

Myalgic encephalomyelitis / Chronic fatigue syndrome

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The Research Team are unable to ensure that the information listed below provides an accurate & up-to-date snapshot of these matters

Research questions:

What are the diagnostic features of ME-CFS?

What is the prognosis for someone diagnosed with ME-CFS? What factors affect prognosis?

What evidence-based treatment or management strategies are most effective for people with ME-CFS?

What is the prevalence of communication difficulties for people diagnosed with ME-CFS?

What evidence-based treatment or management strategies are most effective for addressing communication difficulties caused by ME-CFS?

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2. Summary

Myalgic encephalomyelitis-Chronic fatigue syndrome (ME-CFS) is a condition characterised by excessive fatigue, especially after activity, along with a wide variety of multi-system symptoms. ME-CFS can be debilitating and result in significant functional impairment.

There are important sites of disagreement in research related to ME-CFS preventing strong recommendations about diagnosis or management. The causes and mechanisms are still unclear. There are multiple definitions of ME-CFS with overlapping but distinct diagnostic criteria. Estimates of those that recover or improve after an ME-CFS diagnosis vary widely from 4% to 83%. There is no gold standard management strategy. There are some proposed pharmacological and non-pharmacological treatments, though their efficacy is still debated. Cognitive behavioural therapy, exercise therapy and energy conservation techniques are widely recommended though evidence in support of these strategies is often of low or very low quality.

Communication difficulties are a recognised symptom of ME-CFS. Word finding problems are the most reported speech difficulty. No studies or recommendations were found that directly address problems with language or communication in ME-CFS.

3. What is ME-CFS?

3.1 Symptoms

ME-CFS may include chronic, severe and unexplained fatigue, along with other symptoms affecting bodily functions including sleep, circulation, respiration, digestion, mood, cognition, thermoregulation, and sensory processing (Steiner et al, 2023; Grach et al, 2023; NICE, 2021a-b; Deumer et al, 2021).

According to the UK's National Institute for Health and Care Excellence (NICE), core symptoms of ME-CFS include:

- Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion, and is not significantly relieved by rest.
- Post-exertional malaise after activity in which the worsening of symptoms:
 - is often delayed in onset by hours or days
 - is disproportionate to the activity
 - has a prolonged recovery time that may last hours, days, weeks or longer.
- Unrefreshing sleep or sleep disturbance (or both), which may include:
 - feeling exhausted, feeling flu-like and stiff on waking
 - broken or shallow sleep, altered sleep pattern or hypersomnia.
- Cognitive difficulties (sometimes described as 'brain fog'), which may include problems finding words or numbers, difficulty in speaking, slowed responsiveness, short-term memory problems, and difficulty concentrating or multitasking (2021a, p.12).

3.2 Diagnosis

There are different sets of diagnostic criteria used in research and medical practice (Steiner et al, 2023; Grach et al, 2023; NICE, 2021a-b; Deumer et al, 2021; Bateman et al, 2021; Noor et al, 2021).

The World Health Organisation (WHO) states, "Currently there is no consensus agreement amongst medical professionals as to how chronic fatigue syndrome may be definitively diagnosed" (WHO, n.d.). This is because "Without a biomarker it is not possible to definitively know if a person has or does not have ME/CFS. Without such a reference standard (or 'gold standard') it is not possible to assess the measurement validity of the different criteria" (NICE, 2021b, p.47).

Nevertheless, different sets of diagnostic criteria may be justified on pragmatic grounds, including ability to distinguish between cases and controls or the preference for over- or under-diagnosis (NICE, 2021b).

Emerge, the Australian peak body supporting people with ME-CFS, endorses the United States' National Academy of Medicine diagnostic criteria:

Diagnosis requires that the patient have the following three symptoms:

- A substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social, or personal activities that persists for more than 6 months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion, and is not substantially alleviated by rest
- Post-exertional malaise
- Unrefreshing sleep.

