Reviewer's report

Title: Informing decision-making for universal access to quality tuberculosis diagnosis in India: an economic-epidemiological model

Version: 0 Date: 07 May 2019

Reviewer: William Wells

Reviewer's report:

Sohn et al outline an important area of inquiry: whether TB diagnostics are more cost effective when centralized or decentralized. Unfortunately, the paper is marred by unclear presentation of data, and thus for many readers will be understood primarily on a "common sense" level rather than an analytic level.

Major issues

- The abstract implies that you are modeling completely centralized testing (e.g., all test machines in the capital city). I suggest you clarify in the abstract that you are modeling district vs sub-district testing.

- There is a similar issue in the text, which should be corrected also. Some examples (I'm sure there are more): line 27 of Intro, "in central facilities" should be "in more centralized facilities"; line 29 of Intro, "centralized versus decentralized" should be "more centralized versus more decentralized" {this change also needed on line 34}; Line 32, same page: "either centrally" should be "either more centrally", etc etc. For the later parts of the paper, once you get to the specific methods and results of the paper, you could save some words by initially defining "centralized" and "decentralized" for the purposes of this specific model, so that you can use those terms for the rest of the paper in a way that is clearly understood.

- There is text and data on private sector but it doesn't appear to be used in the calculation or analysis. The text is on line 12-16 of Intro page (the section reading "Nevertheless, in India….non-microbiological tests") - either delete or link this better to the overall topic of the paper, since the connection to the rest of the paper is not clear. Fig 1B is also irrelevant to the paper the numbers and relationships in it appear to never be used in any calculations. Overall, Fig 1 seems to be a figure that was made for a different purpose and it doesn't really fit well with (i.e. support) the current paper.
- Line 47 states that decentralized testing "results in negligible pre-treatment LTFU" and line 62-3 states that it "would avert pre-treatment LTFU that would occur with non-same-day centralized testing". This contains two questionable assumptions.

  o First is the assumption that having decentralized Xpert will result in same-day testing and results. Do we know that patients who currently present directly to facilities with Xpers (i.e., DTCs, for now, or their equivalent in other countries) all get same-day results for the Xpert? I very much suspect not.

  o Second is the assumption that getting a same-day result will completely eliminate pre-treatment LTFU. There will still be indeterminate results, negative results that are not trusted are lead to additional tests or requests to come back later to see a doctor, etc.

  o In sum, it seems reasonable that decentralized testing will have lower LTFU, but not that it will have zero LTFU.

  o A greater discussion of the evidence around this critical point (i.e., does the presence of Xpert in the same facility as the patient reduce pre-treatment LTFU) would also be an improvement.

  o NOTE, other confusions on this topic: the same page refers to something called "P2" in Figure 1, which I don't see.

  o And the legend for Fig 1 says that LTFU is assigned at 13% for both arms, which completely contradicts the main text.

- In general, Fig 1C is unhelpful. What is needed here instead is a graphic of the model comparing centralized vs decentralized and the values that were assigned to these different arms and/or the different scenarios that were tested.

- Fig 2 is missing.
- The selection of scenarios and the way they are presented in Fig 3 is confusing and very non-intuitive. There are so many things varying at once that you get lost. I would suggest that the reader will be better able to digest the results if the authors can keep some things constant and a smaller number of others. As it is, we seem to be simultaneously varying the % of clients who go directly to district (vs subdistrict) facilities; the number and therefore density of DTC sites (although confusingly this is expressed as number of tests needed per day), and the volume of testing in decentralized sites. All that leaves me with a weird blending of numbers, rather than something where I can clearly say, OK, if x and y are held constant, then just varying centralization vs decentralization I can see the clear difference in cost or cost effectiveness.

- As a result of the point directly above, there are sentences like the following (with my commentary in []): "When the volume of centralized testing was low (Figure 3B&C) [Why is it low? Because TB burden or treatment seeking is low, or because there are a lot of DTCs per 100K population, or because you are considering the centralized numbers while assuming that a decentralized testing system co-exists with the centralized testing? There is no clear "scenario" here for the reader to grab onto.], decentralized testing was likely to be preferred, as high levels of cost-sharing are pragmatically unlikely for small DTCs [Why? I don't see this logic at all. Low volume sites are arguably MORE likely to pool their transport methodology with other diseases rather than multiplying their volume-related inefficiency], and decentralized testing was otherwise [otherwise / other than what?] less expensive." These are examples of confusion about the details, but the bigger point is that the scenarios seem to have been set up to make life easy for the modelers, but that makes it very hard for the reader to follow the resulting text or correlate it to a real-world situation as vs an abstract mathematical exercise.


- Line 211 and elsewhere: I do not understand this idea of using smear after Xpert, and I'm not aware of any country that does this. What is the purpose and rationale?

- Discussion section: please add a discussion of the push for truly centralized testing (e.g., full genome sequencing in perhaps only 1-3 sites per country), and any possible implications of your study for the feasibility and cost effectiveness of such approaches.
Minor issues:

- Line 22, introduction page: "pre-treatment losses to follow-up" should be "pre-treatment loss to follow-up"

- Line 23, same page: "among 13% of Asian individuals with confirmed TB" should be "among 13% of individuals with confirmed TB in Asia"

- Methods first para: slightly confusing that the "centralized" and "decentralized" are both at facilities called "district" (which sounds like the same level). You might want to make the explanation of that clearer right away (it does emerge later but by then the reader is already confused).

- Repeated text in reference 11

- References are full of multiple insertions of "[Internet]", which should be removed, along with various other extraneous information

- Line 160-161, can you add two words so it reads "cross-disease cost-sharing of specimen transport under centralized testing" as it gets very confusing who is cost sharing what with whom.
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.

Not applicable

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?
If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

**Statement on potential review bias**

Please complete a statement on potential review bias, considering the following questions:

1. Did you co-author any publication with an author of this manuscript in the last 5 years?

2. Are you currently or recently affiliated at the same institution as an author of this manuscript?

If you can answer no to all of the above, write 'I declare that I did not publish with these authors in the last 5 years and also meet the affiliation criteria". If your reply is yes to any, please give details below.

In 2015 and 2016, I was a co-author on 3 papers (relating to a single project) with three of the authors of this paper (Vassall, Gomez and Dowdy). I was also coauthor on two review articles in 2015 with M. Pai.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license ([http://creativecommons.org/licenses/by/4.0/](http://creativecommons.org/licenses/by/4.0/)). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal