Reviewer's report

Title: Long-term dominance of Mycobacterium tuberculosis Uganda family in peri-urban Kampala-Uganda is not associated with increased virulence.

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Reviewer: Andrew Christopher Whitelaw

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The authors describe a study examining the associations between M. tuberculosis Uganda family, and cavitary disease (used as a marker of virulence). Although they were able to associate a number of factors with cavitary disease (smoking, low income, HIV - negative association), there was no association between M. TB Uganda family and cavitation. The study is well written, and the methodology seems sound. I have a few minor comments, but I do feel the study is worth publishing.

Minor essential revisions / questions:

1: The isolates collected formed part of two separate studies, as described in the Methods section. The first study was performed in peri-urban Kampala; however the location of the second study is not explicitly stated (but is presumably also in Kampala) - could this be added.

2: Only smear positive patients were recruited as index cases - presumably from patients accessing routine health services in Kampala. This could possibly lead to a biased sample collection: if the non-Uganda strains are less frequently associated with cavitation, then it is possible that they may be a more common cause of smear negative disease and thus missed by only including smear positive index cases (with a possible over-representation of cavitary disease in the index cases) Could inclusion of all patients (smear positive and smear negative) possibly have increased the chance of finding an association between cavitation and the Uganda family? Could the authors comment on this possibility? Household contacts were screened by smear and culture - so presumably some of these contacts were smear negative but culture positive. What proportion of the final patients analysed were index cases versus contacts; and what proportion were smear positive versus smear negative? What is the normal proportion of smear negative disease seen in Kampala (if that is known)?

3: How was culture performed (solid or liquid), and were the culture protocols at the two labs (NTRL and JCRC) the same?

4: Please reference the chest X-Ray reading scheme used.

5: When stating that "Basal Metabolic Index" was calculated, do you not mean "Body Mass Index"?

6: How was income stratified?
7: 1746 cultures were stored - what proportion of the total number of patients enrolled does this represent? Was there a significant loss due to culture contamination / loss of viability etc?

8: 533 isolates were excluded from the analysis of clinical associations. Was the distribution of strain lineages in these 533 similar to the overall distribution?

9: Was any association examined between incidence of TB in household contacts and strain lineage?

Minor Discretionary Revisions

1: I do not feel that Fig 1 adds anything to the manuscript - the data is presented in the text. It may be worth deleting this, and adding supplementary Table 3 (and possibly even supp Table 2 if space permits)

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests