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Research priorities for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): the results of a James Lind alliance priority setting exercise

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ABSTRACT

Objective: To identify research priorities of people with myalgic encephalomyelitis / chronic fatigue syndrome (ME/CFS) and those who support and care for them.

Method: Using the James Lind Alliance's protocols, online surveys and workshops were held. The first survey asked participants from the U.K. to submit research questions about ME/CFS which were important to them. In the second, participants prioritised frequently submitted questions from the 1st survey. These were short listed and then workshop discussions were held to reach consensus on the top ten research priorities.

Results: 1565 participated in the 1st survey and 5300 research priorities were submitted. 1752 participated in the 2nd. In both surveys, the predominant demographic was white, middle-aged women with ME/CFS. 15–17% were family/carers of people with ME/CFS and 4–6% were health and social care workers. From the 1st survey, 59 summary questions were identified. These were prioritised and short listed to 18 questions. Of these, the top 10 covered 1. Post-exertional malaise, 2. Use of existing drugs for other conditions, 3. Diagnosis, 4. Autoimmunity, 5. Sub-types, 6. Post-infective cause, 7. Neurological symptomology, 8. Genetics, 9. Severe ME/CFS, 10. Mitochronical dysfunction and 10 (equal) Oxygenation dysfunction.

Conclusion: People with ME/CFS, their families and carers, and health care professionals worked together to identify, for the first time, the research priorities for ME/CFS. These focus on the biomedical causes of ME/CFS and how to diagnose, treat and manage it. Researchers and funding bodies should consider these in their plans for future research.

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ME/CFS is a long-term (chronic), fluctuating, neurological condition that causes symptoms affecting many body systems, most commonly the nervous and immune systems. The illness has been classified as a neurological disease by The World Health Organization since 1969 [1]. It is estimated to affect over 250,000 people in the U.K., and around 17 million people worldwide, regardless of ethnicity, or socio-economic background [2,3]. Most (70–80%) of people with ME/CFS are women. People with ME/CFS experience physical and/or mental exhaustion associated with post-exertional malaise (symptoms caused or exacerbated by physical, mental or emotional effort, which can be delayed). Common other symptoms include pain, cardio-vascular and gastrointestinal problems, sensory impairments and sleep disorders[3,4] . A key feature is that symptoms tend to fluctuate and the onset of post-exertional malaise can be delayed for several days after the triggering activity [4,5]. ME/CFS can have a highly disabling impact on people's everyday lives [6]. A quarter are severely or very severely affected, leaving them housebound, or even bedbound. The economic cost of ME/CFS in the U.K. is estimated to be several billion/year [6]. Quality of life of people with ME/CFS is lower than many other disabling chronic conditions [7]. As a poorly understood condition, there is no definitive diagnostic test, no cure and no universally effective treatments [5]. Consequently, it is unclear how best to support people with ME/CFS and families/carers to manage the condition and there is little evidence to inform clinical services.

Historically, ME/CFS has faced significant under-investment in research, particularly when compared to other severe disabling conditions. For example, funding for research into Multiple Sclerosis (MS) is about 20 times greater than ME/CFS despite MS being far less common [8]. There is a clear need for more research into ME/CFS to address gaps in our knowledge and this has been recognised by Government [9]. Thus, following discussions within the U.K.'s ME Research Collaborative (MERC), and their Patient Advisory Group, the charity Action for ME obtained funding to undertake a James Lind Alliance Priority Setting Partnership as a first step to address this inequity by identifying the research priorities that matter to people with ME/CFS, their families/carers and health care professionals. Action for ME was the grant holder and provided administrative and communications support to the project.

Method

The James Lind Alliance's well-established methodology was followed [10] with adaptations as necessary to accommodate the needs of people with ME/CFS. Firstly, a 'seed' steering group of representatives from the ME Research Collaborative's Patient Advisory Group and other groups promoting and supporting research into ME/CFS (Action for ME, Science for ME and Forward ME) was established. They selected people who responded to advertisements on social media and in print via U.K. ME/CFS charity and support groups' websites and newsletters to make up the main project steering group. Professional bodies such as the British Association of Clinicians in ME/CFS were contacted to ensure representation by professionals. Applications were anonymised and ranked by the seed steering group to ensure balanced representation.

The steering group then established the scope of the priority setting exercise. It included causes, effects, diagnosis, prevention, management and treatment. It excluded chronic fatigue caused by other conditions and studies of ME/CFS using the Oxford Criteria [11], NICE 2007 criteria [5] or Fukuda Criteria [12] without post-exertional malaise as a mandatory criterion.

The first stage of data collection was a survey to identify research ideas that matter to stakeholders. It was open to people with ME/CFS, their carers and families, and health care professionals working with people with ME/CFS in the U.K. over a three-month period. It was publicised through the channels noted above plus the James Lind Alliance's website. People with very/severe ME/CFS were supported to participate by the 25% ME Group (a charity for people with very/severe ME/CFS). Respondents were asked to think about the impact of ME/CFS and what they would like research to find out. Responses were in free text format. Responses were reviewed by an independent information specialist using the James Lind Alliance's established procedures. She worked with a subgroup of the steering committee, comprising people with ME/CFS, carers and health care professionals to group responses so questions which addressed the same issue were summarised into one over-arching (or summary) question. Some responses included more than one question, and were split accordingly, while some unique questions were retained in their original format for inclusion in the next stage.

Then the research literature was searched to check whether the resultant summary research questions had been answered already. The James Lind Alliance considers that a research question has been answered if high quality, recent systematic review(s) addressing the research question have been published. Then a second survey (open for three months) using the same publicity strategies as above was undertaken to establish the highest priority research questions. Firstly, respondents selected all questions they judged to be important, and then reduced their selection to their top ten priorities. Then the most popular priorities were shortlisted for the final workshops by the steering group. Firstly, the top seven most frequently prioritised research questions for people with ME/CFS, carers/family and health care professionals were identified. This involved 11 questions (as there was overlap in the choices between groups). A further seven questions which had been frequently prioritised by people with very/severe ME/CFS and other under-represented groups (ethnic minorities, men, younger people, inhabitants of the devolved countries and people with a short duration of ME/CFS) were also selected.

Finally, the shortlist of research priorities was used during online workshops to decide the final top 10 research priorities (through discussion and ranking until consensus was reached). Attendees were purposively selected from respondents of the 2nd survey who volunteered to participate to ensure broad representation in terms of people with ME/CFS, their carers /families, professionals, severity of ME/CFS, age, gender, ethnicity and location. The James Lind Alliance's standard methodology is to hold a 1-day workshop to finalise the priorities. However, this was adapted to make the energy and cognitive demands more manageable for people with ME/CFS. The workshop ran over three days, with a maximum one-hour commitment on any day. Information and summaries were shared with the participants before and between workshops as an aide memoire, which would not normally be needed in a one-day event.

Results

Uptake for the surveys was strong. One thousand, five hundred and sixty-five responses were received for the first survey; 1332 (85%) of whom reported having ME/CFS. Approximately half were moderately severely affected ($n = 691$, 49%) and had been ill for 5–20 years ($n = 681$, 46%). Two hundred and seventy (17%) were family or carers; 89 (6%)

were health and care professionals and 24 (2%) were 'other'. Note, participants could respond to more than one category, e.g. they could be both a person with ME/CFS and a carer. Of participants who gave an answer, most were female ($n = 1287$, 83%), white ($n = 1462$, 95%) middle aged (45–64 years, $n = 654$, 43%) and lived in England ($n = 1222$, 80%). Of the health care professionals who stated their profession, the largest group were doctors ($n = 26$), including ten who specified they were a general practitioner. Further participants' details are found in Table 1.

