Reviewer’s report

Title: Lifestyle factors, demographics and medications associated with depression risk in an international sample of people with multiple sclerosis

Version: 3 Date: 23 September 2014

Reviewer: Anne Kavanagh

Reviewer’s report:

This is an important paper which provides a wealth of information about associations between lifestyle risk factors for multiple sclerosis. My main problem is that I believe there is a risk of substantial reverse causation which they argue in the discussion is unlikely to be large. It is possible that at least some of the benefits could be overestimated because depression may also cause less healthy behaviours (perhaps through low motivation). In reality the associations are likely to reflect effects occurring in both directions.

The paper is well written, the questions are well articulated and, in the most part, they have used well-validated instruments. The abstract and title are clear.

Major compulsory revisions:

1. Please modify discussion to reflect my concerns with respect to reverse causation outlined above.

2. As all the data is self-report there misclassification (measurement error) is likely. It is also likely that this error is correlated between the exposures and outcomes due to some unmeasured variable such as personality type resulting spurious associations. Please discuss the possibility of measurement error due to self-report and the potential for this to be correlated between the exposures and outcomes (dependent misclassification) thus biasing results. The degree to which this is a problem is not known. Did the authors test the association between doctor diagnosed depression and PHQ2 in this sample? If this is strong this provides some evidence that the findings are robust.

3. Is it possible to test for more categories in the meditation analysis - once a week is still infrequent? It would be interesting to see if more frequent meditation had a stronger association.

4. Throughout the manuscript the authors say “x times the risk” when the estimates on the odds ratio scale. At the start of the results paragraph on demographic risk factors and depression they do present results on the odds ratio scale however later in the paragraph and elsewhere in the manuscript they revert to using language which implies they are estimating the relative risk. (e.g. Participants who were separated or divorced had 1.7 times greater depression risk than those married or co-habiting.)

5. I think marital status should be included in the model as a potential confounder and suggest they collapse the categories and include it.
6. I suggest they delete the sentence on why they did not present analyses separately by gender. The fact that there are no differences in prevalence of depression is not the issue. Stratification is only needed if they believe that there is effect modification (where the lifestyle/depression associations differ by gender).

7. Please include 95% confidence intervals on the odds ratios in Table 2.

8. Spell out SPQ when first used.

9. Under the section on data analysis the authors say “due to variation in item completion, analyses were calculated using item response as the denominator”. I do not understand what they mean by this? Do they mean missing variables or items on a scale (e.g. PHQ2)?

10. Could the authors please provide information on the extent of missing information on all the variables? Also how many people did not complete all items on the scales and what did they do about this. Are there standard procedures for dealing with missingness on the PHQ2?

**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.

**Declaration of competing interests:**

I have MS and have attended the retreat run by Professor Jelinek. I am a highly skilled epidemiologist and have applied these skills in reviewing this paper.