visits. The specific needs of patients with severe ME/CFS need to be considered more by hospital staff when these patients are being treated in-hospital, even for illnesses other than ME/CFS.

	• Whist GPs offer home visits, tele-consults and use of email technology, hospital consultants rarely offer this – yet use of such technology appears to be an essential tool for severe ME/CFS participants to access care and services. • There are few treatments available for patients, thus they have limited choices about the care they receive.
Section 4 *Long-term Care*	• Most patients are not monitored or reviewed regularly by either a GP or hospital specialist. • Most participants report an initial illness followed by long periods of ill health, with some fluctuations, with a general pattern for most of a gradual decline in function over time, often years, whilst few patients recover, although a fair portion improve or stabilize. • Other illnesses, secondary to ME/CFS and/or life stresses, can cause downward spiral and decline in function.
Section 5 *Awareness & Support*	• Many ME/CFS patients with severe status join patient support groups, often online local groups. • Patients want better training of doctors and allied health professionals – information booklets, training courses, severe patient case studies. • Patients find it difficult to access social care support, particularly there is a lack of tailored support for their specific needs. • Patients often offer suggestions for improving care, commonly better professional training, more access to home visits, more regular follow-up and specialist monitoring and help with social care and home support. • Patients often keep up-to-date with research developments.
Section 6 *Important Factors in Care and Management*	• The majority of severe ME/CFS participants state that their doctors lack knowledge of the illness, therefore greater emphasis needs to be placed on training, beginning in medical school and extending to specialist post-graduate training. • Training should include face-to-face contact with severe patients and asking doctors to become cognizant of emerging research evidence on bio-physiological abnormalities associated with the illness. • Patients often ask for NICE guidelines to include severe patients' accounts of the illness and their experiences of treatments such as CBT, GET, Pacing Therapy and Physiotherapy. • Patients want less focus to be placed on psycho-social facets of illness and call on health professionals to be provided with information on new developments in ME/CFS. • Many patients report that they are not treated with respect or empathy by health professionals, doctors and allied health workers.

2.10 Discussion

2.10.1 A unique patient cohort with unique challenges

The ME/CFS literature provides credible evidence that approximately 25% of all sufferers fall into the category of 'severe ME/CFS'. However, no clear and widely accepted definition of severe ME/CFS is given in the literature, thus severe generally refers to sufferers who are mostly home-bound, often bedbound for the majority of the day, and are severely functionally impaired using standardised quality of life instruments. Epidemiological prevalence estimates (that commonly vary between 0.1% to 1%) suggest that there are around 250,000 people living with ME/CFS in the UK. This would suggest that approximately 62,500 sufferers may experience severe illness presentation. A general practice with a population of 10,000 patients is likely to have 30–40 patients with ME/CFS and around half of these are likely to fall into the moderate-to-severe category and may need input from specialist services (Group, 2002).

Findings from this survey show that many participants may move between severe and moderate levels throughout the course of the illness, most gradually getting more unwell and restricted over the years, whilst others improve and a small percentage recover. We noted that many survey respondents self-classify as moderate, that we excluded in our analysis, who may fall into the severe category – we suspect that these patients do not wish to self-identify as 'severe ME/CFS' and retain a level of optimism about their illness status. There are no simple methods available to clinicians or patients to assess illness severity. Research tools such as the *DePaul Symptom Survey* of the *Chalder Fatigue Scale* do not specifically measure illness severity. There is a need for development of a severity scale for ME/CFS.

ME/CFS may be hard to diagnose and is largely defined by generalised fatigue, a characteristic of many other chronic illnesses, idiopathic complaints and is also associated with affective disorders such as depression. Severe ME/CFS patients arguably represent the clearest cohort of 'ME/CFS' cases. These patients experience most of the cardinal symptoms associated with the illness, such as fatigue, pain, sleep intolerance, malaise after minimal exertion, intolerance to light or noise, and cognitive complaints. From our survey, we found that severe sufferers are often socially isolated, are unable to work, or reduce work to part-time or less, often discontinue in education, although with a mean age of 34 years in ME/CFS onset in our survey and a mean age of 45 years in other studies of severe ME/CFS (Pendergrast et al., 2016), many participants have completed third level education before the illness begins. Many severe participants report mental health complaints, such as depression and anxiety, co-morbid to ME/CFS. However, the Pendergrast et al. international study of severe ME/CFS cohorts revealed no significant differences in prevalence rates of comorbid psychiatric conditions (major depression, bipolar disorder, anxiety, schizophrenia, eating disorders, and substance abuse) between individuals who were housebound and those who were not housebound – a surprising finding given differences in social isolation and symptomology associated with severe illness presentation.

