



Title	A Review of the Scientific Literature for Diagnosis and Treatment of Chronic Fatigue Syndrome/Myalgic Encephalopathy (CFS/ME)
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Aim

To assess and synthesize the evidence base for diagnosing and treating chronic fatigue syndrome/myalgic encephalopathy (CFS/ME).

Conclusions and results

Diagnosis: The recommendations for diagnosis are based on guidelines for clinical diagnosis of CFS/ME published by British, Australian, Canadian, and other groups.

- Patient history includes extreme fatigue lasting at least 6 months triggered by disproportional demands, and is unpredictable, does not improve by rest, or is worsened by physical or mental effort. Other symptoms are, eg, sore throat, swollen lymph nodes, painful joints and muscles, headache, and sleeping problems. Comorbidities may include fibromyalgia or irritable bowel syndrome. The course varies.
- Differential diagnoses, eg, metabolic diseases, diabetes, coeliac disease, cancer, bipolar or depressive conditions, neurological disease, and Addison's disease must be ruled out. No diagnostic test can verify the diagnosis, nor point to the best treatment.

Treatment: Cognitive behavioral therapy, graded exercise therapy, pharmacological treatment, immunological treatment, supplements and alternative/complementary treatment. Documentation is low or very low for most outcomes:

- Cognitive behavioral therapy suggests improved physical function and quality of life, but it is uncertain if the treatment influences mental health.
- Graded exercise therapy suggests reduced fatigue, but effects on depression or quality of life are not documented. Dropout was high, especially with high-intensity exercise.
- No evidence recommends pharmacological treatment unless there is relevant comorbidity.
- Immune modulating treatment has uncertain effects, but could have serious adverse effects.

- Effects of supplements and alternative/complementary medicine are uncertain.
- Few studies investigated the effects of treatment in children and adolescents.
- No studies investigated the effects of treatment in the severely ill or disabled.

Methods

The overview of the scientific knowledge is based on systematic reviews and a search of recent primary and qualitative studies. The assessment was done stepwise, starting with 1168 abstracts and ending with 6 systematic reviews, 5569 abstracts of RCTs/CCTs and ending with 4 RCTs on adults and 3 RCTs on children/adolescents. We identified 807 qualitative studies and included 18. Level of documentation was based on GRADE.

A review team performed the assessment, with input from 2 patient organizations. The literature was searched via the Cochrane Database of Systematic Reviews, DARE, MEDLINE, EMBASE, PsycINFO, and AMED. Patients with CFS, ME, postviral fatigue syndrome, and chronic fatigue and immunodysfunctional syndrome were included. Interventions included any kind of treatment for CFS/ME. All outcomes were considered, and fatigue, physical and mental health, and quality of life are reported.

Further research/reviews required

Studies on better treatment for severely ill or disabled sufferers are insufficient. Evidence on children and adolescents is scarce, and for adults the level of documentation is low or very low. Diagnostic criteria vary by study, making comparisons difficult. Empirical studies on treatment experiences are missing. CFS/ME symptoms are subjective. Qualitative studies show that patients feel stigmatized and mistrusted, and doctors find it challenging to diagnose and treat CFS/ME. The prevalence, prognosis, and cause of CFS/ME remain unclear. More research is needed.