

## Abstract

**Background:** Chronic fatigue syndrome (CFS) is a debilitating and serious illness.

Internet-based cognitive behavioral therapy (i-CBT) may help adult patients with CFS.

**Methods:** Our search strategy was based on reports published before September 1, 2021. We searched randomized controlled trials targeting adults with a primary diagnosis of CFS meeting the CDC diagnostic criteria, using PubMed, EMBASE, PsycINFO, and Ichu-shi Web. Patients were assigned to i-CBT condition in comparison with a waitlist group. Two reviewers extracted data on patients, interventions, and outcomes independently, and one author conducted risk of bias assessment of each study. The primary outcome was efficacy in reducing fatigue severity using the mean difference (MD) of the Checklist Individual Scale (CIS).

**Results:** Out of 2504 articles, one RCT (240 CFS participants) from the Netherlands was included in this systematic review. There are two forms of i-CBT, including protocol driven feedback (PDF) and feedback on demand (FOD). Compared with the waitlist group, intention-to-treat (ITT) analysis has shown that both forms of i-CBT reduced fatigue significantly based on the difference in MD (DMD) (PDF: DMD = -8.3, 97.5% CI -12.7 to -3.9,  $P < 0.0001$ ; FOD: DMD = -7.2, 97.5% CI -11.3 to -3.1,

$P < 0.0001$ ). The two forms of therapies, i-CBT(PDF) and i-CBT(FOD), did not show a significant DMD on any of the outcome measures.

**Conclusions:** I-CBT may be effective in alleviating the symptoms of chronic fatigue, compared with patients who were awaiting the treatment. Continued research on comparative effectiveness is required to improve the usability of these programs, allowing for the sustainable implementation of internet-based CBT.

**Keywords:** Chronic fatigue syndrome (CFS), cognitive behavioral therapy (CBT), internet-based cognitive behavioral therapy, (i-CBT)