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: Roderick Joseph Little

Reviewer's report:

1. Abstract, and elsewhere. "The Kaplan- Meier (K-M) probability of drug efficacy." The K-M method does not estimate a probability, it is a curve that estimates the probability of an event (here, recurrence) as a function of time. You are estimating the probability of 28 day recurrence, derived from the K-M curve. Furthermore, this probability is not a measure of efficacy, which requires a comparator treatment.

2. Abstract, 58. Technically IPW and MI estimates are not unbiased, the correct term is "consistent".

3. lines 147-151. "the remaining data … with known outcomes" is confusing, because the use of K-M implies that some outcomes are censored, and the censored outcomes are not known. In fact "complete-case analysis" is a bit of a misnomer since the censored cases are being included but are censored and hence not "complete".

4. What is the extent of censoring in the groups? If minor (I gather only 28 days of follow-up are required), then my analytical results in the previous review still essentially apply; see also next two comments. The use of K-M implies that censoring is "noninformative" or "coarsening at random" - is that a reasonable assumption?

5. While I appreciate the acknowledgement of my analysis of the bias of complete-case analysis in a supplementary file (which, however, I suspect very few people read, including myself -- when I click on the "supplemental material" all I can see is the rebuttal letter). However, it seems that some discussion of the analytical result belongs in the main text. If complete-case analysis is biased without censoring, then it's obviously still going to be biased with censoring, since censoring is just an added wrinkle, and tangential to the main issue with complete-case analysis. The analytical result makes clear the reason for the bias in this method, and is much more powerful than a simulation study, which is limited by the simulation conditions considered.

6. Another comment is that censoring is mentioned in the author's response as a justification for doing a simulation study, but censoring is not varied as a factor in the simulation, it being fixed by the censoring in the full data set.

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

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