Over 5300 research ideas were submitted. These were consolidated to 59 summary questions categorised as:

- Causes and prevention
- Diagnosis
- Lifetime risks and course of illness
- Treatment and management
- Underlying mechanisms and their treatments
- Health services
- Causes of symptoms and their treatments
- Social and psychological impacts and support

Further details are found in Table 2.

Table 1. Characteristics of respondents to the first and second survey.

	First Survey (n/%) n = 1565	Second Survey (n/%) n = 1752
How severe is your ME/CFS or the person you care for, at the	n = 1498	n = 1679
moment?	184 (12%)	194 (12%)
Mild	691 (46%)	821 (49%)
Moderate	520 (35%)	579 (34%)
Severe	74 (5%)	58 (3%)
Very Severe	29 (2%)	27 (2%)
In remission		
Approximately how long ago did you, or the person you care for,	n = 1496	n = 1684
first become ill with ME/CFS?	20 (1%)	32 (2%)
<1year	320 (21%)	313 (19%)
1–5 years	681 (46%)	789 (47%)
5–20 years	475 (32%)	550 (33%)
More than 20 years		
Age of the person with ME/CFS* (years)	n = 1506	n = 1693
Less than 25	168(11%)	157 (9%)
25–44	482 (32%)	631 (37%)
45–64	654 (43%)	706 (41%)
65 +	198 (13%)	192 (11%)
Prefer not to say	4	7
Health Care professionals (n)	n = 89	n = 86
Doctors	26	27
Occupational therapists	13	7
Psychologist/ counsellor	10	20
Nurse	10	6
NHS manager (including of ME/CFS services)	1	2
Social worker	5	0
Physiotherapist	5	5
Alternative health practitioner	5	2
Support worker	2	7
Other	12	10

*NB. Carers of people with ME/CFS responded with the age of the person they cared for.

Table 2. Summary questions in Survey Two.

CAUSE

C1	Is there a genetic link to ME/CFS? If yes, how does it affect the risk of ME/CFS in families? Could this lead to new treatments?
C2	Why do some people develop ME/CFS following an infection? Is it linked to long-covid?
C3	Is ME/CFS caused by a faulty immune system? Is ME/CFS an autoimmune condition?
C4	Are there factors that increase the risk of developing ME/CFS (such as stress, trauma or exposure to toxic chemicals)?
C5	Do hormonal imbalances (such as thyroid hormone or cortisol imbalances) cause ME/CFS and/or affect symptoms? Could this lead to new treatments?
C6	Can ME/CFS be prevented?
C7	Is ME/CFS infectious? Can it be transmitted to others?
C8	What causes ME/CFS to become severe?
C9	What can be learnt about the cause of ME/CFS from clusters of cases?

DIAGNOSIS

D1	How can an accurate and reliable diagnostic test be developed for ME/CFS?
D2	How can the current approach to diagnosing ME/CFS be improved, to reduce delays and include other conditions commonly linked to ME/CFS (such as POTS, EDS and MCAS)?

PROGNOSIS

P1	What is the typical course of ME/CFS over a lifetime, for children and adults? What influences this?
P2	Why do symptoms vary between people with ME/CFS? Why are there short term and long term changes in ME/CFS symptoms?
P3	Why are women at greater risk of ME/CFS than men?
P4	Are there different types of ME/CFS linked to different causes and/or how severe it becomes? Do different types of ME/CFS need different treatments and/or have different chances of recovery?
P5	How do some people recover from ME/CFS? How might this understanding help others?
P6	Do hormonal changes (such as during the menstrual cycle, pregnancy and menopause) affect ME/CFS symptoms in women? Does ME/CFS affect menstrual cycles, risks during pregnancy or menopause?
P7	Which conditions are commonly linked with ME/CFS (such as EDS, POTS, gut disorders and MCAS)? Do they have the same root cause or does one cause the other?
P8	What causes people with ME/CFS to relapse and their symptoms to get worse? Are there ways to prevent or minimise relapses?
P9	Does ME/CFS affect life-expectancy?
P10	Are people from ethnic minorities at greater risk of developing ME/CFS? What barriers do they face to getting a diagnosis and treatment?
P11	Are there long-term effects of repeated post-exertional malaise (symptoms caused by physical, mental or emotional effort, often with a delay)?