Severe sufferers within the wider ME/CFS population, represent the most challenging cases of the illness, particularly for community physicians to manage in primary care. Expert knowledge and careful consideration are needed to engage these patients, yet many studies reveal that many GPs lack training on the illness and lack of confidence in dealing with these patients (Raine et al., 2004). GPs also hold certain value-judgements about these patients, that they are difficult to treat or are combative (Raine et al., 2004).

2.10.2 Their call for recognition and support

Findings from this survey reveal concern among participants that doctors and allied health and social care professionals do not understand their illness or acknowledge their suffering. Many participants report not feeling believed, feeling vulnerable, and having to battle doctors for support, including home visits, referrals to specialist care or with social care applications. This is particularly noteworthy, given ME/CFS patients experience extreme fatigue, emotional fragility and cognitive complaints. Such problems with care and support have been identified in previous reports on ME/CFS (Group, 2002; NICE, 2007). Given that severe patients have lower quality of life scores compared with many other serious chronic health complaints and illnesses, such as multiple sclerosis or diabetes, there is a need to bridge the support gap that currently exists.

The present study provides a snapshot insight into a combative and acrimonious relationship that exists between a portion of severe ME/CFS patients and their doctors. Patients report difficulties getting a diagnosis and suffering severe symptoms for long periods without medical intervention. Previous research has demonstrated that a good relationship with general practitioners from the onset of the illness is essential for avoiding progression to severe presentation of the illness (Pheby and Saffron, 2009) and that getting a diagnosis is the single most helpful event in managing the condition (Drachler Mde et al., 2009), yet current levels of knowledge of ME/CFS among doctors and allied health workers appears inadequate and a cause of ongoing concern and distress for sufferers.

2.10.3 Accessing care and the needs gaps

Patients with severe ME/CFS experience more symptoms, to a higher intensity and for prolonged periods, compared with mild and moderate patients. Unsurprisingly, those patients within the severe category have worse prognosis for recovery. Severe patients may have the greatest need for medical support and intervention but often have the greatest trouble accessing this support, given their housebound status, pain and fatigue symptomology – an classic example of the inverse care law (Tudor Hart, 1971). Our findings mirror those of a survey by patient charity Action for ME that revealed that less than 50% of bedridden patients are monitored by a medical practitioner and 60% are often too unwell to travel to a clinic, yet many GPs refuse home visits. This survey confirms that severe ME/CFS patients have problems accessing both primary care support and specialist care. Despite early management of the illness being an important factor in preventing onset of severe presentation (Pheby and Saffron, 2009). Severe patients also find it physically and emotionally difficult to access all available care, whether medical, psychological, or social. Many participants reported relying on family members, friends and carers for support.

2.10.4 Severe patients absent from research studies

Severe ME/CFS patients are often absent across the majority of research studies on this illness. It is noteworthy, that being bedbound or housebound precludes most severe sufferers from taking part in research studies, whether that be exercise physiology studies or clinical trials of psycho-behavioural therapies. The largest conducted randomised controlled trial of CBT and GET (PACE) required patients to attend multiple therapy sessions in a clinic setting (White et al., 2011). Such trials require ambulatory patients well enough to attend. Wearden et al. attempted to overcome this problem by delivering a combination of CBT and GET to patients at home via practice nurses, but this trial reported much lower levels of benefit (Wearden et al., 2010) using such therapies. We had a strong response to our survey call and received many emails from patients. We found that severe sufferers are keen to get involved in research but are often ignored, meaning patient surveys are often their only avenue to communicate their needs.

2.10.5 Problems with diagnosis

Despite published guidelines for medical professionals to follow to diagnose ME/CFS (Baker and Shaw, 2007), the literature shows that diagnosis remains a challenge for medical professionals and patients often have to wait long periods for a confirmatory diagnosis. Bansal et al. suggest that the ubiquity of general fatigue as a presenting complaint in general practice (around 30% of patients experience some fatigue) makes it difficult for UK GPs to differentiate idiopathic fatigue or fatigue related to other common health complaints from the illness ME/CFS (Bansal, 2016). UK doctors may employ the Oxford Criteria (Sharpe et al., 1991) and/or NICE guidelines (NICE, 2007) to aid in making a diagnosis. The absence of biomarkers to identify ME/CFS means it remains an illness of exclusion diagnosed clinically. This may partly explain why diagnosis is often delayed with an average of 2 years in our study, but this average is much longer than current diagnostic guidelines of 4-6 months after the onset of core symptoms (NICE, 2007). Diagnostic delays may also be caused by doctors, particularly GPs, lacking knowledge of the illness, challenging patients on the origins and severity of their symptoms, denying accommodations such as home-visits and combative doctor-patient relationships.

