Reviewer's report

Title: Prevalence of Chronic Fatigue Syndrome in Metropolitan, Urban, and Rural Georgia

Version: 2 Date: 13 February 2007

Reviewer: Peter White

Reviewer's report:

General

I think the authors have significantly improved this paper. I am happy with all the responses to my queries or suggestions, but with one exception; ascertainment methods, which are central to their main finding.

Major compulsory revisions

1. Possible ascertainment bias may explain their main finding

The authors have “stuck to their guns” with the methods they initially used, in spite of both referees asking for “major compulsory revisions”, particularly in order to avoid an ascertainment bias explaining their main finding of a much larger prevalence of CFS than they and others have shown in the past.

So what to advise?

This is the second largest population survey of CFS ever conducted, the largest having been previously reported by the same group of authors. They have found some important findings, with the most important being the unprecedented prevalence. The authors not unreasonably want to report this prevalence. But I do not think they have overcome the issue of ascertainment bias possibly explaining this main finding. One of the main reasons they have stated for not changing their methods of ascertainment is because they wish to compare their findings directly to other population studies, particularly their own previous survey in Wichita (Reyes et al, 2004). But, in order to fairly compare, they need to report the prevalence using the same ascertainment methods as previously; which they have not done. Reyes and colleagues screened people with fatigue, and did not include people with other symptoms, but without fatigue (a group which may or may not represent CFS). Therefore, I think that they should repeat the same ascertainment method in order to accurately compare prevalence figures. Of course, this only applies to individual screening, and not to the household informant regarding unwell household members.

Is there a compromise solution?

Yes, I think there is. If the authors want to stick to their current ascertainment methods, which they arguably justify on the grounds that people with CFS may report more cognitive or sleep difficulties rather than fatigue, then it could be argued that that is interesting data that should be reported; if CFS is more common than previously thought, this is very important public health information. BUT, in order to allow fair comparisons with previous prevalence rates, including their own Wichita study, they should also report the prevalence figures using the same methods of ascertainment as they and others have previously used, i.e. using fatigue alone as their baseline screening question. Although this will lengthen the paper, I would hope that this would be acceptable to the editor, particularly since the Journal is electronic, so that space is less of an issue.

I am sure that these eminent authors would want to take the opportunity to examine for ascertainment bias, which they themselves admit could at least partly explain their extraordinary findings.

2. Thresholds and criteria used for ascertainment

I would suggest that this alternative prevalence calculation should equally apply to the thresholds they chose, to make them internally consistent. I.e. the lowest/highest quartile from population figures for MFI general fatigue as well as SF36 sub-scales (which they already have done). This would be more consistent with “severe fatigue” and dysfunction than their current choice of the median figure for general fatigue for the population. I think the authors would struggle to justify the case that 50% of the population have fatigue severe enough to be consistent with CFS. I note the other referee is equally concerned about thresholds.
I would argue that this also means excluding emotional role as a criterion on the SF36 for the reasons I stated in my first review, but this is of more minor consideration than thresholds, and I would not stress the importance of this.

Minor essential revisions

The point prevalence of CFS found by Wessely and colleagues (1997) in primary care was 2.6%, not 4.1%, which fell to 0.5% once those with comorbid psychiatric disorders were excluded.

Discretionary
None necessary.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.