

## Reviewer's report

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

**Version:** 1 **Date:** 3 December 2006

**Reviewer:** Peter White

### Reviewer's report:

1. Is the question posed by the authors new and well defined?

Yes, it is, in that the novel aspects are:

- the state-wide sampling
- the study of prevalence across metropolitan, urban and rural populations
- the screen question being unwellness, not fatigue
- the use of standardised questionnaires to measure symptoms

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?

No; see major compulsory revisions.

3. Are the data sound and well controlled?

Not yet; I think the authors need to review their analyses.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

Yes.

5. Are the discussion and conclusions well balanced and adequately supported by the data?

I think the authors need to be more cautious in their interpretation of their findings of a much higher prevalence than previously found. They should also refer to similar findings of prevalence found in other countries.

6. Do the title and abstract accurately convey what has been found?

Yes

7. Is the writing acceptable?

Yes.

Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

1. The methods leave out non-English speaking people, which may have led to an under-sampling of ethnic minority groups, and possibly CFS, if there is a difference in those who do not speak the majority language. I note the authors weighted the sample to allow for ethnic differences. The authors should mention this in discussion.

2. The authors state that, "...those with a score  $\geq$  well-population medians on the general fatigue or reduced activity scales of the MFI were considered to meet fatigue criteria of the 1994 case definition." 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, which require: "clinically evaluated, unexplained, persistent or relapsing chronic fatigue (of least 6 months duration) that is of new or definite onset" (Reeves WC, Lloyd A, Vernon SD, Klimas N, Jason LA, Bleijenberg G, Evengard B, White PD, Nisenbaum R, Unger ER. Identification of ambiguities in the 1994 chronic fatigue syndrome research case definition and recommendations for resolution. BMC Health Services Research 2003;3:25 (published 31 December 2003).

<http://www.biomedcentral.com/1472-6963/3/25> ). In order to provide prevalence data consistent with previous criteria for CFS, the authors need to re-analyse their data for general fatigue alone on the MFI, if that is their preferred sub-scale to measure the severity of fatigue.

3. The authors state that, "Functional impairment was assessed by the medical outcomes survey short form-36 (SF-36) [13]. For classification as CFS, those with a score  $\geq$  25th percentile of population norms in

the physical function or role physical, or social function, or role emotional subscales of the SF-36 were considered to have substantial reduction in activities as specified in the 1994 definition.” The same criticism as in the paragraph above applies to their choice of SF36 subscales. 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”. I note that “role emotional” had the lowest correlation coefficient of any of the SF36 subscale scores with any of the three measures of CFS in one of the authors’ previous studies (Wagner D, Nisenbaum R, Heim C, Jones JF, Unger ER, Reeves WC: Psychometric properties of the CDC symptom inventory for the assessment of chronic fatigue syndrome. Population Health Metrics 2005, 3:8). 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.

4. There is a further problem about the choice of thresholds for both fatigue and functional impairment. For fatigue, the authors have chosen a median split from population norms, i.e. 50 % of the population would have a score of equal or greater than this. In contrast, they have chosen the bottom quartile score of population means. Why the discrepancy? This needs justification. Since the criteria for CFS include “severe” fatigue and dysfunction, it makes sense to make both thresholds the lower quartile from a population sample.

5. Furthermore the authors need to refer to the studies from which they took these population norms. I am aware of several population studies of working age adults using the SF36, but they give slightly different results, and the readers need to know which one they chose and why. I am not aware of any population studies of working age adults using the MFI. This reference should be given.

6. The authors state that, “For classification as CFS, those reporting ? 4 case defining symptoms and who scored > 25 on the SI case definition subscale were considered to meet accompanying symptom criteria of the 1994 case definition.” Having read the relevant paper, I am still uncertain by both what is meant by the “SI case definition subscale” and what a score of 25 means. This needs both clarifying and justifying.

7. What proportion of the three different geographical sample households did not have a working telephone at the time of sampling? This is important information in order to approximate the selection bias towards greater economic income. I would assume that this data would be available.

8. What proportion of those screened by telephone was fatigued but not "unwell"? This should be reported.

9. How did they work out the numeric value of the weightings? It would help the reader to give more details about this.

10. The authors give mainly univariate analyses results with limited interaction data. We need to see multivariate analyses to model all the examined factors that may influence the prevalence of CFS, so that confounding and interactions can be excluded or explored.

11. The authors describe similar findings across black and white people, but do not describe the ethnic groups adequately. What do they mean by “black”?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Reference 12 needs revision.

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

1. The description of the numbers and proportions found in sampling, telephone assessment and clinical assessment is complicated and it is hard to follow the numerators and denominators. I think readers would be helped by an algorithmic figure with the numbers (%) at each stage, with both true and false negatives and positives given at each stage of assessment.

2. The difference between metropolitan and urban areas seems somewhat arbitrary to this non-American referee. I suspect some further justification would help non-American readers

**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 importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.