Author’s response to reviews

Title: Modelling the impact of chest X-ray and alternative triage approaches prior to seeking a tuberculosis diagnosis

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RESPONSE TO REVIEWERS

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"Modelling the impact of chest X-ray and alternative triage approaches prior to seeking a tuberculosis diagnosis"

The authors would like to thank the reviewers and the editor for their time and effort in reviewing our manuscript. We thank them for their support of our paper and for the observation from reviewer 1 concerning the results tables 3 and 4. We have addressed this fully in the Discussion section as advised in the attached revised manuscript in the response below (the point made by the reviewer are shown in italics and our responses immediately after in blue).

In addition to responding to the reviewers comments we have again proof read the manuscript and found a small number of punctuation and labeling errors (e.g. Figures 1 and 2 were the wrong way around) which we have corrected. They are shown in the tracked changed version of the manuscript submitted. We have in addition added one further reference to support the paragraph added to the discussion.

We sincerely hope that with this revision to the manuscript can now be accepted for publication and look forward to seeing it in BMC Infectious Diseases.
Reviewer report:

Nicolas Menzies (Reviewer 1): The authors have done a good job of incorporating the review comments and adjusting their analysis in light of these comments. These changes have resolved the issues described in my original review. I have one new issue raised by these changes: in the updated results tables (Tables 3 and 4) it shows ~30% of TB diagnoses to be false-positive (eg $543/(543+1238) = 30.5\%$). Am I interpreting this correctly? If so, this issue warrants inclusion in the discussion section. Certainly, the ability of the triage test to 'protect' a fraction of TB suspects from the risk of an incorrect positive diagnosis is more important in light of this result.

A. Thank you for your encouraging comments. It is an interesting observation re: false positive diagnosis that we agree should be referred to in the discussion and have therefore added a paragraph – at line 309 and copied below. We point out that much of this reduction in false positive is the result of the use of Xpert as the diagnostic tool rather than the triage approach (e.g. in Table 3 option of Xpert and no triage has false positive % - $419/(419+1375) = 23\%$ in comparison to the 30% with microscopy). However, it is also true that the majority of triage solutions further reduce the false positive rate (e.g. in Table 3 option T5 has false positive % - $285/(285+1369) = 17\%$) and importantly number of cases particularly when the triage test has higher specificity.

Inserted at line 309:

An additional observation from the modeled diagnostic and triage options is the effect on reducing false positive diagnoses (i.e. the number of individuals placed on TB treatment who do not have TB disease). This is an important as the consequences of false diagnosis for TB can be serious for the individual and the TB program (32). As expected the use of Xpert as a diagnostic tool compared to microscopy can reduce the rate of false diagnosis particularly when fewer individuals are clinically diagnosed. Our results also indicate the use of triage can lead to reduced false positive diagnosis (Tables 3 and 4), especially if the specificity of the triage test is high (e.g. in triage tests T3, T4, T6 and T7).