Reviewer's report

Title: Racial disparities in infant mortality: What has birth weight got to do with it and how large is it?

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Reviewer: Enrique F Schisterman

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The authors present here an interesting example that utilizes analytical techniques developed by the co-authors, in order to answer an important question regarding the role of differences in the birth weight distribution in describing racial disparities in infant mortality. The research question is well stated, and an important one in terms of potential policy implications. Considerable attention is given to developing the methodology, and in applying it to the question of interest. However, many questions remain unanswered regarding the implementation, and appropriateness of the applied methods. The authors also fail to acknowledge other important developments in the literature relating to the issue of the pediatric (or birth weight) paradox and effect decomposition. Specific comments are given below.

Discretionary Revisions

1. The authors refer in several places to the “pediatric paradox”. Perhaps the authors could acknowledge that they are referring to what is also commonly known as the “birth weight paradox”.

Minor Essential Revisions

1. The assumptions of the model itself are not made explicitly clear. A discussion of the assumptions, as well as the appropriateness of the assumptions in this scenario would be helpful for the reader to know when the model can/should be applied. Also, a discussion of other possible applications of the method would be useful.

2. The discussion of the pediatric paradox revolves in this case around racial disparities. However, as mentioned in the text, this phenomenon has been observed with various types of stressors. The authors conclude that the direct effect among compromised births is responsible for the pediatric paradox. However, there have been several developments in the literature that demonstrate that the crossing of the curves can be entirely explained by unmeasured confounding factors (Basso & Wilcox 2009), or if not due to unmeasured confounding, then due to an interaction between underlying conditions and birth weight (Hernandez-Diaz et al. 2008). The authors should acknowledge other work done in this area, and describe how their work fits into this body of research. The manuscript also states that a “long term goal is to
categorize the various stressors known to influence infant mortality by their corresponding “direct” and “indirect” effects…” Thus, it seems that if this analysis is truly to be applied for each of the various stressors, there should be more of an in depth discussion of the biological rationale for direct and indirect effects for each of the factors. The biological rationale for the observed results should also be given in this case—how would race directly affect mortality (even if it is a proxy for another factor)?

3. Can the authors provide a bit more explanation regarding the statement: “the ‘compromised’ subpopulation differs slightly from Wilcox’s ‘residual’ subpopulation given that it also accounts for births in the normal range”? In addition, how does this difference impact the results?

4. Conclusion #4 reads a bit awkwardly. Perhaps change “larger 3 or 4 fold” to “3 or 4 fold larger”.

5. It is stated that the model attempts to correct for unexplained heterogeneity in the birth cohort, but no discussion is given to describe how this is achieved. Can the authors speak to this, and for what factors this may account for? In a similar vein, how do the given models adjust for confounding? And which covariates were adjusted for? What impact does this have on the results and interpretation?

6. Model Fitting section: First sentence is missing a closing parentheses.

7. Model Fitting section: The authors state that the bootstrap results are “generally consistent” with conventional bootstrapping. Can the authors expand on what they mean by “generally consistent”?

8. The authors hypothesize that the heterogeneity identified by the CDDmlr model is due to differential fetal loss. Can the authors give more rationale as to why they believe this to be the case? It seems that there could be several other factors that could also contribute to this heterogeneity, and it is unclear how the model corrects for the heterogeneity.

Major Compulsory Revisions

1. The discussion section is lacking a thorough explanation of the strengths and limitations of the application of this method for effect decomposition. The advantages of this approach should be clearly described, and there are also several limitations worth noting. For example, issues of data quality should be addressed, as well as the impact of truncating the data at 500 g or >20 weeks gestation, and the specific advantages/disadvantages to the given analysis method.

2. Can the authors speak to how these methods compare to other common methods for effect decomposition? Placing these results and the CDDmlr method within the context of other methodological work done in this area would be extremely helpful. How do the assumptions of the current model compare to other models, and are they upheld in this case?
3. The conclusion made by the authors that the “true racial disparity is obscured by unobserved heterogeneity, probably due to differential fetal loss” is not substantiated by the data presented. The unobserved heterogeneity could be due to other factors, and the results here do not support this statement.

4. The point is made that “Whatever causes the ‘pediatric paradox’ results in a reduction in the observed relative risk for the ‘compromised’ subpopulation. If it is fetal loss as we have hypothesized then it is possible for secular improvements in health…to cause a secular increase in the observed racial disparity.” The paradox can be explained by a number of factors—even unmeasured confounding—thus the authors should be careful to make such statements regarding the benefits of improvements in health based on the results of this study. It remains to be proven whether the direct and indirect effects can be estimated using the analytical methods used here, and how they compare with other techniques. The authors need to address these methodological issues and restate conclusions as necessary.