TREATMENT & CARE

T1	Based on people's experiences, what needs to be included in a long-term monitoring and follow-up care plan for people with ME/CFS?
T2	What causes sleep problems and sleep pattern changes in people with ME/CFS? How are these best managed and treated?
T5	Can prompt treatment and advice when diagnosed prevent ME/CFS from getting worse over time? What does this mean for people whose illness starts gradually?
T6	Does the immune system continue to over-function or under-function in some people with ME/CFS to cause symptoms? What does this mean for treatment and risks from infections and vaccinations, including with COVID-19?
T7	Which existing drugs used to treat other conditions might be useful for treating ME/CFS (such as low dose Naltrexone, or drugs used to treat POTS)?
T8	Do complementary and alternative therapies benefit people with ME/CFS?

BASIC BIOLOGY

B1	What causes ongoing fatigue (tiredness or exhaustion) in people with ME/CFS? How is this best treated and managed?
B2	What is the biological mechanism that causes post-exertional malaise (symptoms caused by physical, mental or emotional effort often with a delay) in people with ME/CFS? How is this best treated and managed?
B3	Are there changes in the central nervous system (brain and spinal cord) that cause ME/CFS symptoms?
B4	How are mitochondria, responsible for the body's energy production, affected in ME/CFS? Could this understanding lead to new treatments?
B5	What causes gut problems and difficulties with swallowing and eating in people with ME/CFS? How are these best managed, for example with tube feeding for people who are very severely affected?
B6	Do heart problems, changes to blood cells or blood/lymph circulation cause ME/CFS symptoms? If so, how is this best treated?

(Continued)

Table 2. Continued.

CAUSE

B7   What causes brain fog in people with ME/CFS? How is this best treated and managed?

B8   What happens to muscle function in people with ME/CFS?

B9   Do postural or structural problems in the head, neck and spine cause symptoms of ME/CFS? If so, how is this best treated?

B10   What causes pain in people with ME/CFS? How is this best treated and managed?

B11   What causes some people with ME/CFS to become intolerant to alcohol, chemicals and/ or medicines?

B12   What are the links between nervous, digestive and immune systems that could cause ME/CFS symptoms?

B13   What causes transport in and out of cells to be affected in people with ME/CFS? Could this understanding lead to new treatments?

HEALTH SERVICES

N1   What would be the make-up of a high-quality specialist service for people with ME/CFS? Would this improve the treatment and care of people with ME/CFS?

N2   Why don't some health professionals accept ME/CFS is a serious illness? What would help them to recognise and respond appropriately to people's symptoms?

N3   How can the needs of people with ME/CFS best be met when accessing and using health and social care services (for example while in hospital)?

MANAGEMENT

S1   How does ME/CFS impact on people's physical health, and does their physical health impact on their ME/CFS? What can people with ME/CFS safely do to maintain their physical health?

S2   Does changing diet or taking supplements help people with ME/CFS?

S3   Is there a way for people with ME/CFS to monitor and manage their activities (such as using a heart rate monitor) to avoid triggering post-exertional malaise?

S4   What causes sensory problems in people with ME/CFS (such as sensitivity to light, noise, smell and touch)? How are these best managed and treated?

S7   What causes nerve damage in the body in people with ME/CFS? How does this affect the autonomic nervous system causing symptoms such as orthostatic intolerance (e.g. feeling dizzy or unwell on standing or sitting up) or problems controlling body temperature? How is this best managed and treated?

