Author's response to reviews

Title: Role of respondents' education as a mediator and moderator in the association between childhood socio-economic status and later health and wellbeing.

Authors:

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Version: 4 Date: 27 September 2014

Author's response to reviews: see over
Dear Editor-in-Chief,

Please find enclosed our revised manuscript, “Role of respondents’ education as a mediator and moderator in the association between childhood socio-economic status and later health and wellbeing.” by Sheikh, M.A., Abelsen, B., Olsen, J.A..

Please note that we have changed the title of the paper. A very positive discussant on the paper at a recent a conference suggested this alternative title. We think this is a better one and would like to change it, if the editor would agree.

We are grateful to the two reviewers for their detailed comments and suggestions for improvements of the manuscript. Below you will find our response to the reviewers (referred with line numbers in the manuscript). The text from the reviewers is in blue.

Reviewer 1:

The authors made many changes in response to the first set of reviews, and I think generally in the right direction. I remain skeptical that identification assumptions for the natural effects are satisfied, but the authors do raise this dubious assumption as a caveat (lines 437-440), and so at least the paper is honest in this regard. Likewise, although I am not fond of self-rated health as an epidemiologic outcome, the authors also state caveats about these measures, and so the paper discloses these weaknesses appropriately.

I am also not comfortable with all the attention to what is "statistically significant", but we have to pick our battles.

We understand that the reviewer 1 find the paper acceptable in its form. We are very thankful for the comments, and feedback.

Reference 38 is not complete (needs volume, issue and page numbers).

We could not find the paper online on the Stata Journal. The authors informed us that the paper is still in preparation. We have modified the reference accordingly.

Reviewer 2:

1. I agree with Reviewer 1 that the addition of the estimation of the controlled direct effects of childhood SES on self-rated health is worthwhile, but I am not convinced that these have been estimated or interpreted correctly. It is not clear why or how there are two CDEs of CSES on self-rated health – one for high and one for low respondent’s education. My understanding is that there should only be one CDE for the effect of each CSES variable on self-rated health, which is interpreted as how much self-rated health would change on average if respondent’s education were controlled at level m uniformly in the population, but child SES was changed from level a*=0 to level a=1.

It is correct that the CDE will be interpreted as “how much self-rated health would change on average if respondent’s education were controlled at level m uniformly in the population, but child SES was changed from level a*=0 to level a=1”. The level “m” can be any level of the mediator, and can be as many CDE’s for the same binary exposure, as the number of levels of
the mediator. Since the mediator was dichotomized, we have reported two CDE’s for each exposure. This is explained in lines 364-366, and lines 451-456.

2. I don’t think the assumptions required for these analyses hold, particularly that there are no M-Y confounders that are caused by X. The authors provide justification that spouse’s education, presented as an M-Y confounder in the DAG, is caused by X. Age is also likely to influence the other childhood SES variables, which are also M-Y confounders. So the NDE, NIE and CDE are not correctly estimated. The authors report that they have omitted the term ‘causal’ when describing the DAG, but their interpretations of the effects through the results and discussion are written as though the effects are causal.

We agree that the assumptions required for these analyses do not allow us to interpret the estimates as causal. The estimation of CDEs does not require the assumption of no mediator-outcome confounder effected by the exposure. However, we will also like to state that unless both the exposure and the mediator are randomized, these assumptions of unmeasured confounding will never be fulfilled from any observational study. Moreover, these assumptions are not specific to this statistical analysis. Therefore, the same can be said about almost all the papers we have cited, and almost all the papers published in this field, using observational data. Still, we certainly accept the methodological importance of your point and have added the explanation in the text (see line 431-450)

Are there no additional confounders that could be added to the analyses?

Unfortunately, there are no other confounders that we could include in the analysis.

And is paramed the correct method for this research question, when M-Y confounders are caused by X and/or C? Is there another method (along the lines of marginal structural models/g computation) that would deal more effectively with these confounders, and also the interactions that paramed can deal with?

Although a lot has been written about these methods in theory, but software development is still in its infancy. All statistical methods require the assumptions of unmeasured confounding. We believe that PARAMED is the correct method to use here. Each statistical approach (Generalized (G) methods) has its caveats, for example inverse probability weighting of Marginal Structural Models can have the problem of unstable weights. Similarly, the stata command GFORMULA can be used for both the G-formula, and the Marginal structure Models but does not allow estimating RR’s directly. It only provides OR’s, which cannot be interpreted as RR’s in our dataset.

3. The results in the abstract should clarify whether the effects are NDEs or CDEs. This has now been corrected.

4. The fifth paragraph of the Discussion contains much speculation relating parents’ education to their occupation that is not supported by data in the results or other evidence. The authors should refer to other research that supports their theory here.

We had tried to provide some potential explanation of our findings. However, we accept that this paragraph might have a speculative tone and have therefore chosen to delete it.
5. Abstract, Results, line 38: “…while for women the increased risk by 16%...” should read “…while for women the risk increased by 16%...”.
This has now been corrected.

6. In the Statistical Analysis section, sometimes NIEs are written as NIDs.
This has now been corrected.

7. Results, second paragraph: “Men had a higher risk of being classified as unhealthy on the composite EQ-5D measure…” should read something like “Among men, childhood financial situation had a stronger effect on the composite EQ-5D measure…”. The same correction is also required for women in that paragraph, otherwise it reads as though sex is the exposure instead of childhood SES.
This has now been corrected.

8. The final sentence of the conclusion needs some editing particularly on “… in addition to effect adult SES...”.
This has now been corrected.

We are grateful for the helpful suggestions, and hope our revisions are meaningful. We look forward to hearing from you at your earliest convenience.

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