

## **Problems with the New CDC CFS Prevalence Estimates**

At the last IACFS/ME Board meeting in Salt Lake City, we were informed that an article would soon be published concerning the CDC's new prevalence estimates indicating six to ten times more individuals in the US had CFS. On scientific grounds, I had several concerns with these estimates, and after I brought up my concerns, the Board asked if I might post my reactions on the IACFS/ME website. I agreed to do this, and my opinions are below and do not represent the views of the IACFS/ME.

**Leonard Jason, Ph.D., DePaul University**

[The article concerned is entitled [Prevalence of chronic fatigue syndrome in metropolitan, urban, and rural Georgia](#) by Reeves et al.]

## **Problems with the New CDC CFS Prevalence Estimates**

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By the early to mid 1990s, the general consensus was that CFS was a relatively rare disorder affecting primarily white, middle-class women. Prevalence estimates of this illness from the CDC ranged from .002% to .0073% (Gunn et al., 1993) suggesting that there were less than 20,000 individuals in the U.S. with this illness. Toward the late 1990s, Jason, Richman and colleagues (1999) used more rigorous community-based samples and found that approximately .42% of the sample was determined to have CFS, or approximately 800,000 people from the US (Jason, Richman et al., 1999). These overall prevalence estimates were later corroborated by the CDC in another community-based sample (Reyes et al., 2003 estimated the CFS prevalence to be .24%).

In Great Britain, community estimates of CFS rates were estimated to be 2.6% (or 2.6 cases among every 100 people; Wessely et al., 1997). One needs to examine a broadened CFS case definition to understand these CFS rates in Great Britain, and if these rates were applied to the US, there would be about 4 million people in the US with CFS. Wessely et al. (1997) indicated that of the 2.6% with CFS, psychological disorders were absent in only .5%. Individuals diagnosed with CFS in this epidemiologic study were subsequently compared to a sample of people with CFS who had been diagnosed from a hospital unit (Euba, Chalder, Deale & Wessely, 1995). Of the community sample, 59% felt their illness might be due to psychological or psychosocial causes compared to 7% for the hospital sample. In Wessely et al.'s (1996) community based sample, only 64% had sleep disturbances and 63% had postexertional malaise. These percentages are rather low, as both symptoms are critical features of CFS. These findings might provide a clue as to why Wessely and colleagues found CFS prevalence rates that were appreciably higher than those found by a second generation of CFS epidemiologic studies in the United States (Jason et al., 1999; Reyes et al., 2003).

It is of interest that the Great Britain CFS rates are within the range of several mood disorders. Mood disorders are the most prevalent psychiatric disorders after anxiety disorders: for major depressive episode, the one-month prevalence is 2.2%, and lifetime prevalence is 5.8% (Regier et al., 1988). Major Depressive Disorder is an example of a primary psychiatric disorder, which has some

overlapping symptoms with CFS. Fatigue, sleep disturbances and poor concentration occur in both depression and CFS. Some patients with Major Depressive Disorder also have chronic fatigue and other symptoms that can occur with depression (e.g., unrefreshing sleep, joint pain, muscle pain, impairment in concentration). Fatigue and these four symptoms also are defining criteria for CFS, based on the Fukuda et al. (1994) criteria. It is possible that some patients with a primary affective disorder could be misdiagnosed as having CFS. While fatigue is the principal feature of CFS, fatigue does not assume equal prominence in depression (Friedberg & Jason, 1998; Komaroff et al., 1996). Several CFS symptoms, including prolonged fatigue after physical exertion, night sweats, sore throats, and swollen lymph nodes, are not commonly found in depression. Moreover, illness onset with CFS is often sudden, occurring over a few hours or days, whereas primary depression generally shows a more gradual onset. Some individuals with CFS might have had psychiatric problems before and/or after CFS onset and yet, other individuals may only have primary psychiatric disorders with prominent somatic features. Including the latter type of patients in the current CFS case definition could confound the interpretation of epidemiologic and treatment studies.

The CDC has recently released findings from a community-based epidemiologic study that occurred in Georgia (Reeves, Jones, Maloney, Heim, Hoaglin, Boneva, Morrissey, & Devlin, 2007). While the prior CFS prevalence rate was estimated to be .24% in Wichita, Kansas (Reyes et al., 2003), their new estimated prevalence rates were reported to be considerably higher with 2.54% (remarkably similar to the 2.6% rate in Great Britain, Wessely et al., 1997). The CDC now estimates that six to ten times more people have this illness than their previous reports in the US. In this study, the authors screened for persons who reported fatigue, problems with memory/concentration, unrefreshing sleep or pain rather than simply focusing on the single symptom of fatigue, and the authors indicated that these criteria increased the identified cases by 13%. In addition, the authors used what they referred to as standardized criteria to identify cases, and below we evaluate this new empirical CDC case definition of CFS. To meet the new CFS criteria, individuals need to meet criteria on symptoms, level of disability and degree of fatigue, and each of these areas is described below.

