Systematic Review of the Current Literature Related to Disability and Chronic Fatigue Syndrome

Summary

Overview

The purpose of this project, nominated by the Social Security Administration (SSA), and contracted through the Agency for Healthcare Research and Quality (AHRQ) was to develop an evidence base that would provide SSA with the most current medical and scientific knowledge for evaluating disability as defined by the SSA in persons with Chronic Fatigue Syndrome (CFS). This review will also serve to highlight gaps in the current literature and areas ripe for future research.

This database of best available evidence was established through a systematic review of the CFS literature pertinent to diagnosis, measurement, and treatment of disability resulting from any medically determinable physical or mental impairment.

Reporting the Evidence

Several key questions guided this review. Questions were originally posed by SSA and refined in collaboration with expert panel members and representatives from SSA and AHRQ to focus on the issues of disability and impairment in CFS. The revised key questions are as follows:

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.)

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?

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

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

Methodology

A multidisciplinary panel of professionals with a broad range of clinical expertise in CFS was assembled early on to provide guidance and direction regarding:

- Establishing a working definition of CFS for purposes of this task order.

- Refining the original key questions as posed by SSA.

- Making recommendations regarding the breadth of the literature to be reviewed, analyses that should be performed, and sources of data to be accessed to ensure an evidence report that would be responsive to SSA's concerns.

Members of the panel served throughout the course of the project as the Technical Expert Panel (TEP), responded to questions during the review, and commented on the draft evidence report. The systematic review followed a prospective protocol that was developed *a priori* and shared with the nominating partner (SSA), the TEP, and the Task Order Officer at AHRQ. The protocol outlined literature search methods, study eligibility criteria, data elements for extraction, and methodological

strategies to minimize bias and maximize precision during the process of data collection, extraction, and synthesis.

The published literature was searched from January 1, 1988 to November 15, 2001, using Medline®, Current Contents®, Cochrane Library, and PsychINFO databases. In addition, the bibliographies of all accepted studies and review articles from the past 2 years were searched for potentially relevant citations. The retrieval cut-off date was March 15, 2002.

English language published literature from 1988 to 2001 was sought, utilizing the following search strategy:

fatigue syndrome, chronic [MeSH] or *chronic fatigue* [*syndrome*].

Limits: English language, human subjects.

All citations and abstracts were printed and screened at MetaWorks. Full papers were obtained for all abstracts that mentioned CFS and disability. The electronic searches noted above were supplemented by a manual search of the reference lists of all accepted studies and relevant review articles. To be included in the review, studies were required to report CFS as diagnosed according to one of the four accepted CFS definitions, evidence of a medically determinable physical or mental impairment, and data regarding employment or work in at least two adult patients.

Data from each accepted study was extracted by one investigator and reviewed by a second. Key data elements sought for extraction from each study included study, patient, and intervention characteristics, as well as outcomes of interest. All eligible papers were evaluated and scored for both internal and external validity, with possible scores ranging from 2 to 8.

No quantitative analyses were performed beyond descriptive statistics to summarize findings. Eleven peer reviewers, drawn from clinicians with expertise in CFS and professional organizations, along with eight TEP members reviewed and provided comments on the draft evidence report. Feedback was incorporated into the final report as appropriate.

Findings

Of all 3,840 citations identified, 53 studies met all eligibility criteria. The majority of studies were conducted in the United States or Western Europe. There were 17 interventional and 36 observational studies, covering 4,558 primarily female adult patients with CFS. Twenty-two of these studies described comparator groups of healthy controls totaling 775 patients.

No quantitative syntheses were possible because of insufficient and/or inconsistent reporting or results. The evidence supports the following conclusions:

- Some individuals with CFS have discrete cognitive or affective impairments on neuropsychological tests, but these results are not consistent, nor can any causality associated with decreased rates of employment be inferred due to the cross-sectional design of most of the studies.

- 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 proven to be effective in restoring the ability to work, and interventional trials describing both baseline and outcome data were sparse. The most commonly reported interventions included drug therapy and cognitive behavioral therapy; the latter lending a possible association between improvement in the ability to work and an increase in the number of patients employed.

- No specific patient characteristics have been defined that serve as best predictors of positive employment outcomes in CFS patients.

- It is important to compare the patient's level of functioning at the time of diagnosis to his/her level of functioning prior to the onset of illness especially as it relates to work, school, social, and home activities.

- The major limitations of this review are related to the weaknesses inherent in the current medical and scientific published literature related to CFS. Study designs were not sufficiently homogeneous to allow quantitative synthesis of individual study results, and external validity was low. While some studies reported test and scale results, this was highly variable with relatively sparse and inconsistent reporting of both baseline and outcome data. Longitudinal studies which would allow for assessment of effect of baseline characteristics on long-term work outcomes were extremely rare.

Future Research

It is clear from this review of the literature addressing work status in patients with CFS that more studies are needed to enable researchers to better assess and evaluate disability in this population. Following are priorities for future research:

- Longitudinal, interventional studies are mandatory in order to determine what baseline characteristics are associated with inability to work and which interventions are effective in restoring the ability to work.

- Authors should report more detailed information about impairment and work status at baseline and after intervention, preferably stratified by patient characteristics.

- Future studies of employment status should clarify if employment means full or part time, prior work or new work, and also provide information on duration of return to work.

- Further research is needed to determine the impact of cognitive behavior therapy, graded exercise, and other interventions on the issue of disability.

- The literature would be enhanced if standardized measurements of impairment were developed, defined, and used to evaluate the impact of all interventions, and if

2

some assessment was made regarding the impact of impairment on employability in this specific patient population.

- Further research is needed to determine validity and reliability of self-reported instruments in assessment of impairment and disability in CFS patients who are often formerly high functioning individuals, unlike chronic mentally ill patients or low functioning patients with physical impairments. Validity and reliability of these instruments should be determined in patients with concurrent or prior neuropsychological diagnoses, given the high lifetime incidence of same, and particularly in patients who may have different motivations for determining disability. Instruments should also be validated in compensation settings.

- Further research is needed to determine whether and which validated neuropsychological non-self-reported assessment tools yield sufficient evidence to evaluate functionality as it relates to ability to work.

- Further research in needed to determine whether there are characteristics of care providers or prior work experiences that relate to ongoing CFS disability.

Availability of the Full Report

The full evidence report from which this summary was taken was prepared for the Agency for Healthcare Research and Quality (AHRQ) by MetaWorks Inc. Evidence-based Practice Center (EPC), Medford, MA, under Contract No. 290-97-0016. It is expected to be available in the winter 2003. At that time, printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 66, *Systematic Review of the Current Literature Related to Disability and Chronic Fatigue Syndrome*. In addition, Internet users will be able to access the report and this summary online through AHRQ's Web site at www.ahrq.gov.