At least one of the two following manifestations is also required:

- Cognitive impairment
- Orthostatic intolerance (Institute of Medicine, 2015, p.6)

This contrasts with the 2021 NICE clinical guideline in three ways. According to the NICE criteria:

- Diagnosis can be made when symptoms are present for a minimum of 6 weeks for adults and 4 weeks for children.
- Cognitive symptoms are necessary for diagnosis.
- Symptoms cannot be explained by another condition (NICE, 2021a).

4. Management and recovery

Researchers disagree about whether there are effective treatments for ME-CFS (Vink & Vink-Niese, 2023; NICE, 2021a). There is still ongoing debate regarding the use of cognitive behavioural therapy and graded exercise programs. Seton et al (2024) identify a number of antivirals and other pharmacological treatments that may be effective but require further investigation.

Most clinical guidelines focus on symptom management and lifestyle changes. Lifestyle interventions include strategies such as scheduling activities and rest, ensuring good sleep hygiene and appropriate diet.

Reported recovery rates for people with ME-CFS are likely low, with one study reporting 8% recovery rate in a sample of 168 people (Ghali et al, 2022). Reported improvement rates vary

widely from 4% to 83% (Lim & Torpy, 2023; Ghali et al, 2022; Moore et al, 2021). The wide variance in improvement rates may be due to different definitions of improvement and different outcome measures used (Ghal et al, 2022; Moore et al, 2021).

Table 1 Symptom management strategies (Source: Grach et al, 2023, p.1549)

Symptom	Management
Post-exertional malaise	Pacing/rest, stimulus reduction, tracking devices or diaries for symptoms
Fatigue	Pacing, low-dose naltrexone, low-dose aripiprazole, anti-inflammatory diets, supplements, vitamin deficiency treatment
Sleep issues	Melatonin, trazodone, suvorexant, doxepin/tricyclic antidepressants, gabapentin/pregabalin
Cognitive dysfunction	Journaling, memory aids, occupational therapy, low-dose naltrexone, low-dose aripiprazole, careful use of stimulants
Orthostatic intolerance	Fluids/electrolytes/compression, fludrocortisone, midodrine, propranolol, pyridostigmine, guanfacine (best guided by postural orthostatic tachycardia syndrome subtype or tilt vital signs)
Dizziness (frequent)	Consider persistent postural-perceptual dizziness diagnosis, vestibular therapy, low-dose selective serotonin reuptake inhibitor or serotonin-norepinephrine reuptake inhibitor
Muscle or joint pain	Over-the-counter medications, duloxetine, milnacipran, pregabalin, gabapentin, tricyclic antidepressants, low-dose naltrexone
Neuropathy	Pregabalin, gabapentin, tricyclic antidepressants, compression or brace therapy

Symptom	Management
Sensory amplification	Noise-cancelling headphones, tinted glasses, crowd exposure reduction, low-dose aripiprazole
Gastrointestinal symptoms	Anti-inflammatory diets, small meals, pro/synbiotics, antidiarrheals or antihistamines for diarrhea, fibre or motility agents for constipation

4.1 Pacing

Pacing is a self-management technique for energy conservation that incorporates planned periods of activity and rest. It is recommended for all people with ME-CFS. Users plan activities around periods of rest and incorporate rest breaks where possible. Gradual increases in activity are a possible but not essential element of this strategy. The aim is to reduce the symptoms of post-exertional malaise and may improve quality of life and functional independence. This strategy makes possible regular activities that are part of a healthy lifestyle (good diet, exercise, social engagement etc.) by avoiding the over-exertion/exhaustion cycle of ME-CFS. It is not intended to be a cure or rehabilitation strategy (Barakou et al, 2023; Grach et al, 2023; NICE, 2021a). While this strategy is recommended in clinical guidelines, recent reviews suggest that further research is required to address heterogeneity of study designs, inconsistent findings and poor study quality (Sanal-Hayes et al, 2023; Barakou et al, 2023).