S9   Are there ways to objectively measure how severely someone is affected by ME/CFS and whether their symptom levels are changing over time?

S10   Does poor delivery or use of oxygen within the body cause ME/CFS symptoms? If so, how is this best treated?

S11   Does continuing viral or bacterial infection cause ME/CFS symptoms? If so, are antivirals or antibiotics effective treatments?

S12   What causes headaches and migraines in ME/CFS? How are they best treated and managed?

S13   What causes skin problems in ME/CFS? How are they best treated and managed?

PSYCHOLGICAL AND SOCIAL IMPACT

Y1   What are the impacts of ME/CFS on people's quality of life, including work, finances and family and social life? What practical support would be most effective, particularly in terms of social care and welfare benefits?

Y2   What are the psychological impacts of ME/CFS? How are these best treated and managed?

Y3   What harms do people with ME/CFS experience as a result of the lack of professional recognition and stigma from the condition? How can these best be addressed?

Y4   What practical and emotional support do carers/ parents of people with ME/CFS need and how can these needs be met?

Y5   What support do pupils and students with ME/CFS need to help them in their education?

It was noted that many of the submissions were out of scope (as per the definitions of the process) but raised important issues. Many referred to the need for information about how to cope with ME/CFS, greater awareness and understanding from professionals, and the need for biomedical, rather than biopsychological research. These were collated to be used as the basis for information and publicity by the funding organisations.

Searches of the health literature showed none of the summary questions had been adequately answered. and all were included in the second survey. There were 1752 respondents to the second survey including 1464 (81%) people with ME/CFS, half of whom were moderately severely affected ($n = 821$, 49%) and had been ill for 5–20 years ($n = 789$, 47%). Two hundred and sixty-nine (15%) respondents were family/carers, 86 (4%) health care professionals and 20 'others'. Note, participants could respond to more than category. Of those who answered, most were female ($n = 1401$,

81%); white (*n* = 1633, 95%), middle-aged (aged 45–64 years, *n* = 706, 41%) and lived in England (*n* = 1407, 85%). Of the health care professionals who stated their professional background, the largest group were doctors (n = 27); seven of whom specified they were a general practitioner. Further details in Table 1.

One hundred and forty-seven people volunteered to take part in the workshops. Participants were selected using pre-determined criteria and their names blinded during the selection. Thirty-six were invited to take part, including 18 people with ME/CFS; nine family/carers and nine health care professionals. In total, the group represented a broad range of demographics, severity of ME/CFS and role. Thirty-five participated in the first workshop, 34 in the second and 33 in the final workshop. Drop-outs were due to illness or unforeseen circumstances.

The final research priorities were:

1. What is the biological mechanism that causes post-exertional malaise (symptoms caused or made worse by physical, mental or emotional effort, which can be delayed) in people with ME/CFS? How is this best treated and managed? [Underlying mechanisms and their treatments; Causes of symptoms and their treatments]
2. Which existing drugs used to treat other conditions might be useful for treating ME/CFS, such as low dose naltrexone, or drugs used to treat Postural Orthostatic Tachycardia Syndrome (POTS)? [Treatment and management; Underlying mechanisms and their treatments; Causes of symptoms and their treatments]
3. How can an accurate and reliable diagnostic test be developed for ME/CFS? [Diagnosis]
4. Is ME/CFS caused by a faulty immune system? Is ME/CFS an autoimmune condition? [Causes and prevention; Underlying mechanisms and their treatments]
5. Are there different types of ME/CFS linked to different causes and how severe it becomes? Do different types of ME/CFS need different treatments or have different chances of recovery? [Causes and prevention; Treatment and management; Lifetime risks and course of illness; Underlying mechanisms and their treatments]
6. Why do some people develop ME/CFS following an infection? Is there a link with long-COVID? [Causes and prevention; Underlying mechanisms and their treatments]
7. What causes the central and peripheral nervous systems (brain, spinal cord and nerves in the body) to malfunction in people with ME/CFS? Could this understanding lead to new treatments? [Causes and prevention; Treatment and management; Underlying mechanisms and their treatments; Causes of symptoms and their treatments]
8. Is there a genetic link to ME/CFS? If yes, how does this affect the risk of ME/CFS in families? Could this lead to new treatments? [Causes and prevention; Lifetime risks and course of illness; Underlying mechanisms and their treatments]
9. What causes ME/CFS to become severe? [Causes and prevention; Lifetime risks and course of illness; Underlying mechanisms and their treatments; Causes of symptoms and their treatments]
10. How are mitochondria, responsible for the body's energy production, affected in ME/CFS? Could this understanding lead to new treatments? [Causes and prevention; Treatment and management; Underlying mechanisms and their treatments]
11. 10+ Does poor delivery or use of oxygen within the body cause ME/CFS symptoms? If so, how is this best treated? [Causes and prevention; Treatment and management; Underlying mechanisms and their treatments]

