Reviewer’s report

Title: Identification of ambiguities in the 1994 chronic fatigue syndrome research case definition and recommendations for resolution

Version: 3 Date: 5 September 2003

Reviewer: Susanne Merz

Reviewer’s report:

Like the authors, I find it necessary to improve the precision of case ascertainment in order to obtain better results in CFS-research. I have thus in my first review of the article made the following recommendations (among others):

1. The article should clarify that different research groups use different CFS definitions, which describe different groups of patients. Many reports claiming to study CFS actually study chronic fatigue (CF).
2. To as best as possible prevent CFS-research from including patients with diagnoses of exclusion, the article should summarize current knowledge regarding differential diagnosis.
3. The goal of being able to compare the patient material in different studies can best be reached if the Study Group recommends one single scale for rating CFS symptoms.
4. For research results eventually to find clinical application, it is illogical for CFS to be a diagnosis of exclusion for researchers but not for clinicians.
5. To avoid further confusion surrounding the term CFS, it is of utmost importance to summarize The Study Group’s recommendations in an easily surveyed fashion.

In my review of the article’s revised version (25 Jul 2003), the above five points of criticism still remain. I thus find that major changes are still required before the article can be published. (For that reason, I do not list the misprints, which are still present.)

To support my contention that the differences between different CFS-definitions are relevant (point 1 above), I cite recent publications of two members of The Study Group:

Jason et al:
“One factor that has contributed to the slow progress in research concerning CFS is a lack of consensus among health care professionals regarding the diagnostic criteria for CFS” (1, p 412).

“... it might be inappropriate to synthesize results from studies of this illness that use different definitions to select study populations” (2, p 3).

Evengård et al:
“Because CFS patients (compared to patients with CF) have more somatic symptoms, more often report an infectious, sudden onset and have less psychiatric comorbidity, and CF patients seem to have more of an emotional, burn-out-like component one could speculate about the existence of different pathogenetic backgrounds behind the two diagnoses” (3, p 361).

If the authors’ goal is to improve “the precision of case ascertainment” (according to the article’s p 3), it is therefore fundamentally wrong to refer to “considerable overlap in all of the case definitions” (Author’s response to reviews, compulsory revision 3a).

Many of the article’s references use different CFS-definitions than that from 1994. If one
nevertheless chooses to cite such studies (which is questionable from a scientific point of view), one
should at least add that patients fulfilled for example the Oxford criteria for CFS. It should not be
assumed that the reader knows that there are fundamental differences between the different
CFS-definitions and how the definitions differ. Rather, that should be explained by the article’s
summary of CFS-research’s background. Only after these differences have been clarified is it
meaningful to tackle the ambiguities in the 1994 CFS research case definition and make
recommendations for their resolution.

Regarding points 2-5 above, I refer to my first review, where I supported those points with
references. In response to the authors’ comments on my criticism, I would like to add the following:

Much new knowledge concerning CFS differential diagnoses has come in recent years. Regarding
diagnosis of exclusion, in today’s state of the art there is certainly more to recommend than just a
sleep workup. A minimum requirement is to make the reader aware of the importance of thorough
differential diagnosis and cite references, for example, those I cited in my first review. The authors
write that none of the investigations I recommend are “clinically indicated tests for CFS”. Indeed! If
there were clinically indicated tests, which support a diagnosis of exclusion (e.g. CFS), it would not
be a diagnosis of exclusion!

The FibroFatigue scale was published in June 2002. To expect that scale to be internationally
recognized a year later seems absurd. That scale (in contrast to the scales the authors describe)
was developed for patients meeting the CFS-criteria of 1994 and therefore spans the entire range of
CFS symptoms. The authors discard The FibroFatigue Scale because it is not standardized and
validated. But the Centers for Disease Control and Prevention Symptom Checklist they recommend
has (likewise) “not been formally validated” (p 9). The authors themselves admit where the problem
lies when they comment on my suggestion that they recommend a single rating scale: “To follow her
recommendation would obviate our reason for preparing the article” (author’s response to reviews,
compulsory revision 3d).

The authors greet me as Dr. Merz, so I assume that the information on my background, which I
provided the editors when I accepted this peer review, has not reached them. I am not an MD but
have long experience in medical rehabilitation and a special interest for unusual diseases. Since
1997, I have mapped out different CFS differential diagnoses (6, 7) and am therefore familiar
with the difficulties of evaluating and diagnosing CFS. I have also developed a CFS diagnosis form (7),
which is quite doable. A requirement is that it be revised as new knowledge accumulates.

References:
1) Jason LA, King CP, Frankenberry EL, Jordan KM, Tryon WW, Rademaker F et al. Chronic fatigue
2) Jason LA, Helgerson J, Torres-Harding SR, Carrico AW, Taylor RR. Variability in diagnostic
criteria for chronic fatigue syndrome may result in substantial differences in patterns of symptoms
and disability. Eval Health Prof 2003;26:3-22.
3) Evengård B, Jonzon E, Sandberg A, Theorell T, Lindh G. Differences between patients with
chronic fatigue syndrome and with chronic fatigue at an infectious disease clinic in Stockholm,
4) Sharpe MC, Archard LC, Banatvala JE, Borysiewicz LK, Clare AW, David A, et al. A report -
chronic fatigue syndrome: guidelines for research. Journal of the Royal Society of Medicine
1991;84:118-121.
5) Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A and the International Chronic
Fatigue Syndrome Study Group. The chronic fatigue syndrome: a comprehensive approach to its