2.10.6 What patients say helps, what doesn't and what they want

Many of our respondents were too unwell to participate in treatments such as cognitive behavioural therapy (CBT) or graded exercise therapy (GET). However, for those who undertake such therapies, few participants reported significant benefit from such therapies. Many participants state that psycho-behavioural treatments are inappropriate, particularly GET. A large proportion report that GET causes a worsening of symptoms. This finding runs contrary to evidence from clinical trials that report few adverse outcomes with GET (Dougall et al., 2014). However, as we noted above, patients with severe ME/CFS status are often absent from clinical trials. A small percentage of patients state that CBT helps with the psychological stresses that comes with chronic illness.

The greatest proportion of our patient cohort state that pacing therapies help most often, but mainly to ameliorate symptoms or prevent deterioration – most severe patients report little change in their illness status over the long-term. This finding may fit with Jason's Envelope Theory (Jason et al., 2013), of staying within energy limits until stronger. This may be particularly useful for severe sufferers. However, a question does arise as to how doctors and allied health professionals, particularly physiotherapists and occupational therapists, can support these patients in moving limbs and avoiding deconditioning. Long periods of confinement to the home will result in profound loss of physical conditioning and other problems, physical and psychological. There may be a need to develop tailored exercise or movement programmes other than GET, given many patients report problems with GET, perhaps some form of supportive physiotherapy as described by patients in '*Participants' experiences of management and treatment of ME/CFS*' p23-24.

Many patients report having tried alternative therapies, but again the majority report that these treatments only help manage symptoms. Many of our survey cohort recognise that anxiety and depression are common mental health complaints that can arise during the course of their illness, but many are unwilling to seek help with these complaints because they believe the medical profession views ME/CFS as a predominantly psychological illness and disclosure of mental health complaints might bias their doctors views of the illness. GPs should consider alternatives to CBT only for dealing with mental health complaints in ME/CFS.

Many severe participants mention the need for home-based visits with GPs, tele-calls with GPs and hospital specialists, as very important to them. GPs and hospital-based staff should consider using such technologies with these patients. Patients also talk about the need for specialist follow-up and monitoring, and support with symptoms, particularly orthostatic intolerance (often called POTs).

The importance of social support, in all its forms, home care assistance, support from family and friends, occupational therapy, support from local and national agencies with disability benefits and mobility aids – emerged as an important theme in our study. We found that many severe ME/CFS patients join patient support groups, but not all join national groups; many participate in online forums and local patient groups. Almost all of our sample claimed disability or social care benefits, but a large number recount difficulties in accessing such benefits. Many patients want doctors to do more to support them with their claims, including providing medical evidence and letters of support.

Blease et al. wrote about how ME/CFS patients often feel a sense of injustice, both epistemic and hermeneutic, that their illness is not understood and they feel unsupported. We detected patient frustration at not being believed and having their symptoms dismissed. We believe doctors could do more to support patients and small changes in patient management and doctor-patient communication might overcome many of the issues we identified.

2.10.7 Building better doctor-patient relationships with severe ME/CFS patients

Severe ME/CFS patients wish to be treated with dignity, respect and empathy. Many report difficult and distressing experiences with doctors and other health and social care professionals. There is a lack of understanding of the illness and often a lack of empathy for the patient and their plight. Empathy is important in building effective doctor-patient relationships and has been shown to improve outcomes, particularly in general practice (Derksen et al., 2013). Empathy lowers patients' anxiety and distress and delivers significantly better clinical outcomes (Derksen et al., 2013), and given anxiety and distress are common complaints for severe ME/CFS patients, doctors must do more to avoid causing or adding to patients' distress. All ME/CFS sufferers are at enhanced risk of suicide (Roberts et al., 2016), but severe ME/CFS sufferers are particularly vulnerable to severe depression and suicide given they experience the highest levels of social isolation and debilitating symptoms, therefore health professionals need to take extreme care in communicating with and managing these patients.

Many severe patients become 'expert patients' and attempt to inform their GP or specialist, however whilst some doctors form good relationships with their patients, others fail to engage these patients. Raine talks about how GPs often lack confidence in dealing with ME/CFS patients and how they view these patients as challenging and combative (Raine, 2004). GPs and other health professionals clearly need more training on the illness and face-to-face patient exposure, particularly within patients' homes to see the impact the illness has on people with severe ME/CFS. Participants in our survey consistently stated that doctors need to stay abreast of the latest developments in ME/CFS research.

