

Evidence Report

Chapter 1. Introduction

Purpose of Review

In 2001, the Agency for Healthcare Research and Quality (AHRQ) commissioned the San Antonio Evidence-based Practice Center to conduct a systematic literature review entitled “Defining and Managing Chronic Fatigue Syndrome (CFS)”.¹ This earlier report focused on diagnosis and management of CFS and established a foundation for the current report, the objective of which is to evaluate the best available evidence on detecting and managing disability in persons with CFS. We seek to add to the groundwork laid by the earlier Evidence Report, without repeating the same information.

This topic was nominated by the Social Security Administration (SSA), which defines disability as “the inability to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment (or combination of impairments) which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than 12 months”.² Patients must have a severe impairment that makes them “unable to do (their) previous work or any other substantial gainful activity”.² The impairment “must result from anatomical, physiological, or psychological abnormalities which can be shown by medically acceptable clinical and laboratory diagnostic techniques. A physical or mental impairment must be established by medical evidence consisting of signs, symptoms, and laboratory findings, not only by a statement of symptoms”.²

While these requirements may be easily documented for some illnesses, assessing disability for CFS, a condition for which there is no accepted diagnostic test or widely effective treatment,¹ presents a greater challenge. The goal of this evidence review is to ensure that the SSA is using the most current medical knowledge for evaluating disability in persons with CFS.

Prevalence and Diagnostic Criteria

The prevalence of CFS is difficult to quantify, due to the lack of validated diagnostic tests and the heterogeneity of the CFS population.³ It is estimated that CFS affects approximately 0.2 to 0.7 percent of adults in the United States and the United Kingdom,⁴⁻⁶ and that women are affected more often than men.⁷ CFS occurs in all ethnic groups and in people of every socioeconomic status.^{4, 7, 8} The societal implications of CFS constitute a significant public health problem.⁴

Fatigue is frequently reported in primary care settings, but the vast majority of patients who complain of fatigue do not suffer from CFS, which is defined by specific diagnostic criteria.⁹ Several operational case definitions of CFS have been developed by consensus groups in the United States, United Kingdom, and Australia.¹⁰⁻¹³ The Centers for Disease Control (CDC) first developed diagnostic criteria for CFS in 1988,¹¹ with the most recent revision in 1994.¹⁰ CFS is defined by the CDC as a syndrome of severe, disabling physical and mental fatigue lasting for at least six months, exacerbated by minimal exertion, and unexplained by a conventional medical diagnosis. CFS represents a diagnosis of exclusion. The differential diagnosis of CFS includes symptoms of depression, somatization disorder, anxiety disorder, hypochondriasis, activity-induced chronic fatigue, fibromyalgia, hypothyroidism, Lyme disease, and multiple sclerosis.

While people with CFS may report a variety of symptoms in many organ systems, extensive research has not revealed any serious underlying pathology.¹⁴

The diagnostic work-up for CFS recommended by the CDC includes a history and physical examination, including mental status examination, and laboratory tests including complete blood count (CBC) with differential, erythrocyte sedimentation rate (ESR), liver function tests, total protein, albumin, calcium, phosphorus, glucose, blood urea nitrogen, creatinine, electrolytes, thyroid function tests, and urinalysis.¹⁰ None of these tests are diagnostic for CFS, but they may point the clinician toward an alternative diagnosis. No causal agent and no diagnostic laboratory tests or biological markers have been verified for CFS. Earlier reports suggested a role for Epstein-Barr Virus (EBV) in the pathogenesis of CFS.¹⁵ Some physicians persist in ordering serial EBV titers to diagnose and follow patients with CFS; however, available evidence indicates that EBV serology has no role in standard laboratory evaluation of persons with CFS.⁴ The diagnosis of CFS remains one of exclusion, since a diagnostic laboratory marker or pathognomonic biopsy specimen has not been identified.⁴

Treatment of CFS

No treatment for CFS has proved to be effective. A systematic review of interventions for treating CFS showed mixed results of effectiveness for all treatments, with promising results with cognitive behavioral therapy (CBT) and graded exercise therapy.^{1, 16} Numerous pharmacologic approaches have been tested, including antidepressants,¹⁷ corticosteroids,^{18, 19} mineralocorticoids,²⁰ anti-viral medications, anti-fungal agents, and immunotherapy. Many alternative treatments have also been tried, unsuccessfully.²¹ In addition to CBT²² and graded exercise,²³ a myriad of other non-pharmacological approaches have also been tested, including massage therapy, prolonged bedrest, biofeedback, stress management, anti-allergy and anti-yeast diets.²¹

Challenges in Determining Disability

Determining levels of disability, as a manifestation or consequence of fatigue, presents an important research challenge. Evaluating disability in CFS patients is hampered by the difficulties in defining and diagnosing CFS, the unknown etiology, and the heterogeneity of the population. The core complaint, fatigue, is entirely subjective, and does not readily fit the SSA definition of “anatomical, physiological, or psychological abnormalities”² that can be demonstrated by objective testing. Impairment is also variably defined and measured. Interpretation of the clinical significance of specific impairment measurements is limited by the many different impairment scales used, the different health domains measured, and the relatively small numbers of patients studied. As a result, studies of impairment and disability in CFS often cannot be readily compared, even in study cohorts with homogenous case definitions. There are thus numerous unanswered questions regarding CFS disability. This review of the current medical and scientific research related to CFS disability was nominated by the SSA, and a Task Order was commissioned by the AHRQ to assist in answering several key questions related to assessment and management of disability in people with CFS. This research will assist

the SSA in ensuring that it is using the most current medical knowledge for evaluating disability in persons with CFS.