Discussion

Using the James Lind Alliance's gold standard systematic and transparent processes, we have elicited the views of a diverse range of people with ME/CFS, their families and carers and health care professionals with an interest in ME/CFS to establish the top 10 priorities for research. To our knowledge, this the first time the ME/CFS community have been engaged in a research priority exercise of this scale. The response rate was strong, with over 2000 respondents, demonstrating that engagement with this 'hard to reach' community is both possible and welcomed. This was facilitated by simple actions to make it easier for people with ME/CFS to participate such as ensuring the tasks involved could be broken into small chunks and extra time given to complete tasks so people with ME/CFS could work at their own pace, take breaks and rest as necessary. Advice was also taken from people with ME/CFS regarding the format and layout of any survey materials so it was as easy to follow as possible. The success of this priority setting partnership in engaging people with ME/CFS across the severity spectrum indicates similar techniques should be considered by other ME/CFS researchers to maximise recruitment and engagement, particularly of those who are very/severely affected.

Although a convenience sample, the participants are broadly representative of people with ME/CFS and professionals working with them. Participants were most commonly white, middle-aged women with moderately severe illness [2,4,13,14], while the professional participants were most frequently doctors, occupational therapists and psychologists. Thus, we are confident that the views expressed here represent most of the ME/CFS community and those that support them. However one area which was relatively unrepresented was people with ME/CFS from ethnic minorities. Although some participants from ethnic monitories were involved in all stages of the study, the numbers involved were small. Only 5% of participants with ME/CFS were non-white. The prevalence of ME/CFS in people from ethnic monitories is unclear but estimated to 7.5% in the U.K. [2]. In the U.K., the 13% of the population are from ethnic minorities [14] indicating that we may have under-recruited this group. Further research is needed to better understand the demographics of ME/CFS in the U.K. and elsewhere, and the factors which may contribute to inequitable access to diagnosis and treatment in under-represented groups.

The identification of the priority research questions is a landmark for the ME/CFS community and researchers in the field. It is the first time that a broad range of the people affected by or involved with ME/CFS have come together to define what is important to them. The priority for people with ME/CFS is to understand the biological mechanisms explaining why people develop ME/CFS and the associated symptoms, and how to diagnose and treat or manage it. Unlike priority setting exercises for many chronic conditions, we found broad concordance with the community's priorities and the 'direction of travel' of most current research. These focus on the biomedical cause of the condition and its treatment, rather than a further exploration of psychological approaches, which also align with the recommendations for further research in the recent NICE Guidance for ME/CFS [5]. This is encouraging and will act as the catalyst for future research efforts. We call on researchers, funding bodies and government to consider the priorities highlighted here and to address the historic underinvestment in ME/CFS research. This exercise focussed on the U.K., and the priorities in other countries and health care systems may differ, however, our experience of engagement with ME/CFS charities and forums

internationally indicate the need to understand the biomedical causes of ME/CFS and how to treat it are universal. Thus, international researchers and funding bodies should also consider these priorities unless and until those from their own countries are reported.

