**Author’s response to reviews**

**Title:** Identifying Priority Technical and Context-Specific Issues in Improving the Conduct, Reporting and Use of Health Economic Evaluation in Low- and Middle-Income Countries

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Reviewer’s comments  Response

Reviewer 1

The Discussion is in my view the strongest part of the paper - despite a rather thin Limitations section which doesn't capture some critical conceptual issues (see below) - the case for more targeted methodological research and development as well as capacity building efforts is well argued, the conclusions very much policy-relevant and useful for guiding next steps by academic and international partners.

****First of all, we would like to thank you for the useful comments and thought-provoking points which benefits our manuscript improvement significantly.

My reservations about the paper are more fundamental ones: what research question(s) does the study set out to ask, and what questions are actually asked of respondents in the survey? I feel that the conceptual clarity and specificity is missing upfront and throughout the paper, perhaps until the Discussion section. Principally, "methodological issues" appears to conflate a range of things, some of which neither appear to relate strictly to methodology, nor do they necessarily warrant a methodological solution.

For instance, the highest ranking technical issue was "lack of high quality local clinical data". I would however argue that the lack of high-quality local data may make a study's findings and conclusions less useful, but this does not necessarily mean the study would be methodologically poor. To use an analogy: if I were to conduct a systematic review of a treatment's efficacy but
found zero relevant RCTs, it would make my review not very useful but that doesn't mean that I used poor methods for my systematic search.

****Thank you for pointing out. We have made improvement on clarifications, so the reader will benefit most from our study. Also, the focus has been changed from ‘methodological issues’.

Among the context-specific issues, most if not all of these relate to issues around "lack of capacity" to generate or use relevant evidence for policymaking (see Li et al 2017). Indeed even within the technical issues, some of the issues appear to relate to (lack of) technical capacity. E.g. "Inappropriate choice of comparator(s)" seems to reflect a lack of awareness or understanding, on the part of health economic researchers, of fundamental methodological principles in health economic evaluation. As the authors point out in the Discussion, a solution may not be in terms of methodological advancement; rather capacity building and awareness raising / knowledge translation might play a more important role.

****Thank you for the insight and for pointing to a useful literature. We have added at the end of paragraph 8 of Introduction section (page 6 line 17-18) and the Discussion section (page 23 line 16-23) that most context-specific issues are at their fundamental issues in the lack of capacity, and that capacity issue is an overarching problem. Information from Li et al. is incorporated.

The divide between "technical issues" and "context-specific issues". Again the authors themselves acknowledge that the latter are "not easily changed with adjustment in the methodology or the conduct of the study" (p5, line 58), so why include them in a survey aimed at understanding "methodological" issues in the first place? The authors later observe that "context specific issues were considered the bigger barrier which impede the use of economic evaluations" (p17, line 15-16) - so we are no longer (only) talking about the methodology or conduct of economic evaluations, instead we're talking about their usefulness and use in policy - which is a wholly different issue with potentially different solutions. ****Our original objective was to explore ‘methodological issue’, but we think it would be interesting to explore context-specific issues based on the assumption that they will also affect the methodology and eventually the use of economic evaluation. However, we agree that moving the focus from ‘methodological issues’ to be on the problems at each process of economic evaluation (conduct and use) would be clearer to the reader.
Is the study asking "What reasons, in your view, negatively affect the quality of LMIC health economic evaluations (as a whole)?", or "What factors have you found hindered your own experience of conducting and reporting LMIC health economic evaluations?" (or both)? The two are slightly different questions - even disregarding the aforementioned distinction between evidence generation and use - and again the questionnaire as described in the manuscript appears to fail to make this distinction, instead asking about "issues" in a generic way. The specific question(s) asked should be clearly spelled out in the Methods section, and any limitations acknowledged in the Discussion section as necessary.

****The research question has been explicitly stated in the Introduction section (page 6 line 5-7), and questions that the respondents were asked have been added to the Methods section (page 7 line 16-21) and the limitations of the approach has been discussed.

I appreciate the thrust of the paper is inherent in the first line of the Abstract ("The use of economic evaluation… might be promoted through the improvement of methodological quality of the studies") - the assumption being that if studies are better, then they will are more likely to be used. This assumption is questionable, as the authors find from the results of their survey; and in the Discussion they go on to articulate a convincing case that there are in fact a range of technical and non-technical constraints, but importantly methodological innovation (including adaptation of methods to LMIC contexts) could help to address many of those. Yet in the same Discussion, the authors readily point to non-methodological solutions (capacity building in the broadest sense - see Li et al. 2017). In all, I feel that the framing of the study around "methodological" quality rather undersells the evident importance of the non-methodological factors, and adds confusion rather than conceptual clarity.