2.11 Study strengths and limitations

One of the main strengths of this study is that is has been carried out by an experienced team of professional researchers with expert knowledge of myaglic encephalomyelitis/chronic fatigue syndrome and clinical experience. Our research team included two medical doctors and a nurse. The objectives and methods applied throughout are clearly specified, and thus enhance the reliability and credibility of findings. Given that other studies reported difficulties in recruiting and engaging patients with severe ME/CFS, such as poor response rate reported by Newton and colleagues at Newcastle (Strassheim et al., 2018) or high time and cost demands reported by Lacerda and colleagues at LSHTM (Lacerda et al., 2018), our study opted for a survey methodology that allowed us to engage severe ME/CFS patients within a short timeframe and the accessibility of a survey enhanced our response rate, we had far more responses than required, in excess of 340 in under 1 week. Our survey method also minimised input requirements on the part of respondents compared to face-to-face interview with a home visit.

Our study has some inherent limitations. First, the use of a survey questionnaire as a data collection instrument may exclude very severe participants who are too unwell to complete such surveys. We attempted to overcome this limitation by instructing respondents to seek the assistance of family members, friends or care assistants, to complete the survey. Surveys of this kind are open to response bias. Patients who have recovered from ME/CFS or who have moved from severe to moderate or mild symptoms might be unwilling to engage in such studies. There is also a risk that patients with negative experiences of medical care are more likely to participate then those with positive experiences, however this factor applies to all such patient experience research. We attempted to overcome such bias by advertising our survey via social media to widen participation beyond patient advocacy group members. We emphasized that responses would remain confidential and we were careful not to encourage negative responses by using neutrally framed semi-structured and open-ended questions that allowed respondents to give a full account of their views and experiences, both positive and negative.

We did not obtain confirmation of ME/CFS status by independent medical professional assessment, instead we relied on respondents to attest to their ME/CFS. This is common practice in this field, given it is often too costly and time consuming to medically screen every patient for a confirmatory diagnosis. However, respondents in our survey had to confirm if they had an ME/CFS diagnosis from a medical professional. Respondents who did not, were excluded from our analysis.

Another potential bias within our survey concerns the self-rating of 'severe ME/CFS'. It was not feasible within the remit of our study to measure the severity levels of each respondent's illness. Indeed, measuring the severity of ME/CFS is inherently difficult given the lack of biomarkers or guidelines to assess severity. To avoid complexity, we opted to allow participants to self-rate as 'severe', however we did structure questions in order to explore severity factors, such as asking participants if they were housebound or not, if they could or not and so on. We found that a large percentage of patients self-classified as 'moderate' who may well meet a 'severe' categorisation. For example, some moderate respondents stated they were housebound and spent most of the day in bed. However, we excluded these patients due to their 'moderate' self-classification, but they could perhaps have been included. As we had enough responses with clear severe status to analyse, exclusion of moderate participants has no impact on our findings, but it does reveal that patients' severity status is highly subjective and patients may be poor judges of their actual functional status. Finally, our thematic analysis of responses is open to selection or interpretation bias. We sought to minimise such bias by using two independent researchers to extract and analyse data, overseen by a senior academic. We also included direct quotations from patient respondents alongside data and themes identified and presented.

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3 Drawing on the report to inform the recommendations

A member of the NGC technical team presented the findings of the report to the committee and 1 member of the research team was available on the telephone to answer questions from the committee. The committee had received the study report two weeks before the meeting. The themes that emerged from the report were taken into consideration alongside other identified evidence when drafting recommendations. This was the most applicable evidence for a number of topics and influenced the recommendations directly. Where relevant this is referenced in the committee discussions of the evidence reviews.

4 The committee's overview of the research

The committee assessed the report and agreed it is a valuable report providing information on a population that are very difficult to identify and access. The lay committee members noted that the report findings that reflected their own experiences and is reflective of other surveys seeking the views of people with severe ME/CFS.

Although the limitations of the research are described well in the report the committee noted the additional points:

- the sample was a self-selected group
- the diagnosis of ME/CFS and severity of the condition was self-reported. The definition of severe could be different for different people making it difficult to attribute a commonality to the results
- people with very severe ME/CFS are unlikely to have participated. The committee recognised the difficulties with recruiting and researching people with severe ME/CFS.
- the empirical basis for the project was not clear. The methodology was described as qualitative and a survey and a mixed methods approach was described in the results with limited qualitative analysis
- it isn't clear who had therapies, what therapies they had, or when or where these where implemented and the relationship to their symptoms at the time. This made it difficult for the committee to attribute any positive or negative effect to the therapies mentioned in the report.
- the research team were restricted by the areas of the scope and the time to conduct the research, This did not allow for deeper probing and questioning potentially missing some important issues.
- the survey could be completed with assistance from a family member/carer. The committee recognised and supported the rationale for this, but also acknowledged that it may have influenced the responses.
- issues of sample size and data saturation were discussed in relation to qualitative interview studies, but there was no clear rationale for the sample size selected for the design that was used.

