Author's response to reviews

Title: Performance criteria for verbal autopsy-based systems to estimate national causes of death: development and application to the Indian Million Death Study

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Author's response to reviews: see over
Reviewer: Peter Byass
Reviewer's report:
Thank you for the opportunity to re-review this manuscript. I find it considerably improved on the basis of the earlier reviews. It is good to see the MDS forms appended as Additional File 4, but I cannot find any reference to this file in the main text. I think these forms should be mentioned in the opening section of Methods - and it would be helpful to the reader to note that these forms are only suitable for determining cause of death by physician review, which is of course the approach used by MDS.
REPLY 1. Yes, forms now referenced.

Quality of written English: Acceptable

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

Declaration of competing interests:
I have no related financial interests.
I do have some scientific contact with the author group (which is not surprising given the relatively small number of scientific groups working on verbal autopsy methods). However, I have no connection whatsoever with the Indian MDS, nor with this manuscript.

Reviewer: Gary King
Reviewer's report:
I have read this paper again, including the revisions and authors comments. I have no doubt that these are serious people, doing a large project, and working hard and earnestly to do as well as they can. However, the authors have made no major changes in response to my first review. Their response to the critique I provided there seems to be that, among others (1) they can't fix the problems, (2) the problems are too difficult to tackle given their research design, (3) coming up with an gold standard even on a subset of data is too difficult or impossible for them in how they set up their research, (4) there isn't a better approach available to them, (5) other papers in "this series" (to which I do not have access by the way) do the same thing, (6) this meets the standards of the field.

REPLY 2. We disagree with the reviewer completely. There simply is no gold standard that can be applied when deaths occur out of hospital and at home. Deaths without medical attention are the vast majority of cases in any VA study, and the lack of an accurate gold standard applies to any VA study, not only the MDS. The reviewer appears to argue that hospital-based deaths should be used as a gold standard. This is incorrect, as hospital and non-hospital differ in various important ways, including the types of diseases for which medical attention is sought, the symptomatology for a given disease, the recall of signs and symptoms by family members, etc. Additionally, rates of major diagnostic errors in hospitals, even in high-income countries, are high -- from 8-24% of deaths (see Shojania et al., Changes in rates of autopsy-detected diagnostic errors over time. 2003 JAMA)

Therefore, several indirect approaches have been used to assess the performance of the MDS. This includes the comparison of the MDS to a completely independent resample of deaths (which establishes reproducibility), and comparing MDS deaths between hospital/non-hospital and rural/urban areas (which establishes the important role of obtaining a random sample of deaths in any national VA study).

These justifications may each be correct, but I'm afraid none are relevant to whether the fundamental question: Does the science behind this article justify the scholarly (and policy) community relying on its results? To that question the answer seems absolutely unambiguous: The huge uncertainties -- well described in this paper by the way -- are considerably larger than almost all the "results" claimed in the paper. As such, the authors have made no detectable substantive contribution.
Perhaps there is some small contribution in terms of describing how difficult it was to do this study or something, but I would very much hope that no one follows in their footsteps at least when it comes to the research design. If it is true that everyone else is doing this in the field, then maybe it will turn out I'm singling them out for inequitable, but not incorrect, criticism since I'm only reviewing this one paper; however, "everyone is doing it" is no justification for a research design that cannot support its conclusions. With regret, I recommend rejecting this paper, and encouraging the authors to develop a research design that tackles not only the very low levels of reliability but also gives direct measures of validity.

REPLY 3. The reviewer has not statistical basis on which to claim that uncertainty in the results exceeds the key findings - if this were true, and if physician coding was random and unreliable, then the completely independent resampling would not produce the same results as the original study, and the expected differences in causes of death between rural/urban settings and hospitals/home would not be seen. Nor would the population-level results show plausible age- and sex-patterns.

Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
I have a patent in a related methodological area, although we give access to the software that implements the patent ideas for noncommercial activities, including for verbal autopsy analyses; I don't regard it as a conflict of interest, but don't know whether this meets the formal definition in this case.

Reviewer: Michel Garenne
Reviewer's report:
None specific.
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

ADDITIONAL REVIEW (UNAMED)
My feeling is that the authors answered properly the comments made. I guess that the authors did the best they could from the data they had, knowing that no "gold standard" was available. They may gain by being more careful in their wording, emphasizing "consistency", "replicability", and "plausibility" of their method rather than "high quality", "accuracy" or "precision". Verbal autopsies are never very accurate nor very precise, but as still very useful despite their limitations.

REPLY 4. Done. We have altered the wording throughout to be more precise on consistency and reliability.