Reviewer’s report

Title: Adverse childhood events and risk of diabetes onset in the 1979 National Longitudinal Survey of Youth Cohort

Version: 1 Date: 07 Jan 2019

Reviewer: Susan Marshall Mason

Reviewer's report:

This study examines the association of adverse childhood events with later onset of Type 2 diabetes. Because this association has been examined in several other studies, the major contribution of this analysis is assessing the role of a range of health risk behaviors as possible mediators. This is a significant topic, although I had some questions about the methods and presentation of results. Comments below:

Major

1. The authors state that ACEs were measured in 2012, but then describe their modeling approach as censoring individuals who were lost to follow-up before 2012. Am I correct that those individuals lost to follow-up would not have had info on ACEs? It seems that they should have been excluded. Please clarify.

2. Please provide more information on response rates over time and exclusions. Does the analytic sample include all those enrolled in 1982, or just those with ACE reports from 2012? I assume those with diabetes at enrollment were excluded? Any other exclusions?

3. Please examine whether there are any interactions between ACEs and risk behaviors in predicting T2DM, because the presence of interaction between the exposure and mediators complicates mediation analysis and interpretation (see, e.g., VanderWeele TJ, Mediation Analysis: A Practitioners Guide. Annu Rev Public Health. 2016;37:17-32).

4. Change in significance is not a useful metric for assessing mediation, since p-values are driven both by magnitude of effect estimates and power/sample size. In results text, please report differences in ORs in models with and without adjustment for risk factors and base interpretation on the magnitude of differences.

5. I am not sure what stratification by race/ethnicity adds, as it is clearly underpowered (overall there is an association of ACEs with T2DM but no one group shows this). I think
the authors should either eliminate this analysis or consider it to be exploratory and present ORs and 95% CIs without relying on significance testing to interpret results.

6. Results would be improved by greater clarity about which models results are from and what these are trying to estimate. For example, Model 1 in Table 4 might be referred to as a 'total effect' or 'confounder-adjusted' estimate as it is adjusting only for covariates thought to be confounders. Model 2 would be estimating the 'direct effect' after adjustment for BMI. Likewise Model 3 would be the 'direct effect' estimate after adjustment for BMI, tobacco, and alcohol. (See Tyler Vanderweele's papers on mediation analyses for information on these terms.)

Minor

7. In results, there are numerous findings presented having to do with how each covariate is associated with T2DM. It would streamline the paper to pare this down, and focus only on the central questions the paper addresses. Specifically, it would be appropriate to examine the ways that the exposure (ACEs) is related to potential mediators, and from mediators to T2DM, and this could be presented as an analysis of the proposed pathways along this mechanism. Information on other covariates is less relevant and somewhat distracting to the flow of the paper.

8. The difference between 'current smoker' and 'daily smoker' is not clear, particularly in abstract and results.

9. The p-value for comparison of number of ACEs in women with T2DM versus those without is different in results (bivariate results) than in abstract.

10. Throughout, it would help to give age at 2012 to better understand T2DM risk.

11. At the top of p 13 the authors present crude ORs instead of confounder-adjusted ORs for individual ACEs. Is there a reason they preferred crude ORs? It seems that seeing the confounder-adjusted ORs would be helpful.

12. Page 15 - ACEs did not predict T2DM in men. Is this after confounder adjustment? Earlier results say that 4+ ACEs were associated with T2DM in men.

13. In discussion, it should be noted that findings of an ACE-T2DM association only within women is consistent with prior literature finding sex differences in ACE effects with regard to obesity and other outcomes.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Unable to assess

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

Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes

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I am able to assess the statistics

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