This was taken into account when considering the findings of the research.

Appendix A: Research guide and questionnaire

Scope area	Review questions	Area to be explored in interviews/questionnaires with people with severe ME
Identification and assessment before diagnosis	• What are the most clinically effective and cost effective precautionary management strategies that should be adopted while being assessed for a diagnosis of ME/CFS? • In people with suspected ME/CFS, what are the criteria used to establish a diagnosis? • What are the barriers and facilitators to the diagnosis of ME/CFS?	Experience of : • Initial illness ○ Being believed • Initial illness and impact on life (including family, friends, school, college, university, work) • Initial contact with a health and social care professional about symptoms • What worked well • What didn't work well
	Questions	1. At what age were you first diagnosed? 2. How long have you had ME/CFS? 3. Have you received a firm diagnosis of ME/CFS? 4. - Was this from a GP, specialist or other - specify? 5. How long did it take you to get a diagnosis? 6. Did your illness start suddenly, or gradually worsen over time? 7. What was your experience of getting a diagnosis (please detail)? 8. What factors do you feel helped you get a diagnosis? 9. Did any factors delay your diagnosis? 10. Did your primary care doctor/GP agree with a diagnosis of ME/CFS and offer you appropriate support? 11. Is your illness relatively stable, have you experienced any periods of improvement or remission? 12. Would you classify yourself as mild, moderate or severe ME/CFS currently? 13. Did or does your illness prevent you from: 14. …Attending school or college/university/training or work? 15. …Participate in social events? 16. Are you able to get outside your home to shop or undertake outside activities? 17. Do you receive support from family members? 18. Do you have a carer or care assistant? (how often per week)

Diagnosis of ME/CFS	• What are the predictive accuracies of specific tests, or clinical symptoms/signs, to identify people who will subsequently be given a definitive diagnosis of ME/CFS? • In people with suspected ME/CFS, what are the criteria used to establish a diagnosis? • What are the barriers and facilitators to the diagnosis of ME/CFS?	Experience of : • Continuing illness and severe ME/CFS • Continuing illness and impact on life (including family, friends, work, college, university) • Contact with health and social care professionals to get a diagnosis, approach taken • Time to get a diagnosis • What worked well • What didn't work well
	Questions	Above
Management of ME/CFS	• What is the clinical and cost-effectiveness of pharmacological interventions for people with ME/CFS? • What is the clinical and cost-effectiveness of non-pharmacological interventions for people with ME/CFS? (includes self-management strategies) • In people with ME/CFS, what is the clinical and cost-effectiveness of different models of multidisciplinary care? • What are the barriers and facilitators to the care of people with ME/CFS? (will include access to care)	Experience of: • Interventions (benefits and harms) o For ME/CFS and symptomatic relief o Outcomes: benefits and harms o If offered interventions have not been taken up, why • Contact with health and social care professionals and services o Are your basic needs met? o Co-ordination of care o Referral to specialists o Hospitalisation o Involvement in decision making ▪ Feelings of control and choice o Access to services ▪ Access to appointments and getting to appointments (distance to clinics) ▪ Home visits ▪ Support services (mobility aids) • What worked well o Experience of recovery if appropriate o Experience of reintegration if appropriate (for example, work, friendship groups) • What didn't work well o Experience of relapse
	Questions	19. Have you been prescribed any drugs by your doctor or a specialist specifically for your ME/CFS or related symptoms – list? 20. Have these helped improved symptoms? – please specify 21. Have you been offered any other treatments for your illness? - Cognitive Behavioural Therapy (CBT) - Graded Exercise Therapy (GET)