As one part of the standardized CDC criteria, the Symptom Inventory is used to operationalize the symptoms of CFS (Wagner et al., 2005). For each of 8 critical Fukuda et al. definitional symptoms, patients are asked to rate the symptom on perceived frequency (1 = a little of the time; 2 = some of the time; 3 = most of the time; 4 = all of the time) and severity or intensity of symptoms (the ratings were transformed to the following scale: 1 = mild, 2.5 = moderate, 4 = severe). The frequency and severity scores were multiplied, and the sums for the 8 critical Fukuda et al. (1994) symptoms were summed. Even with summed scores for the empirical case definition needing to be greater or equal to 25 (Reeves et al., 2005), the overall level of symptoms seems relatively low for patients with classic CFS symptoms (the criterion would be met if an individual rated only 2 symptoms as occurring all the time, and one was of moderate and the other of severe severity). In addition, the 8 case definition symptoms were based on a time period comprising the last month compared to what is specified in the Fukuda et al. (1994) criteria, which states that: "There needs to be the concurrent occurrence of 4 or more of the following symptoms, and all must be persistent or recurrent during 6 or more months of the illness and not predate the fatigue." This change in the case definition has the potential of including more individuals.

Also, part of this new CDC empirical CFS criteria is the use of the Medical Outcomes Survey Short Form-36 (SF-36) to assess substantial reductions in

occupational, educational, social or recreational activities. Using the SF-36, these criteria were defined as scores lower than the 25th percentile on the physical function, role physical function, social function, or role emotional. Because the individual only needs to meet one of these areas to meet the CFS criteria, the individual might not have any reductions in key areas of physical functioning, and only impairment in role emotional areas (e.g., problems with work or other daily activities as a result of emotional problems), and then the person could meet disability criteria for CFS. Ware, Snow, and Kosinski (2000) found that mean for role emotional for a clinical depression group was 38.9, indicating that almost all those with clinical depression would meet criteria for being within the lower 25th percentile on this scale (which was a score of less than or equal to 66.7). In Peter White's Dec. 3, 2006 review ([http://www.biomedcentral.com/imedia/1083914155124266\\_comment.pdf](http://www.biomedcentral.com/imedia/1083914155124266_comment.pdf)) of Reeves et al.'s (2007) article, he states: The use of physical function, role physical and social function sub-scales is consistent with the International Study criteria for CFS, which states that the illness "results in substantial reduction in previous levels of occupational, educational, social, or personal activities..." (Reeves et al, 2003). The use of role emotional is not, since it specifically asks about change in function "as a result of any emotional problems". And later White states that "In order to make these important criteria consistent with other studies, I think the authors need to re-analyse their data, omitting this sub-scale."

The last instrument used with the new CDC empirical CFS criteria is the Multidimensional Fatigue Inventory (MFI) (Smets, Garssen, Bonke, & DeHaes, 1995). Severe fatigue was defined as greater than or equal to 13 on the MFI general fatigue or greater than or equal to 10 on the reduced activity. In Peter White's Dec. 3, 2006 review of the Reeves et al.'s (2007) article ([http://www.biomedcentral.com/imedia/1083914155124266\\_comment.pdf](http://www.biomedcentral.com/imedia/1083914155124266_comment.pdf)), he wrote: "This means that it would be possible to meet the fatigue criterion without significant fatigue; i.e. with reduced activity alone. This is inconsistent with the international study criteria for CFS." In support of this criticism by White, I believe that the general activity items refer to issues that a person with depression might easily endorse. If a person indicated that the following two items were entirely true: "I get little done", "I think I do very little in a day"; they would meet the fatigue criterion for the new CDC empirical case definition. Our group is currently studying individuals with major depressive disorder versus those with CFS, and we are finding individuals with a purely affective disorder being classified as having CFS with this new empirical case definition (Najar, Porter, & Jason, 2007).

It is important to better understand the two CDC community based studies (Reyes et al., 2003; Reeves et al., 2007), and this is particularly important as their CFS estimated prevalence rates have changed so dramatically. Of the individuals who were identified as having CFS during the first study (Reyes et al., 2003) that occurred over a three year period (1997 through 2000), 58 were brought back for a two day inpatient study that occurred from December 2002 to July 2003, and only 16 (28% of the original group diagnosed with CFS) had a current consistent diagnosis of CFS, using traditional methods of making this diagnosis. When these investigators employed an empirically derived system (that was used in deriving the higher prevalence rates of 2.54% in the Georgia community based study), 43 rather than 16 individuals who had been traditionally diagnosed as having CFS met this new system. Clearly, this newly developed empirical system brings in many additional people to a CFS diagnosis. It is very possible that this new empirical classification does identify a group of individuals with high levels of fatigue, impairment, and symptoms, but it might

also be identifying a group with high chronic distress and illness, rather than CFS as a unique disorder.

