Reviewer’s report

Title: Comparison of nuisance parameters in pediatric versus adult randomized trials: A meta-epidemiologic empirical evaluation

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Reviewer: Hsin-Chou Yang

Reviewer's report:

In this paper, the authors examined and identified significant differences in nuisance parameters between pediatric and adult randomized control trials (RCTs). Authors concluded the extrapolation of nuisance parameters from adult RCTs to pediatric RCTs should be used cautiously. Significant efforts have been put to collect and analyze the data.

I have only one major concern about this study: In addition to significant differences/heterogeneity between pediatric and adult RCTs, the data also showed significant differences/heterogeneity among pediatric RCTs. It may have two implications. First, a use of the nuisance parameters from one to another pediatric RCT should be made cautiously too. This observation will lead to a stronger suggestion than the current conclusion of this study, but this is not the purpose of this study. Second, this study may not be able to assume that all of the meta-analyses of a Cochrane review are similar enough for an imputation of nuisance parameters. The current result cannot exclude that the differences between RTCs came from the different populations. A random effect model cannot overcome this limitation. In practice, a further refinement of the inclusion criteria and a re-analysis based on the refined RTC data with a similar population structure (e.g., considering more matching factors) may yield a more concrete conclusion. At least, an evaluation over this study limitation and detailed discussions on this limitation will be useful.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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?
If not, please explain in your comments to the authors.

No
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
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Acceptable

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