		- Pacing Therapy (Adapted Pacing Therapy – APT) - Physiotherapy - Other therapies (please specify) 22. For each treatment or therapy undertaken, please detail if this therapy helped, made no difference, or made symptoms worse? 23. Have you ever refused to undertake a specific therapy or treatment (please specify which ones and your reasons for not undertaking)? 24. Have you ever required specialist support such as tube feeding, IV fluids, speech therapy, - please list? 25. Have you ever tired any alternative treatments or therapies (not offered by your doctor or the NHS) y/n – please specify which ones? E.g. massage, supplements, psychotherapy, and so on. 26. Did any of these alternative treatments or therapies help improve your symptoms, did any make things worse? 27. Does your GP visit you at home, if you are unable to attend a GP practice/surgery? 28. Are you able to attend hospital appointments or appointments with specialists? 29. Do GPs/specialists offer any alternative arrangements if you are unable to attend? 30. Are hospital staff aware of your condition and do they accommodate your needs on hospital visits? 31. Have you had any hospital in-stays – how many per year or since you developed the illness? 32. Do you make decisions about your care, do you feel you are able to make choices about the types or care you receive? 33. Do doctors consult you and take your views on board during treatment? 34. Have you had any support form a social worker/social services? 35. What type of support or care do you receive from them? 36. Did you receive any Government disability of sickness benefits? 37. Do you use mobility aids or a mobility scooter? 38. Have you encountered any difficulties in accessing social care and or sickness benefits – please specify any issues? 39. Has your illness and symptoms remained relative stable or changed since it began – specify if it has remained relatively the same, has worsened over time, has improved over time, or fluctuates frequently? 40. Have you been able to return to work, study if prevented to previously? 41. Have you received any special medical or social care assistance that has helped you undertake work or education/training?

		42. Have you been able to take part in social activities recently if prevented previously? 43. What types of medical or social support have been most useful to you in managing your illness - please specify?
Monitoring and review	• What is the most clinically and cost-effective method of monitoring/reviewing people with ME/CFS? • What are the barriers and facilitators to the care of people with ME/CFS? (will include access to care)	Experience of : • Continuing care • Follow up Who does this? Information about prognosis or future planning
	Questions	44. Is your ME/CFS regularly monitored by either a GP or hospital specialist, if so who and how often? 45. Do you feel your illness receives adequate ongoing medical support? 46. What more do you feel your doctors or care support workers could do to assist you living with ME/CFS?
Information, education, and support for people with suspected or diagnosed ME/CFS and their families and carers	• What information, education and support do people with ME/CFS and their families and carers need? • What information, education and support do people with suspected ME/CFS and their families need before formal diagnosis?	Experience of : • Accessing information, education and support ○ What was useful and what wasn't ○ Information and support networks
	Questions	47. Do you feel there is enough information or educational material available relating to your illness? 48. How accessible is this information or educational material? 49. Where did you go to get or access information or educational material – please detail? 50. Are you a member of an ME/CFS patient organisation or support group – please detail which ones? 51. What information or educational material have you found most useful to you in dealing with your illness? 52. Is the material you used tailored for your needs? 53. Is there material available tailored to family members and carers?
Information, education and support	• What information, education and support do health and social	Experience of : • Knowledge of the health and social care professionals

for health and social care professionals.	care professionals who provide care for people with ME/CFS need? • What are the barriers and facilitators to providing information, education and support for health and social care professionals?	○ Where do you think they get information from • Health and social care professionals attitude to ME/CFS • Do they have the ability to provide support and what has been useful
	Questions	54. Is or was your primary care doctor or hospital specialist knowledgeable about ME/CFS – please detail? 55. If you feel their knowledge or awareness was lacking in any way, what could be done to improve raising awareness of the illness among health and social care professionals? 56. When visiting your GP or hospital were you able to convey any special needs or requirements to staff, were these needs accommodated e.g. quiet area, short waiting time, and so on? 57. Were you treated with respect and empathy/understanding by health and social care professions – please detail any response? 58. What do health and social care professionals need to specifically take into account when dealing with patients with severe ME/CFS – please detail any response? 59. Is there any other relevant information you wish to share that is not covered in the questions above – please feel free to detail in this section?

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Appendix B: Consent form

UoM Participant Consent Form

This research project is compliant with the GDPR (General Data Protection Regulation) and the Data Protection Act 2018.

Title of Research

Involving adults with severe ME/CFS symptoms in developing a NICE guideline on Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management

If you are happy to participate please complete and sign the consent form below

	Activities	Initials
1.	I confirm that I have read the attached information sheet (study information sheet version 1, 1st Oct 2019) for the above study and have had the opportunity to consider the information and ask questions and had these answered satisfactorily.	
2.	I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving a reason and without detriment to myself. I understand that it may not be possible to remove all of the data I provide, from the project once it has been anonymised and forms part of the data set or a report. I agree to take part on this basis.	

