Reviewer's report

Title: Clinical Correlates of Chronic Cerebrospinal Venous Insufficiency in Multiple Sclerosis

Version: 3 Date: 16 January 2012

Reviewer: Brenda Banwell

Reviewer's report:

Weinstock-Guttman et al have revised their prior submission according the comments of the reviewers. The manuscript has been improved, however a few points remain:

1. Abstract: data that only trends to significance is best removed from the abstract. The concluding sentence should read “...but has no or very limited”, rather than “...none or very limited”.

2. Introduction, last sentence, would be more accurate to state “.venous hemodynamic findings according to the Zamboni CCSVI criteria with clinical disease severity and classification of disease status as relapsing or progressive.” The authors did not look at CCSVI criteria at presentation, and Zamboni did not provide a clinical classification (as would be inferred based on the current placement of his name in the sentence).

3. Page 11, “CCCVI” should be “CCSVI”

4. Page 14, “.and the CCSVI” should be “...and CCSVI criteria”

5. Page 14, 1st paragraph “...than the originally reported sensitivity and specificity” should be made clear “...than the 100% sensitivity and 100% specificity reported by Zamboni et al (ref)…”

6. Page 14, paragraph 2 is extremely poorly written and should either be re-written or removed.

7. Page 15, paragraph 1 “.. no association between disease status and MS”?? Do the authors mean “no association between disease status and CCSVI”??

8. Page 15, paragraph 3 is poorly phrased and is pure conjecture. I would advocate that this paragraph be removed.

9. Page 16, paragraph 2 remains highly theoretical and is not addressed directly by the authors’ work. The paragraph dilutes the key messages of the paper and would be best removed.

10. Reference 39 does not appear to address MS pathology, and certainly does not evaluate whether venous valve changes over time contribute to CCSVI VH scores. Please revise this statement and reference appropriately.

11. The authors comment on the absence of CCSVI findings in degenerative diseases, such as Parkinson’s. However, they also state that some aspects of CCSVI might contribute to the neurodegenerative components of MS. How do
they marry these points? Furthermore, are venous drainage issues and/or hemosiderin in the brain not core components of several dementias? This section of the text should either be more fully addressed or removed.

12. The final paragraph should state the core finding of the present work- that features of CCSVI have no relationship to disability. This is the most important statement of the paper and warrants emphasis.

**Declaration of competing interests:**

My only conflict is that I have a funded CCSVI study research grant (as disclosed previously).