Reviewer's report

Title: Associations between air pollution and perceived stress: the VA Normative Aging Study

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Reviewer: Rakesh Ghosh

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This study is interesting because perceived stress has mostly been investigated as an exposure in epidemiological studies. The authors investigated if there is an association between air pollution exposure and perceived stress in a setting with relatively low air pollution and demonstrated associations. Whether this association is causal is far from being established.

Major Compulsory Revisions

1. On page 7 and table S1 the authors note significant differences between those included in the analysis vs. those who were eligible but not included. What is the possibility that this might induce selection bias and whether the authors think it deserves to be acknowledged?

2. There is huge loss to follow-up from visit 1 to visit 3 or 4. The authors estimated the probability of participation in future follow-up, calculated the inverse probability weights and used it to adjust for survivor bias. The logistic regression model included PSS scores.

   Is this adjustment sufficient to account for attrition or is there any attrition bias i.e. are those with higher (or lower) stress less (or more) likely to participate in subsequent follow-up visits?

3. An interesting aspect of this paper is that the authors chose to present the results for two types of exposure – estimates from central site monitors and modeled exposures. However, the two types of exposures are not presented or compared before the exposure-response associations were presented. A thorough presentation of the distributions and correlations of the two types of exposure would put the two types of results in context of exposure misclassification.

4. What do these results, from the two types of exposure models, mean in terms of bias due to exposure misclassification. PM2.5 association was higher from LUR based model compared to the association from the central site exposure model. Does that mean there is a higher degree of non-differential exposure misclassification in the latter models, leading to a classic example of bias towards null? But less precise LUR estimate (with wider confidence interval) demands perhaps more complex consideration of Berkson error.

   For BC the results are opposite i.e. LUR model estimates have lower magnitude
compared to the central site exposure results. This brings up the point that PM2.5 is generally considered to be a regional pollutant and BC is a near-roadway pollutant (mobile sources). Does the exposure modeling despite using these variables “cumulative traffic density within 100 m” and “distance to nearest major roadway” capture the near roadway spatial gradient of BC adequately (for these 987 participants), because BC generally has more measurement error in regional models (see Lancet 2009; 374: 2091–2103).

Minor Essential Revisions

1. The authors chose to present 6 different pollutants from the central site monitors but only 2 from the LUR. Were there no predictions for the other ones?

2. The authors adjusted for covariates available at both individual as well as area level (e.g. race and education) in their models. Please explain the need for such adjustment and if there was some unexplained variance in the one level model that was explained by the inclusion of the area level indicators (additional level).

3. When the authors mention that the total score for perceived stress was obtained by adding the scores and higher scores indicate higher stress, please also mention that the scores of the positive items in the 14-item scale was reversed prior to these steps.

4. Table 4 and the text gives the impression that the actual PSS scores was the response variable but y axes in figures 1 and 2 used the difference in scores implying some difference in PSS scores was used. Given the high attrition, this seems unlikely. The y axis label is confusing, please consider rewording.

5. Please clarify wording while comparing the estimates from the two types of exposures. Higher or lower associations that refers to the magnitude of the regression coefficients and separate it from the strength (stronger or weaker) of the associations, which refers to the p values. Consider rewording the sentence on page 20 (end of the paragraph before conclusion) – “……..however the associations for predicted PM2.5 and BC were of stronger and weaker magnitude………..”. And the same for the last few lines of results sections before the discussion section. The clearest way it was described was the first two lines on page 17.

6. Please check sentences:
   Pg 5, 2nd paragraph – “Less is known the potential effects …”
   Pg17 middle of the paragraph - “Air pollution was also more strongly with emotional symptoms………..”.

Discretionary Revisions

1. Please consider adding the range of distances of the central site monitors from participant homes in the methods where the median was presented.

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:

No conflicts of interest.