Reviewer’s report

Title: Midlife insomnia and mortality. The Hordaland Health Study

Version: 2 Date: 30 May 2014

Reviewer: Tetyana Kendzerska

Reviewer’s report:

Thank you for the opportunity to review this study.

In the study “Midlife insomnia and subsequent mortality: The Hordaland Health Study” performed by Sivertsen et al, having an insomnia as defined by the Karolinska Sleep Questionnaire had been found to be associated with mortality risk controlling for potential confounders.

In a light of conflicting evidence on the relationship between insomnia and mortality, this study is very important; however, I have some concerns with the manuscript as written.

Major issues:

1. The sample size (number of events of 160) of this study is relatively small, as was nicely described by authors in the limitation section, introducing uncertainty around estimated effect of insomnia and restricting number of potential confounders to be included in the statistical model. As such, it is very important to include the phrase from the limitation section “Therefore, the findings, and especially those from the fully adjusted analyses, should be interpreted with caution and repeated by studies based on larger samples.” in an abstract to bring a reader attention.

Further, through the abstract and discussion section authors emphasized the positive results based on the subgroup analyses with the number of events not sufficient to perform statistical adjustment (men subgroup, n of events = 67; short sleep duration <6.5 hours subgroup, n of events = 34). With such a small number of events I would recommend to avoid subgroup analyses. Instead, authors may visualize effect (present plots for interactions) of gender and sleep duration on an association between insomnia and mortality or may report HRs for men with insomnia compared to women with insomnia etc.

Consequently, the results from subgroup analyses couldn’t be used to make a strong conclusion “Insomnia was associated with a four-fold risk of mortality in men during 14 years follow-up.”; how it was done in this study without emphasizing that results from subgroup analyses should be interpreted with caution.

Subsection, sample size consideration or power calculation, is required for clarity.

2. Lack of information on self-reported data completeness. Amount of missing values need to be described in the manuscript. As well as information how
missing data was handled.

3. In discussion section authors stated that “we cannot disregard the possibility of multicollinearity”. Did the test for multicollinearity was performed? The results from the multicollinearity test will be beneficial to include, as well as from testing model characteristics: model internal validation, model predictive and discriminative abilities.

4. The Karolinska Sleep Questionnaire Scale was used to define insomnia – this information needs to be included in an abstract. Also brief description of the measurement properties of this scale including validation against clinical diagnosis would strengths this study.

Minor issues:
1. Did all participants have follow-up of 14 years? If no, medium follow-up or range needs to be provided.
2. In an abstract, authors stated “Adjusting for several possible confounders” – details would be beneficial for readers to understand the model.
3. Did you consider U shape relationship? Did you test for linearity? If so, details need to be provided in the methods section.
4. In the results section authors stated: “The interaction between insomnia and gender was statistically significant (P = 0.023)” – in which direction?
5. In the discussion section authors stated: “The effect of insomnia was especially strong for men, and among insomniacs who also reported short sleep duration.” - based on the underpowered subgroup analyses that needs to be mentioned.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:
I declare that I have no competing interests