Reviewer’s report

Title: Sex differences in dementia: On the potentially mediating effects of educational attainment and experiences of psychological distress

Version: 1 Date: 23 Dec 2019

Reviewer: Eva Hogervorst

Reviewer's report:

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This is an interesting paper attempting to investigate the association of sex differences in dementia by including distress, age and education in the model. The introduction is well written and gives a good overview of the rationale.

On page 6: row 46 I would not talk about the 'effect' of sex but rather the association of sex with dementia. I do think the authors skip a little bit too fast over the age effect. If women reach an older age than men and age is one of the strongest risk factors for dementia and men are no longer part of the statistics because they died of CVD or in fact survived because they did not have CVD risk factors which are also dementia risk factors, then surely age is a major factor as is also shown in the analyses. I would like a little more attention to that age-effect.

On page 9 it is not clear whether the 'longstanding stress' includes 3,4 and 5? Please describe. Also how valid is the depression question? Why was not a standard questionnaire used?

My main concern is the lack of crucial other variables such as SES related to education and distress as also outlined in the introduction and related to SES, distress and dementia other in particular CVD risk factors which could have explained the association such as smoking drinking obesity (stress eating) etc and on the other hand engaging in psychosocial activities (exercise, meeting people etc) which could have offset and explained the effects n reverse.

In the results I would have liked to have seen in text the % of women with depression and dementia and difference in education

I am not clear what was done with the FA results and the schema in fig 1. The results could benefit from a good look from a SEM specialist also considering the low numbers of people with dementia. I found them not so easy to follow. I gathered the female sex is related to an older age, lower education and more distress but distress in further analyses and from the table but not fig 2 no longer relates to dementia. So in the final model, education and distress are no longer related to dementia? For education as the authors surmise that can happen when you include APOEe4. So I am not sure whether we can conclude that the female association with dementia is mainly explained by education and age? Distress itself
is associated with the female sex and education but no dementia in controlled analyses? There is also the reverse causality issue of distress being caused by dementia onset which was addressed by the authors.

An interesting read but may need some additional checks, apologies it is too close to XMas maybe. Merry XMas and a happy 2020

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Unable to assess

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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