Author's response to reviews

Title: The impact of drug resistance on the risk of tuberculosis infection and disease in child household contacts: a cross sectional study

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Author’s response to reviews:

Dear Editorial Team,

We would again like to thank the editorial team and the reviewers for going through our revised article. We apologise that this has taken so long to reply but we have re-extracted data for both cohorts and undertaken a comprehensive re-analysis with methodology to include clustering as suggested by Reviewer 2. We set out below our responses to the comments and attach a revised manuscript as well as one with the changes marked as tracked.

REVIEWER 1

Comment 1

I believe that the authors have addressed all my concerns about this paper including the potential influence of various confounders. I believe this paper is a useful addition to the literature in this field especially given the caveats that are well outlined in the article. It is unlikely that better data for a pediatric population will be available in the near future to better address this question. I think this paper deserves publication in its current (revised) form.

Response 1
Many thanks

REVIEWER 2

Comment 2

My primary remaining concern is the lack of statistical method used to account for household level clustering. To my knowledge, methods like GEE are now the standard for household contact studies and other similar scenarios. I disagree that your study design adequately controls for this, given that 50% of your households have multiple children enrolled. By assuming independence of observations, your standard error estimate is likely to be too small which would impact the precision of your odds ratios and, possibly, statistical inference. If, for whatever reason, you choose not to use a method to account for within-household clustering, you should indicate your choice to assume that outcomes are independent across individuals in the Methods section and/or the limitations discussion.

Response 2

We appreciate R2’s concern. We have now conducted a sensitivity analysis accounting for clustering at the household level, and this did not have any material impact on the results. We have now indicated this in the text.

Comment 3

One additional minor comment is regarding the discussion of previous relevant studies. You did a great job of identifying and listing the outcomes of previous studies, but seemed to gloss over the possible reasons for discrepant findings. A more thoughtful discussion of why results may be different and how your study strengthens the evidence for lower infection risk / higher disease risk among MDR-TB contacts would strengthen the paper. Perhaps a suggestion for a future study design that could more definitively answer this question might be helpful.

Response 3

Thank you for this point. We have further expanded our discussion around why the different studies may have been different and have suggested a future study that might provide a more definitive answer.