3.	I agree that any data collected may be published in anonymous form in academic books, reports or journals.	
4.	I understand that data collected during the study may be looked at by individuals from The University of Manchester or regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data	
5.	I agree that any anonymised (that does not identify me) data collected as part of this study may be shared with researchers at other institutions.	
6.	I agree that researchers from Manchester or given permission by the research team running this study may contact me in future about other research projects. (this is not expected but we are asking just in case there is ever a need to contact you in future)	
7.	I agree that the researchers may retain my contact details in order to be able to remove me from the study if I change my mind regarding my participation.	
8.	Where I have assistance filling in my answers to questions in the survey, this will be indicated.	
9.	I understand that there may be instances where during the course of the study information or data is revealed which means that the researchers will be obliged to break confidentiality and this has been explained in more detail in the information sheet.	
10.	I agree to take part in this study.	

Data Protection

The personal information we collect and use to conduct this research will be processed in accordance with data protection law as explained in the Participant Information Sheet and the Privacy Notice for Research Participants.

_____ _____ _____

Name of Participant Signature Date

_____ _____ _____

Name of the person taking consent Signature Date

[Consent forms will be securely kept at the University of Manchester. Online version consent forms will be electronically stored, whereas hardcopy consent forms will be stored in our secure offices at the University.]

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Appendix C: Participant information sheet

University of Manchester
Research Participant Information Sheet

Title of Research

Involving adults with severe ME/CFS symptoms in developing a NICE guideline on Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management

You are being invited to take part in a research study to explore the views and needs of patients with severe ME/CFS. This project has been commissioned by the National Institute of Health and Care Excellence (NICE). Before you decide whether to take part, it is important for you to understand why the research is being conducted and what it will involve. Please take time to read the following information carefully before deciding whether to take part and discuss it with others if you wish. Please ask if there is anything that is not clear or if you would like more information. Thank you for taking the time to read this.

About the research

- Who will conduct the research?

The project is being led by Dr. Keith Geraghty, working with colleagues at the University of Manchester Centre for Primary Care.

- What is the purpose of the research?

The purpose of the study is to explore the needs of patients with severe ME/CFS. Our wish is to better understand the needs and views of patients with severe ME/CFS presentations and to provide NICE with up-to-date information that might help inform the NICE Guideline Committee as they undertake a review of treatment guidelines for this illness. We plan to recruit a selection of patients, in the time period available to us between October 2019 and November 2019 and to write up a report based on our findings that we will pass to NICE at the end of the project.

- Will the outcomes of the research be published?

We also hope to publish a research paper from this project.

- Who has reviewed the research project?

This project has been reviewed by The University of Manchester Research Ethics Committee (September 2019).

- Who is funding the research project?

The National Institute of Health and Care Excellence

What would my involvement be?

- What would I be asked to do if I took part?

We are asking people with severe ME/CFS to take part in this study. This involves completing a short online survey. We anticipate that the survey will take you between 30 minutes to 1 hour to complete, however you may not want to do this in one sitting if it makes you feel unwell or aggravates your symptoms. We advise that you pace yourself and complete the survey in your own time. A family member or carer can assist you if needed. The survey will ask you a range of short questions about your illness, your care needs and your experiences of accessing health and social care.

- Will I be compensated for taking part?

We are not offering any compensation for taking part as we do not have funding for this. We greatly appreciate your participation in this project.

- What happens if I do not want to take part or if I change my mind?

It is up to you whether or not you decide to take part. If you decide to take part, you will be given this information sheet and a consent form to sign (confirm you agree). You can contact us at any stage if you do not wish to take part of if you wish to withdraw from the study. However, it will not be possible to remove your data from the

project once it has been anonymised as we will not be able to identify your specific data. This does not affect your data protection rights. If you decide not to take part, you do not need to do anything further.

Data Protection and Confidentiality

- What information will you collect about me?

In order to participate in this research project we will need to collect information that could identify you, called "personal identifiable information". Specifically we will need to collect:

- Your name
- Age
- sex
- How long you have suffered from ME/CFS
- Other less identifiable information

- Under what legal basis are you collecting this information?

We are collecting and storing this personal identifiable information in accordance with data protection law which protect your rights. These state that we must have a legal basis (specific reason) for collecting your data. For this study, the specific reason is that it is "a public interest task" and "a process necessary for research purposes".

- What are my rights in relation to the information you will collect about me?

You have a number of rights under data protection law regarding your personal information. For example, you can request a copy of the information we hold about you. If you would like to know more about your different rights or the way we use your personal information to ensure we follow the law, please consult our Privacy Notice for Research.

- Will my participation in the study be confidential and my personal identifiable information be protected?

In accordance with data protection law, The University of Manchester is the Data Controller for this project. This means that we are responsible for making sure your personal information is kept secure, confidential and used only in the way you have been told it will be used. All researchers are trained with this in mind, and your data will be looked after in the following way:

Important note: UoM requires identifiable data to be anonymised as soon as the objectives of the project allow. The standard retention period for data once anonymised is 5 years unless funders or regulators have specified longer retention requirements.