Conclusions

People with ME/CFS, their families and carers, and health care professionals worked together to identify, for the first time, the research priorities for ME/CFS. These focus on the biomedical causes of ME/CFS and how to diagnose, treat and manage it. Researchers and funding bodies should consider these in their plans for future research.

Disclosure statement

Vinod Patel has worked with most of the large pharmaceutical industry groups over the years with the majority of the work being in education of Healthcare Professionals in Diabetes Care. This includes Novo Nordisk, Eli Lily, MSD, BI, Sanofi, Napp, Internis, Takeda and AZ. I have been part of Advisory Board work on occasions. From these companies I would have received Conference Arrangements and Lectures Fees. He is a trustee of the SAHF Charity (South Asian Health Foundation).

Funding

Competing interest

Sonya Chowdhury is CEO Action for M.E.

Notes on contributors

Sarah Tyson is a physiotherapist and emeritus Professor of Rehabilitation at the University of Manchester U.K. She lives with ME/CFS and acts as an academic, patient and carer representative in ME/CFS research and advises on the development and delivery of ME/CFS services.

Kristina Stanley is Director of TwoCan Associates, a consultancy specialising in patient and carer involvement in health and social care, established in 2004. She has worked as an Information Specialist on several JLA PSPs including the ME/CFS PSP.

Toto Anne Gronlund is a freelance consultant, facilitating consensus processes, and working with several James Lind Alliance Priority Setting Partnerships. Toto supported the ME/CSF JLA PSP. Previously Toto had a 30-year career with the National Health Service in the U.K. as a Medical Physicist including research into non-invasive diagnostics; and in national projects in health informatics and health economics.

Sian Leary is an advocacy and communications specialist working in the charity sector. She also lives with ME and acts as a patient representative in ME research.

Claire Dransfield is Research Manager with Action for M.E. Claire worked with the Steering Group throughout the ME/CFS PSP.

Helen Baxter is an advocacy worker for the 25% ME Group.

*Rachel Elliot*t is the mother and principal carer of a young adult with very severe ME who has been ill since 2015. Rachel is also Education Director of a national arts organisation and charity.

Rachel Ephgrave is a former physics teacher living with ME/CFS. Other members of her family have also been diagnosed with ME/CFS. She is active in the ME/CFS community including as a member of the Patient Advisory Group to the ME Research Collaborative, and Gloucestershire's ME/CFS Friendship Group. She has co-authored, as patient partner, a paper on the quality of life of people with ME/CFS and their family members. *In accordance with* Taylor & Francis policy and my ethical obligation as a researcher, I am reporting the following non-financial interests. I have disclosed those interests fully to Taylor & Francis. Member of the Patient Advisory Group to the ME Research Collaborative (MERC, formerly CMRC). The Patient Advisory Group to the MERC is a member of Forward ME and had one representative on the steering group of the James Lind Alliance ME/CFS Priority Setting Partnership. The PAG was a NICE stakeholder for the ME/CFS Guideline and the Managing the long-term effects of COVID-19 Guideline. The PAG is to co-chair the UKCRC ME subgroup. Member of the ME/CFS Friendship Group in Gloucestershire. The ME/CFS Friendship Group sends representation to the Physical Disability and Sensory Impairment Partnership Board in Gloucestershire and the Neurology subgroup of this board. The Friendship group has organised Millions Missing events and advocacy with MPs. Workshop participant in the James Lind Alliance ME/CFS Priority Setting Partnership. Supporter of Action for ME by providing my patient input into summarising Action for ME national strategy.

Monica Bolton I have had ME/CFS for 33 years, initially very severe but now mildly affected. I was previously a doctor, working as a GP in an inner city practice. I have been interested in clinical trial research in people with ME/CFS, particularly in the repurposing of existing drugs, since my own excellent response to the drug low dose naltrexone 12 years ago.

