Reviewer’s report

Title: Dealing with indeterminate outcomes in antimalarial drug efficacy trials: A comparison between complete case analysis, multiple imputation and inverse probability weighting

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Reviewer: Temesgen Zewotir

Reviewer's report:

Review Report

Manuscript Number: BMRM-D-18-00204

Full Title: Dealing with indeterminate outcomes in antimalarial drug efficacy trials: A comparison between complete case analysis, multiple imputation and inverse probability weighting

The manuscript used the data from the four artemisinin-based combination (4ABC) trial and compared the performance of multiple imputation (MI) and inverse probability weighting (IPW) against the CC analysis for dealing with indeterminate recurrences.

The manuscript is written plainly and it is easy follow and understand the message. This has compromised the expected scientific writing with concise evidence based arguments. To highlight some of these points

Statistical:

1.1 Missingness mechanisms determine the suitability of MI, however the authors ignored to explore the missingness mechanism test. It is a common knowledge that under MCAR or MAR, MI outperforms CC {see Hendry and references there in among others: GM Hendry, RN Naidoo, T Zewotir, D North, G Mentz (2014). Model development including interactions with multiple imputed data. - BMC medical research methodology 14 (1).}

1.2 Unlike MI and IPW, CC has a reduced sample size and the standard error is apparently high. In other words, IM and IPW mimic the CC and algorithmically filled the missing values. Accordingly there is nothing new with result except minimum MSE due to the sample size advantage with homogeneously imputed values.

1.3 The IPW outperforms any model if we have good (near to perfect) prior knowledge about the propensity score. If the missingness mechanism is random, the IPW performance depends on the number and the strength of association with the covariates used. The authors need to elaborate and account IPW performance in accordingly. Under no clear...
cut on the number of covariates as well as evidence for the relevance of the covariates with the outcome variable comparison IPW with IM and CC is not justifiable.

Implication to health professionals and practitioners:

2 Who suggested CC as a standard approach, is it because of no other methodology? The authors need to give a full consideration of the reasoning and fill the missed information or complement it. In other words the authors should scientifically argue that by using CC instead of MI or IPW, WHO's conclusion/decision making went wrong.

Write Up:

3.1 The manuscript mishmash between being statistical and epidemiological. The paper has excellent elements but the statistics and epidemiological arguments are not strongly bonded.

3.2 When referring to a Figure in the text as "Figure" and the number and Table as "Table" and number.

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

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

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

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