Reviewer's report

Title: A three generation study of the intergenerational mental health relationships between grandparents, parents and children

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Reviewer: Rolieke AM Cents

Reviewer's report:

Dear editor,

thank you for the opportunity for reviewing this manuscript.

Up to know, there are few studies that assessed the transgenerational effects of psychiatric disorders beyond two generations. By including over 4600 families with data on grandparental, parental and child psychiatric problems, the authors aimed to examine the transgenerational effects of psychiatric problems over the course of three successive generations.

The authors are correct in stating that, up to now, there are few studies examining the effects of psychiatric history on children's development beyond the parent-child relationships, and findings of those studies are mixed with some reporting direct effects of the grandparental generation on the child generation, and others reporting indirect effects, i.e. effects that are no longer significant once corrected for psychiatric problems of the parental generation.

As the introduction currently reads, one of the main selling points of the current manuscript is the availability of data on how much time the grandchild spent with his or her grandparents. However, in my opinion, this information is currently not optimally utilized: the measure of child contact with their grandparents is dichotomized into two very broad categories 'frequent contact' and 'infrequent contact'. Maybe the authors can elaborate more about the original report form (amount of categories), and create more categories to optimize the variability of the measure.

The study sample included children, parents and information on grandparents from two cohorts: children aged 4-5 years, and children aged 8-9 years. For the analyses, the data on the two cohorts are put together and a cohort-variable is added as a covariate. As it reads from Table 4, the effect of cohort, and therefore the child's age, is statistically significant. What happens to the reported effects once the cohorts are tested separately? Also, children aged 4 to 5 are in a different phase of development (transition to school) than children aged 8-9, maybe parental or grandparental psychiatric problems have different effects on different ages. Maybe the authors can comment on this?

The measure of child outcome, the Strength and Difficulties Questionnaire was assessed at Wave 3. As I understand from the manuscript, there was also data
collected at two earlier waves. Did these waves also include data on behavioral outcome? If so, would it then be possible to look at time/age effects using repeated data?

As for the measure of child outcome, the authors choose to dichotomize the data. However, with such a large sample size, isn't it possible to analyse the data continuously? This would increase power.

Similarly, the measure of parental psychiatric problems could also be assessed continuously.

If I understand correctly, information on child and parental psychiatric history is assessed at the same wave and is therefore assessed cross-sectionally. It is therefore more difficult to draw causal conclusions from the current study, and also reporting bias is an important issue as the same parent also reported on child outcome. Authors should comment on this and also state this as an important limitation of their study.

What I find a major drawback of the current study is that information on grandparental psychiatric history is assessed retrospectively by asking the parent 'whether or not his/her father/mother suffered from nervous, emotional trouble, or depression' yes or no. Besides the fact that this information is not assessed by using a standardized method, it is a very broad measure, and also very likely to be subject to reporter bias. Is there any information available about the parent-grandparent relationship or the state of mind of the parent at the moment of reporting about grandparental psychiatric history, so that an effort can be made to adjust analyses and try to diminish reporter bias?

There are some questions on covariates used in the analyses:
Why isn't maternal age at birth of her first child used continuously?
How are 'ongoing medical conditions of parent or child' assessed? What does this measure include, and what is the rational for including medical conditions as a covariate?

I miss a table with descriptive statics including all variables, also the covariates.

The presentation of the descriptives of psychiatric problems in the grandparent-parent and parent-child generations are not very clear; from the table 1 and table 2, statistically significant differences cannot be read, no p-values are reported. Also, in the text and above the tables it should be stated that values are based on crude analyses.

As for the analyses including face-to-face contact with the grandparents, page 13, I do not understand why the analyses are stratified? Why not perform adjusted regressions? Similarly for table 3, as for Tables 1-2, the format is not clear; it is hard to read from the table which differences are statistically significant, and which are not. It follows that children with maternal grandparents with a history of psychiatric problems, and not children with paternal grandparents with a history of psychiatric problems, have more behavioral
problems. Then, why not assess the association (as presented in table 4) separately for maternal and paternal grandparents? Do the authors have an explanations for this finding? It would be interesting to elaborate some more on this in the discussion.

As the face-to-face contact variable is a selling point of the current article, why not include it in all analyses. it was hypothesized before-hand that it is an important covariate....

In the introduction as well as in the discussion, the authors talk about direct and indirect mechanisms of transmission of risk, and about genetic and environmental mechanisms. However, they give little background on how they hypothesize the different mechanisms work. A bit more elaboration would help the reader to better understand the hypothesized pathways.

Do the authors have information on whether or not the parents or the grandparents are the biological (grand)parents of the child?

Some minor points:
the grammar of the first sentences of the results-section of the abstract is incorrect.
references should be included in the introduction where the authors discuss limitations of previous studies (second paragraph, page 6).

I hope my comments were helpful.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

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