Reviewer’s report

Title: Within- and between-group regression for improving the robustness of causal claims in cross-sectional analysis

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Reviewer: Wolf-Peter Schmidt

Reviewer’s report:

This article proposes an extended multilevel modelling approach for the analysis of cross-sectional studies with particular emphasis on environmental exposures that display a large degree of spatial clustering. Some of the details of this paper go a bit above my own statistical expertise which is modest. I am reviewing this paper from the statistical amateur’s perspective. In general the paper is a good read. As an amateur I would suggest a few clarifications.

1. I am not sure I understand the following: “However, the observed macro-level regression coefficient, i.e. the coefficient obtained from an aggregated analysis, is not exactly the same as the between-group regression coefficient derived from a multilevel analysis. This is because the observed group averages, can be regarded as observed with measurement error.” I would think both aggregated and individual level analysis is observed with measurement error. Perhaps outline better the specifics of measurement error in aggregated analysis. Why would the BGE and macrolevel coefficients become similar with increasing sample size? I would have thought that most measurement error is not dependent on the sample size.

2. “Model parameterisation of WBGR “: It would seem bold to me to reject one or the other type of based on a hypothesis test, with a clear cut off. Aren’t there many grey areas where BGE and WGE are somewhat different but not significantly so? Or where they are significantly different but where the size of the difference is not clinically relevant?

3. “In most epidemiological applications, true context effects are unlikely”. Please explain further why this is so.

4. “The concept underlying the approach is the one of instrumental variables”. This statement comes a bit out of the blue to me. Why was IV regression not explained in the methods sections? Is the modelling approach actually an IV regression, or just similar in terms of the idea behind it? I think the reader might benefit from some more explanation of the principles of IV.

5. “An additional limitation of the approach is that the average exposure concentrations of geographical areas are often non-perfect instrumental variables.” Perhaps briefly outline the problem with weak instruments.

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

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