

Chapter 4. Conclusions

Summary of Answers to Key Questions

1. *What is the evidence that some individuals with CFS have discrete impairments that are associated with disability? (Note that impairments include both physical and mental impairments).*

CFS patients represented in the database have measurable physical and mental impairments; however this is based primarily on a variety of “self-report” instruments, most of which have been validated. These instruments; however, although “validated,” have not been validated in a “compensation setting,” have not been validated as measures of disability, and have not been validated in CFS patients who are often formerly high functioning individuals, unlike chronic mentally ill patients or low functioning patients with physical impairments. The majority of the CFS patients represented in the 37 studies reporting employment status are unemployed. However, due to the heterogeneity of CFS, small study size, and wide variations in reporting the data, it is not possible to determine whether those CFS patients with discrete impairments and/or measurable disability are those who are unemployed. We could not compare employment status of healthy controls with impairment, as the healthy controls in these studies did not have measurable impairments. No particular measure of impairment appears superior to others in CFS patients, and no measure of disability appears as objective and reproducible as work status.

2. *What is the evidence that in the CFS population, current neuropsychological tests reliably detect cognitive or affective impairments associated with decreased ability to work?*

The evidence suggests that some individuals with CFS have self-reported discrete cognitive or affective mental impairments, as measured on validated tests in the mental or cognitive domain. The majority of CFS patients in studies reporting work outcomes have decreased ability to work. CFS patients with a greater degree of depression are unemployed more often than those with mild or no depression, although no cause and effect relationship can be claimed.

3. *What is the evidence that in individuals with CFS, treatments are effective in restoring the ability to work?*

Some CFS patients who underwent a variety of interventions ranging from individualized rehabilitation programs to CBT demonstrated improvement in functioning and were able to return to work; however, the sample sizes are too small and the study designs too disparate to enable comparisons of different treatments in their association with returning CFS patients to work. Furthermore, a substantial number of CFS patients with no treatment returned to work with the passage of time. So, while some treatment interventions may provide symptom relief,¹ no evidence for efficacy as defined by work outcomes is available.

4. *What are the patient characteristics that best define improvement or positive outcomes in the CFS population such that they experience improvement in functioning? Where it occurs, how is this improvement in functioning related to the ability to engage in work activity?*

No specific demographic, clinical, or psychiatric traits have been shown to be consistently predictive of CFS patients' ability to return to work.

Strengths and Limitations of the Evidence Base

The strengths of this review include the clear definition of the research questions, adherence to an explicit research protocol developed prior to the analysis, the comprehensive nature of the data search (employing both computer databases and manual bibliography searches, resulting in the inclusion of all relevant published materials), consensus between two reviewers of all data elements prior to entry into the database, and a quality control review of every element of this report.

Another primary strength of this evidence base derives from the collaboration of multidisciplinary researchers who participated in its development. The expert panel meeting held early in the project enabled the researchers to focus their attention on areas which the experts believed to be relevant. The report was compiled by investigators who are skilled in employing highly systematic and unbiased methods to collect, review and synthesize data from published clinical literature. Throughout the course of this project, the team received frequent input from the co-investigator (a clinical content expert) representatives from SSA, and the AHRQ Task Order Officer. In addition, the draft report was evaluated by a panel of nine peer reviewers as well as the TEP, and their comments are incorporated as appropriate into this final version of the Evidence Report.

There are many limitations to this review. CFS is a heterogeneous disorder, even within the strict operational definitions used, and it may not be possible to make any generalizations about disability associated with this condition.

The major limitations of this review are those related to weaknesses of the available current medical and scientific published literature related to CFS disability. It should also be noted that cultural differences may exist within this international database. Data summaries do not account for any cultural variances. As with any qualitative analysis, our coding system was inherently subjective, despite developing the quality scale *a priori*, and using two independent researchers to grade each study. However, given the limitations of the grading systems used, study designs were poor and external validity was low. Due to the variety of study designs, scales used, and outcomes reported, results from different studies could not be combined in meaningful ways. Study designs were not sufficiently homogeneous to allow quantitative synthesis of individual study results.

Fundamental gaps exist that hamper an objective assessment of CFS and disability. This stems from the fact that CFS is an illness without clear biological concomitants and therefore relies on a non-objective and often inadequate self-reporting of symptoms and functional limitations as a means of determining the actual extent of impairment and work capacity.

Another limitation of the literature was that it lacked a clear stratification of subjects' employment status according to the onset of illness (acute, gradual or insidious), duration of illness, medical and/or psychiatric comorbid conditions, or quantifiable fatigue scores.

Findings showed an insufficient use of standardized measurements which could be compared across studies and which had the ability to detect (or not) any exaggeration/inadequacy of effort. Numerous patient outcomes were reported, and although we attempted to assign each measurement to a specific domain, it was clear that the different instruments/scales may not have measured precisely the same phenomenon. These instruments although "validated," have not been validated in a "compensation setting," have not been validated as measures of disability, and have not been validated in CFS patients who are often formerly high functioning individuals, unlike chronic mentally ill patients or low functioning patients with physical impairments. While some studies reported test and scale results, the results were reported in a wide variety of formats, with relatively sparse reporting of both baseline and outcome data. Many otherwise eligible studies we reviewed did not report the employment or disability status of CFS patients. Even more rare were studies reporting work data for patients over time, e.g. at baseline and followup for an interventional trial. These missing data mean that, while relationships between various impairment measures and work/disability status might be explored in some cases, causality could not be determined.

Conclusions

This systematic review of the current published research related to CFS disability identified 53 primary studies published between 1988 and 2001 that met prospectively determined inclusion criteria.

The evidence suggests that some individuals with CFS have self-reported cognitive or affective impairments on neuropsychological tests, but these results are not consistent. And while people with CFS may frequently have co-morbid psychiatric conditions, it is unclear whether the neuropsychological test results are due to CFS, or to coexisting psychiatric disorders. Patient's scores on an instrument used to measure depression, indicates that depression of greater severity is associated with unemployment, but no other impairment appeared to be consistently associated with disability or work outcomes. No specific interventions have been proven to be effective in restoring the ability to work. No specific patient characteristics have been defined that best predict positive employment outcomes in CFS patients.

"Whatever one presumes chronic fatigue syndrome (CFS) to be, people suffer with it and because of it."⁶⁶ While the diagnosis of CFS is based on patient self-reports and exclusion of other causes of the complaints, a group of patients meeting the case definitions for CFS can be identified. Some of these patients have severe symptoms, and are disabled, according to the SSA definition. In practice, a functional capacity evaluation has been useful in defining what a patient can or cannot do. It is important to evaluate how a patient's current activities compare to activities prior to the onset of illness, and compare their functioning in terms of work, school, social, and home activities.