4.2 Cognitive behavioural therapy

NICE recommends discussing CBT with patients and carers (2021a). The evidence-review that informed their recommendation found all studies reviewed provided either low or very low quality evidence for the effectiveness of CBT in ME-CFS (2021c). The authors note:

Based on criticisms in the qualitative evidence of cognitive behavioural therapy (CBT) being described as a 'treatment' (cure) for ME/CFS, the committee considered it was important to highlight that CBT is not a cure for ME/CFS and should not be offered as such. Instead, it aims to improve wellbeing and quality of life, and may be useful in supporting people who live with ME/CFS to manage their symptoms and reduce the distress associated with having a chronic illness. It should therefore only be offered in this context, and after people have been fully informed about its principles and aims (pp.84-85).

This recommendation caused some controversy as other guidelines recommend more strongly in favour of CBT as a way to manage core symptoms of ME-CFS (Vink & Vink-Neise, 2023). Two recent reviews (Kuut et al, 2024; Bempohl et al, 2024) argue that CBT can lead to

significant reductions in fatigue, depression, anxiety and improvements in functional impairment and physical activity.

Kuut et al (2024) performed a meta-analysis incorporating data from 8 randomised controlled trials and including 1298 participants. They found statistically significant effects on fatigue, functional impairment and physical functioning. Effects were smaller for older people and people with more severe functional impairment. The authors found no significant effects on physical functioning for people with low levels of self-efficacy. Of note, none of the studies reviewed had low risk of bias and all 8 studies were conducted by the authors' own research group.

Berpohl et al (2024) performed a meta-analysis incorporating data from 15 randomised controlled trials and including 2015 participants. They found small to moderate effects on fatigue, depression and anxiety. Of note, the studies reviewed were rated as either high risk of bias or as having some concerns.

4.3 Exercise and physical activity

Regarding exercise programs, the NICE guidelines do not recommend graded exercise programs or unstructured exercise programs. Instead, if the patient understands and requests a personalised exercise program, the program should begin with activities below their baseline level and ensure that they can tolerate that level for a period of time. The authors state:

The committee concluded any programme using fixed incremental increases in physical activity or exercise (for example, graded exercise therapy), or physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories, should not be offered to people with ME/CFS. The committee also wanted to reinforce that there is no therapy based on physical activity or exercise that is effective as a cure for ME/CFS (2021a, p.78).

These recommendations were controversial. Some researchers argued that the recommendation against graded exercise therapy does not reflect the definitions of that approach used in the studies that NICE reviewed, and ignores some studies that show benefit of low intensity exercise for some people with ME-CFS (White et al, 2023). Wormgoor and Rodenburg (2021) found some evidence that graded exercise therapy improves fatigue as measured by participant self-report measures. However, objective measures of fitness, level of physical activity and employment showed no benefit.

5. Communication difficulties in ME-CFS

Cognitive difficulties are either common in or essential to ME-CFS, depending on the set of diagnostic criteria. Five of the nine sets of diagnostic criteria reviewed by NICE (2021b) include word finding problems as an example of cognitive symptoms (Grach et al, 2023; Lim & Torpy, 2023; NICE, 2021a-b; Maksoud et al, 2020; Institute of Medicine, 2015). Grach et al (2023) suggest that word finding and language processing problems could be a feature of post-

exertional malaise, which is a core symptom of ME-CFS on several definitions. However, the extent or severity of linguistic problems in ME-CFS is not clear. One study found around 75% of subjects experienced difficulties with words, though the authors do not elaborate on the type, frequency or severity of the difficulty (Institute of Medicine, 2015).

Evidence presented in a 2022 meta-analysis of cognitive impairments in ME-CFS shows an uneven picture of linguistic ability (Sebaiti et al; 2022). The authors found a moderate to large effect of ME-CFS on language processing speed (as measured by Colour/Word tests) and long-term verbal memory (as measured by California verbal learning test recognition, Weschler logic and reading tests). They found no significant effect on instrumental linguistic skills (as measured by the Boston Naming Test and Weschler Adult Intelligence Test), short term verbal memory (as measured by Digit Span Forward and Backward) or linguistic efficiency (as measured by National Adult Test Reading and Weschler Adult Intelligence Test).

No studies were found that address management of language or communication impairment for people with ME-CFS.

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