Only the study team at The University of Manchester will have access to your personal information, but they will anonymise it as soon as possible. Your name and any other identifying information will be removed and replaced with a random ID number. Only the research team will have access to the key that links this ID number to your personal information. Your consent form and contact details will be retained for 5 years (electronic copies will be securely kept at our University data storage facility and hardcopies will be kept in a locked office within our faculty building. Data may be transferred electronically between researchers on and off-site, however only data that has removed personal identifiers will be shared in this way. All data sharing will involve password protected files.

We have a duty of care to participants which includes breaking confidentiality if you disclose information that indicates that your health and well-being are at serious risk. In such cases we might share the relevant information with qualified medical and or social care professionals.

Data Sharing Requests from Other Parties (other than our research team):

When you agree to take part in a research study, the information you provide may be liable to data sharing requests from other researchers and interested parties. We will only share data that does not include any personal identifiers (such as your name or contact details). We will only share data if requesters can guarantee data security, with a plan for data storage. We will only share data if you have given consent to do so.

Opt-Out Reminder: You are able to opt out of this study within 2 weeks after you complete the online survey. After this time your data may form part of a report or dataset that cannot be changed. You can have your personal details deleted at anytime. We will retain your contact details on a secure University server/storage facility in order to be able to remove you in future, if you so wish. This data will be kept for 5 years, before being destroyed/deleted permanently.

Please also note that individuals from The University of Manchester or regulatory authorities may need to look at the data collected for this study to make sure the project is being carried out as planned. This may involve looking at identifiable data. All individuals involved in auditing and monitoring the study will have a strict duty of confidentiality to you as a research participant.

What if I have a complaint?

You may contact any member of our research team at any time if you have a complaint or concern about your participation in this study or any other matter relating to this study. Email contact details are provided below.

CONTACT DETAILS FOR COMPLAINTS:

Dr. KEITH GERAGHTY or Prof. ANEEZ ESMAIL (Project principal investigator and Project lead)
Email:keith.geraghty@manchester.ac.uk
Email: Aneez.esmail@manchester.ac.uk
Tel: +44(0) 161 306 3990

If you wish to make a formal complaint to someone independent of the research team or if you are not satisfied with the response you have gained from the researchers in the first instance then please contact TheResearch Governance and Integrity Officer, Research Office, Christie Building, The University of Manchester, Oxford Road, Manchester, M13 9PL, by emailing: research.complaints@manchester.ac.uk or by telephoning 0161 275 2674.

If you wish to contact us about your data protection rights, please email dataprotection@manchester.ac.uk or write to The Information Governance Office, Christie Building, The University of Manchester, Oxford Road, M13 9PL at the University and we will guide you through the process of exercising your rights.

You also have a right to complain to the Information Commissioner's Office about complaints relating to your personal identifiable information Tel 0303 123 1113

CONTACT DETAILS:

If you have any queries about the study or if you are interested in taking part then please contact the researcher(s)

Dr. KEITH GERAGHTY or Prof. ANEEZ ESMAIL(Project principal investigator and Project lead)
Email:keith.geraghty@manchester.ac.uk
Email: Aneez.esmail@manchester.ac.uk
Tel: +44(0) 161 306 3990

Appendix D: Abbreviations

CBT	cognitive behavioural therapy
CCBT	computerised cognitive behavioural therapy
CDC	Centers for Disease Control
CFS	chronic fatigue syndrome
CI	confidence interval
CMO	Chief Medical Officer
DoH	Department of Health
EBV	Epstein–Barr virus
ECG	electrocardiogram
ESA	employment support allowance
GDG	Guideline Development Group
GET	graded exercise therapy
GRP	Guideline Review Panel
HCP	healthcare professional
LSHTM	London School of Hygiene and Tropical Medicine
ME	myalgic encephalomyelitis or myalgic encephalopathy
ME/CFS	Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome
MRI	magnetic resonance imaging
NCC-PC	National Collaborating Centre for Primary Care
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NSAID	non-steroidal anti-inflammatory drug
PCT	Primary Care Trust
PIP	Personal Independence Payment
PIS	Participant Information Sheet
PVFS	post-viral fatigue syndrome
QALY	quality-adjusted life year

QoL	quality of life
RCGP	Royal College of General Practitioners
RCT	randomised controlled trial
SG	support group
SMC	standard medical care
SSRI	selective serotonin reuptake inhibitor
UC	Universal Credit

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