Reviewer’s report

Title: Comparing methods to estimate treatment effects on a continuous outcome in multicentre randomized controlled trials: A simulation study

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Reviewer: Valerii Fedorov

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Review

“Comparing methods to estimate treatment effects on a continuous outcome in multicentre randomized controlled trials: A simulation study”
Rong Chu, Lehana Thabane, Jinhui Ma, Anne Holbrook, Eleanor Pullenayegum and Philip J Devereaux

BMC Medical Research Methodology Research article

The authors made a formidable job applying the Monte-Carlo simulation to compare the usage of various models and estimators while “data” are generated by the simplest mixed effect linear normal model that does not include the “treatment-by-center” interaction.

There a few things which do not allow me to recommend the manuscript for publication:

1. The background model is too simple to be of practical interest.
2. The analytical results are either known or can be relatively easily derived for the most of the reported findings (see, for instance, S.R. Searle, 1987, Linear models for unbalanced data, Wiley, Ch.13 in particular, V. Dragalin et al, 2002, Estimation of combined response to treatment in multicenter trials, JBS, 11, 275-295, and Sections 2&3 from V. Fedorov & B. Jones, 2005, The design of multicenter trials, SMMR, 14, 205-248).
3. “Grouping”, see p.14 is a rather dubious procedure and often if it is not defined in the protocol can be viewed as “fishing”.
4. The number of tables is impressive but I doubt that there are a lot readers who will force themselves to read them. Try to use more graphs instead.
5. Figs 1 & 2 are trivial.
6. It is a standard to report the precision of MC calculations, or at least to say that its evaluation was not done. For instance, I doubt that any comparison of 95% confidence intervals will be reliable if it is based on 1000 MC runs. The statement about 1% precision for the “90% power” calculation should be better supported.

Conclusion: - Major Compulsory Revision
Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

'I declare that I have no competing interests'