Author's response to reviews

Title: Agreement between QuantiFERON(R)-TB Gold In-Tube and the tuberculin skin test and predictors of positive test results in Warao Amerindian pediatric tuberculosis contacts

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Author's response to reviews: see over
Reviewer's report - Referee 2

Minor revisions

Introduction:
1. Need to make explicit that IPT is not offered to childhood contacts of adult Tb cases (SSP or culture confirmed) as this is not clear

Response to comment 1 Reviewer 2:
We agree with this reviewer that it is important to mention this fact in the Introduction section and we therefore added the sentence 'Isoniazid preventive therapy is currently not routinely provided for childhood contacts of adult TB patients in the Orinoco Delta.' Since we have now mentioned this fact in the Introduction section, we deleted the sentence 'Preventive chemotherapy was not provided for childhood contacts in the Orinoco Delta at the time of this study.' from the Methods section.

Methods:
2. Following sentence needs shortening:
A previously published cross-sectional analysis reported on the association of TST and QFTGIT positivity with helminth infections and cytokine profiles in asymptomatic Warao childhood TB household contacts 1-15 year of age of sputum smear-positive pulmonary TB patients between May 2010 and May 2011 residing in the same region [23].

Response to comment 2 Reviewer 2:
We shortened the respective sentence into 'A previously published cross-sectional analysis reported on the association of TST and QFT-GIT positivity with helminth infections and cytokine profiles in asymptomatic Warao childhood TB household contacts [23].'

Some minor corrections in use of English
3. Line 14 discussion: change
The proportion of children that WAS lost – change to WERE

Response to comment 3 Reviewer 2:
This word was changed accordingly.

4. Both in the Brazilian as well as in our study population reported TB rates are EXTRAORDINARY high (>30 times – change to EXTRAORDINARILY

Response to comment 4 Reviewer 2:
This word was changed accordingly.

Discussion
5. Somewhat overlong and some discussion could be shortened. For example, most of the first paragraph could be shortened and the extensive discussion related to follow up rates in a German study could shortened to say that the authors had a very high rate of loss to follow-up compared with previous studies (ref).

Response to comment 5 Reviewer 2:
We agree with the Reviewer that the first paragraph and the discussion concerning the German study can be shortened. Therefore, we changed the paragraph:

'Two earlier prospective studies including child TB contacts in Japan [35] and Germany [36] also reported high negative predictive values (100%, 95% CI 99-100% and 100%, 95% CI 99.5-100.0% respectively) and low positive predictive values (0%, 95% CI 0-46% and 13%, 95% CI 8-19% respectively) for progression to active TB disease. However, in the Japanese study only 41/313 children were close contacts of the index case and in the German study only 141/1414 participants were children <16 years of age. Furthermore, almost 30% of the study subjects in the German study moved away from the study region during the observation period of 2 years and no follow-up data were available for these participants. The proportion of children that was lost to follow-up in our study was even higher (62%) and estimations and comparisons of positive and negative predictive values should thus be interpreted with caution.'

into:

'Two earlier prospective studies including child TB contacts in Japan [35] and Germany [36] also reported high negative predictive values and low positive predictive values of QFT assays for progression to active TB disease. However, the proportion of children that were lost to follow-up in our study was very high (Figure 1) compared with previous studies [35,36] and estimations and comparisons of positive and negative predictive values should thus be interpreted with caution.'

In order to shorten the discussion further, we also deleted the following sentences/paragraphs since the information discussed in these paragraphs was not directly related to our primary research objectives:

'Because the development of calcifications requires at least six months and may often take up to four years [25], calcifications observed on CXRs taken at inclusion probably reflect earlier TB exposure. In contrast, the calcifications that were observed on follow-up CXRs but not on initial CXRs in six children are more likely to be associated with their recent TB exposure.'

'Unlike CXRs, a HRCT scan can accurately describe the pattern and distribution of bronchiectasis including descriptions of the bronchoarterial ratio and bronchial and pleural wall thickening.'