Author's response to reviews

Title: Association between Tuberculin Skin Test Result and Clinical Presentation of Tuberculosis Disease

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Author's response to reviews: see over
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Dear Editors,

Please find attached our revised manuscript entitled, “Association between Tuberculin Skin Test Result and Clinical Presentation of Tuberculosis Disease” for consideration for publication in *BMC Infectious Diseases*. In this revised version we have responded to the comments and concerns raised by the reviewers following the primary submission. Specific responses to their comments are found on the following pages.

We thank you and your reviewers for your consideration and continue to believe that this report contributes to the growing body of literature regarding the host-pathogen relationship in TB disease and indicates that the role of the TST may extend beyond serving as a marker of infection and may be relevant to the pathophysiology and presentation of active TB disease.

Sincerely,

*Sara Auld, MD*

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Response to Referee 1:
Thank you for your feedback and comments on this manuscript. We agree with your point that this analysis raises important questions and hypotheses concerning TB immunity and TST reactivity that warrant further investigation and exploration.

Response to Referee 2:
Thank you for your careful reading and helpful commentary on this manuscript. With regards to your question about statistical review, one of our co-authors (C.M.H.) has a PhD in statistics and over 20 years of experience in biostatistics and methodology and provided substantial guidance with regards to our statistical models. We agree that the poor sensitivity of the TST remains underappreciated in clinical medicine and are hopeful that this analysis will lead to testable hypotheses in tuberculosis immunology.

Discretionary revision responses:
1. We appreciate that the second section of the results section is more challenging to read because of the four subgroups (HIV positive/negative and US-/foreign-born) and that the differences between the subgroups are often subtle. However, we feel that it is important to include this level of detail because of the presence of statistically significant interaction and also because of the differences seen between the strata for cavitary pulmonary disease (i.e. that foreign-born persons without HIV with a positive TST were less likely to have cavitary pulmonary disease while all other strata with a positive TST were more likely to have cavitary pulmonary disease).
2. Thank you for pointing out that the wording was unclear in the second paragraph of the discussion. We have removed the first sentence of the paragraph to try to simplify and clarify the paragraph.
3. We have changed the wording of “robust immune response” to “active immune response” and also added the word “direct” to the immune system engagement that is referenced later in the same sentence. We believe this phrasing is clearer and remains in line with the referenced articles.