Reviewer’s report

Title: Stress mediates the relationship between sexual orientation and behavioral risk disparities

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Reviewer: Edwin van Wijngaarden

Reviewer’s report:

This manuscript examines the presence of excess behavioral risk among sexual minorities, and aims to determine which factors may be mediating this excess risk.

Major Compulsory Revisions:

1. The authors used NHANES 2005-2010 data for their analysis. While this is a nationally-representative database with a large sample size, it does not lend itself very well to examine the mediation question that the authors are interested it as cross-sectional data are ill suited to address questions that are longitudinal in nature. While the authors appropriately acknowledge this limitation, it is a real substantial limitation to evaluating the causal mechanisms they intend to identify.

2. The conceptualization of the issue at hand and construction of variables and analysis plans are somewhat unclear. The use of a theoretical framework (Theory of Minority Stress) is a strength of the manuscript, but which particular constructs based on this framework are key is not clear ("stress" is a bit too broad). Consequently, defining constructs of mediators that are meaningful and that have been captured in the dataset appears to have been a challenge, and I am not convinced that the mediators chosen are the best measures. For example, depression (as a measure of psychological stress) could be considered a correlate or even consequence of risky health behavior rather than a precursor. There is little evidence provided for their choice of this measure, and the NHANES dataset does not allow one to assess the temporality or causal mechanism. As for physiological stress, the authors chose CRP and cite a recent meta-analysis. However, multiple articles have now been published (include those using NHANES) that have used a more comprehensive measure of cumulative physiologic dysfunction as a proxy for the allostatic load concept. CRP is only one indicator of this broader construct. It should also be noted that CRP could be a consequence of some of the risky behaviors such as smoking. The NHANES dataset will not allow one to distinguish these possibilities.

3. Related to the previous point, it is unclear to me how biological indicators of stress could be mediating the relationship between psychological stress resulting from societal and other aspects of being a sexual minority. It could be a consequence of such stress or be a correlate of it, but I have difficulty understanding how it would be in the causal mechanism with behavioral
The authors would do well to draw up a directed acyclic graph (DAG) to better outline the causal paradigm which in turn can guide the statistical analysis plan.

The limitations brought up in points 1-3 make it difficult to interpret the findings or judge their contribution to the literature.

4. Why were data from NHANES 2005-2010 chosen. Did cycles prior to or after this period not have the data necessary available?

5. Sexual orientation: what was the N for those who answered "something else", "not sure" or "don't know"? It seems that it may be meaningful to include these individuals in the analysis as they would likely also experience psychosocial stress (i.e. they did not identify as heterosexual, the majority group).

6. I disagree with the authors' conclusion that the "findings support the theory that stress may be a driver in health-related disparities among sexual minorities." While the theoretical framework used certainly seems to suggests so, the study design does not really lend itself to shed adequate light on this issue and the findings shown in Table 3 suggest such a small impact of magnitudes of association (regardless of statistical significance) that it questions the clinical/public health significance of the results.

Minor essential revision:

7. Please clarify why the Sobel test was used; this test has been common in analyses of mediation, but there are more sophisticated modeling techniques available (such as structural equation modeling) to identify causal mechanisms.

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