It is at least possible that the 2.54% to 2.6% CFS rates both the United States and Great Britain are due to a broadening of the case definition and possible inclusion of cases with primary psychiatric conditions. Some CFS investigators would not see this as a confounding problem because they believe that high rates of psychiatric comorbidity indicate that CFS is mainly a psychiatric disorder (Abbey, 1993). CFS and depression are two distinct disorders, however, even if they share a number of common symptoms. Most importantly, the erroneous inclusion of people with primary psychiatric conditions in CFS samples will have detrimental consequences for the interpretation of both epidemiologic and treatment efficacy findings.

Reeves et al. (2005) claims that the empirical definition identifies people with CFS in a more precise manner than can occur in the more traditional way. It is primarily the use of this new empirical case definition that has led to the increase in CFS prevalence rates in the United States. In their use of the empirical case definition, several changes occurred to what had been previously recommended by an international expert committee (Reeves et al., 2003) of recommendations for the case definition of Fukuda et al. (1994). First, rather than excluding those with depressive disorder with melancholic features, only those with a current condition were excluded as opposed to what had been recommended. Of interest, of those 16 within the Reyes et al. (2003) study who had been classified with CFS using the more traditional methods, 6 had a past history of major depressive disorder with melancholic features (Reeves et al., 2005); and it is unclear how many of those 43 who were diagnosed using the empiric case definition had past depressive disorder with melancholic features. These individuals should have been excluded, and by including them, the broadening of the case definition has the potential to bring into the CFS category those with a primary psychiatric condition. More importantly, there was little agreement between the empirical method of classifying individuals with the more traditional method of comparing whether an individual met the case definition on their critical symptoms. Rather than assuming that this might be a problem with the CFS empirical case definition, they concluded that the more traditional way of diagnosing patients was flawed. As an example of this problem, one individual who was classified as being in remission for CFS using the traditional method was diagnosed with current CFS using the CDC's empirical approach.

Papers are now appearing in the literature using this empirical case definition of CFS, and many have received considerable media attention. For example, Heim et al. (2006) recently used this new empiric case definition and the Wichita study to explore the influence of early adverse experience on risk for developing CFS. The authors concluded that childhood trauma is an important risk factor for CFS. In fact, among those with CFS, 62.8% had some type of early abuse. This is in contrast to findings reported by Taylor and Jason (2002) who found prevalence rates of sexual and physical abuse history among individuals with CFS were comparable with those found in individuals with other conditions involving chronic fatigue, including medically based conditions. Relative to those with CFS who report such history, most individuals with CFS did not report histories of interpersonal abuse.

The Reeves et al. (2005) article clearly used instruments (such as the SF-36) to make diagnostic decisions, rather than encompassing more specific criteria involving aspects of the illness (for example, whether with rest, all symptoms disappear). Given the high variability in symptom severity among persons with

fatigue, standardized procedures should be employed for determining whether or not a particular symptom is severe enough to qualify as one of the symptoms required for the diagnosis of fatigue. But one needs to be extremely careful about deciding whether standardized instruments and scores need to include contextual issues, and often they do not. For example, if a patient endorses a symptom such as post-exertional malaise, standardized questions should include duration, frequency, and severity of the symptom including onset, pattern, intensity, and associated factors (see Hawk et al. 2007). Clinical judgment, which has been used in most past studies to diagnose CFS, remains an important role even for diseases like lupus, which use a combination of clinical judgment, patient report, and objective measures to come up with a diagnosis. This currently is not occurring with the CFS empirical case definition developed by the CDC.

Some researchers have posited that FMS, CFS, and IBS can be considered functional somatic syndromes (Barsky & Borus, 1999). Functional somatic syndromes are characterized by diffuse, poorly-defined symptoms that cause significant subjective distress and disability, cannot be corroborated by consistent documentation of organic pathology, and are highly prevalent even in healthy, non-patient groups (Barsky & Borus, 1999). Accurate measurement and classification of CFS, FMS and IBS is imperative when evaluating the diagnostic validity of controversial disease entities alternatively labeled, 'functional somatic syndromes'. For example, results of a study by Taylor, Jason and Schoeny (2001) provided support for distinctions between the five conditions of FMS, CFS, somatic depression, somatic anxiety, and IBS, but this will only occur when using symptom criteria that matches actual diagnostic criteria for these illnesses. Measurement that fails to capture the unique characteristics of these illnesses might inaccurately conclude that only distress and unwellness characterize these illnesses, thus inappropriately supporting a unitary hypothetical construct called functional somatic syndromes. Ultimately, using a broad or narrow definition of CFS will have important influences on CFS epidemiologic findings, on rates of psychiatric comorbidity, and ultimately on the likelihood of finding biological markers.

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