Annette Barclay lives with ME.

Gemma Hoyes MSc, A PhD researcher in marine science and offshore wind and an ME patient for over 15 years.

Ben Marsh is a Consultant Paediatrician with sub-specialism in Neurodisability and Community Child Health. He is medically retired. He lives with ME/CFS, is an associate of Doctors With ME and when able advocates and campaigns for improved research & medical education into ME/CFS.

Russell Fleming enjoyed a career as an independent financial adviser, private client investment manager and marketing manager for Lloyds Private Banking before early retirement due to ME/CFS. He now works for the ME Association doing his best to help others as they battle this devastating neurological condition.

Joan Crawford is a Chartered Counselling Psychologist in the NHS and private practice. Her research encompasses the neuropsychological difficulties people with ME/CFS face along with the optimal ways to support patients. She was Chair of the Chester ME self-help group for 9 years and she is a clinician, academic, patient and carer representative in ME/CFS practice and research. She was misdiagnosed with ME/CFS in 2003.

Ann West is a practising architect. She is also carer for family members with ME/CFS, both of whom are severely affected. She has been involved in advocacy work re educational access for children with ME/CFS in Scotland.

Opal Webster-Phillips is an educator and a former Training Manager of Southampton University. She has lived with ME for 30 years and has acted as an expert patient. She is Chair of a local ME think tank, ME/CFS Alliance https://mecfsalliance.org.uk . In 2008,in partnership with Professor Sir Holgate, Opal organised a ground-breaking international conference on ME. Sir Stephen credits her with starting him and others on the journey to research which led to him establishing and chairing the CFS/ME Research Collaborative (CMRC). She's a founder Member of the original CMRC Patient Advisory Group (PAG). She's currently a Patient Advisor on MERC (formerly CMRC) and Co Author of 'The History of ME/CFS, the Evolution and the Role of the @CMRC (A Patient's Perspective)'. This was commissioned by the CMRC Board and promoted as a highly recommended

introduction to ME. It has been widely distributed to academics, researchers, other stakeholders and the public-available via The ME/CFS Alliance website.

Cristina Betts is a Chartered Physiotherapist delivering physiotherapy and symptom management for individuals diagnosed with neurological and/or a long term health condition. Practicing physiotherapist where 50% of my work is face to face patient contact, and the remainder is managing and developing the two services of ME/CFS and Long COVID.

Susan O'Shea is a member of the patient advisory group (PAG) to the ME Research Collaborative (formerly CMRC) and taken part in the medical education and Nurses for ME sub groups. I am also a research student studying for an MRes Clinical Health Research qualification at the University of Birmingham. I am passionate about furthering research and education for this long neglected illness.

Vinod Patel is Professor in Diabetes and Clinical Skills at Warwick Medical School, University of Warwick and Honorary Consultant Physician in Endocrinology and Diabetes at the George Eliot Hospital NHS Trust in Warwickshire. He is also Clinical Director for Diabetes for NHS England and Improvement (West Midlands). He is jointly qualified in Hospital Medicine and General Practice which allows him to work across the primary /secondary care interface and improve the effectiveness of diabetes care. He set up one of the first CFS Clinics in the West Midlands with other physicians, occupational therapists and physiotherapists.

Sonya Chowdhury, has been CEO of Action for M.E. for nine years. Prior to this, Sonya worked in senior management roles, including as Head of Business Support and National Lead for the Family Strategic Partnership for leading children's charity Barnardo's. Previous experience includes working as a local authority social worker in fostering and adoption and child protection teams, management and trustee roles with children and families voluntary sector organisations and consultancy and training with charities and the public sector. A year after Sonya joined Action for M.E. a family member was diagnosed with the condition so she has lived experience of M.E. as a parent.

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