*****This is a very good and valid point. However, we partly agree, and partly disagree with this. We perceive this as: if there is a quality study in policy-makers’ reach, the policy-makers would want to use it to inform their decision-making. However, we definitely agree that having good quality evidence by itself does not directly induce its use, and much more needs to be done, e.g. awareness raising. This has been made clearer and explicit in the Introduction section (page 5 line 16-26)

My advice would be to move away from the terminology "methodological issues" throughout the paper (even if such wording was already used in the survey and couldn't be changed, I would include this as a Limitation). Rather, I would much prefer that the authors spell out the distinctions between: evidence generation and evidence use in policy; technical and non-technical issues; problems/solutions that are methodology-related versus those that are capacity related. To help the reader appreciate the importance of the study, such conceptual clarity really
needs to be set out from the beginning; i.e. the distinctions made upfront in the Abstract and the Introduction, rather than left till the end of the paper in the Discussion section.

*****The amendment has been made as suggested. Further, the term methodological issues has not been used in the survey but instead we just used the terms ‘technical issues’ and ‘context-specific issues’. We originally decided to use the terms ‘methodological issues’ because we perceive that all of the issues will eventually compromise the methodology of studies. However, we agree that including the terms ‘methodological issues’ may bring about confusion. The term has been deleted throughout the text. The distinction between evidence generation and evidence use, technical and non-technical issues, and problems/solution for technical and non-technical issues were emphasize throughout the Introduction section.

Finally, I would also suggest the following title for the paper which attempts to capture some of the above distinctions: "Identifying priority technical and context-specific issues in improving the conduct, reporting and use of health economic evaluation in low- and middle-income countries".

*****The study title has been amended as suggested.

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Reviewer 2

The authors justify the research question by citing several systematic reviews which highlight lower quality methods used in low- and middle-income settings. This is indeed true in many settings, but it would be more revealing to highlight the fact that researchers working in LMIC face different methodological challenges, rather than simply being worse at their job (as is currently implied).

*****Thank you for the useful comments and help our manuscript better reflect reality. This point has been made clear in the Introduction section (page 4 line 21-23).

The authors should state in the introduction why they chose to explore the opinion of economic evaluation practitioners, and what this adds to the debate. For example, why is this approach better than a survey of users of economic evaluations, or a review of methods in existing economic evaluations?
This has been made explicit in the paragraph before last in the Introduction section (page 6 line 23 – page 7 line 2).

The authors should have a look at the Health Economics Supplement on methods in low- and middle-income settings, which was published last year. This is a key reference in this field, and gives a very good overview of specific methodological issues faced by researchers in LMIC.

Thank you for pointing out to this useful article. We have added a number of relevant, very useful information from this paper in throughout Introduction and also Discussion sections.

The methods section does not mention whether ethical approval was given for the study. Please can you also state whether the survey was conducted anonymously.

We have added statements in the Study design subsection under the Methods section (page 7 line 24-27).

Table 1 Characteristics of respondents - this table should be moved to the results section

Table 1 has been moved to the start of the Results section as suggested (page 13).

Table 2: Ranked technical issues - these issues as currently presented seem a large jumble of many different types of problems. Perhaps it would be helpful to split out the 'technical issues' under subheadings such as 'lack of data', 'inappropriate use of data', 'lack of commonly-accepted methods', 'inappropriate use of methods'.

Amended as suggested (page 14).

It seems a lot of work was done to identify methodological issues in economic evaluation through review of methods in existing economic evaluations in low- and middle-income countries. It would strengthen this paper to add the results of that work, for example so that readers could compare the frequency of methodological issues in published data against the perceptions of practitioners as to which issues are the most prominent.

Thank you so much for the useful insight, the results from the review has been added to the Methods section (page 9 and 10).
It would be helpful to include more in the discussion on the solutions that practitioners proposed for these issues - as this seems to be a real benefit of the survey which is not currently substantially addressed.

*****The proposed solution has been rearranged and discussed as suggested (page 17-18 and throughout the Discussion section).

I believe the approach of suggesting a list of issues and asking respondents to rank them introduces substantial bias - as respondents will be less likely to consider methodological issues which are not in the list (even if given the chance to add them). The authors should consider including a discussion of this in their limitations section.

*****A statement has been added in the limitation part in the Discussion section (page 25 line 1-4).

It would be helpful to ground the discussion section more within the context of existing methods for economic evaluation, policy, and the decision-making process. For example, researchers think that lack of high quality local clinical data is the biggest problem - can the authors give an idea of what data people tend to use instead, and how this impacts the quality of economic evaluations and therefore decision making? What actions are needed to address this - is it generation of local data, or better education of the applicability of global data, or something else entirely?

*****More discussion points on this has been added throughout the Discussion section as suggested.