Author’s response to reviews

Title: Host iron redistribution as a risk factor for incident tuberculosis in HIV infection: an 11-year retrospective cohort study

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Author’s response to reviews: see over
Please consider the following point-by-point response to the Editorial Requirements and Referee comments/concerns that were kindly provided in regards to our initial manuscript submission:

**Editorial Requirement:**

- “Please include source of funding in Competing Interest section.”
  
The Competing Interests section has been modified as suggested.

**Referee 1:**

**Overall**

- “…present abbreviations in full the first time they are used…”
  
The manuscript has been checked and changed to reflect this suggestion.

**Abstract**

- “Avoid starting a sentence with absolute numbers as in the results of the Abstract.”
  
The wording but not the concepts or information has been slightly modified to accommodate grammatical and abbreviation suggestions made elsewhere in order to keep within the 350 word limit for the abstract.

**Background**

- “Clearly state the purpose of the study after the objective”, and, “The purpose of the study needs to be clearly stated in the Background.”
  
The purpose of the study has been stated after the objective in the Background section.

- “A reference needs to be stated after the first sentence of the article”.
  
  This sentence has been reworded as this information seems to be generally accepted as common knowledge and typically not referenced. Data and references on the most recent global burden of TB including the estimated incidence of new TB cases and cumulative lifetime risk have been added from which this concept is derived to provide additional support for the statement.

- “The hypothesis needs to be rephrased and removed from the Methods and taken to the Background.”
  
The hypothesis has been modified and moved from Methods to the Background section.

- “Last paragraph and last sentence of background should read…else the second half of this sentence needs to be rephrased…”
  
The wording of this text has been clarified to better reflect the intended meaning of the second half of the sentence.
Methods

- “Probably, this study was not the purpose of the setting up of this cohort. We will like to know how this was taken care of ethically, especially considering the fact that, laboratory analysis were performed on patient sample collected back then...” and, “Participants gave a written informed consent...Was it open consent that permits research to be carried out in their samples indefinitely?”

The main HIV Clinical Cohort from which this study recruited participants from was established shortly after the first HIV diagnosis was made in The Gambia in 1986 and it continued recruitment until 2010 when the cohort was closed. The main purpose of the Cohort was to study the burden and natural history of HIV-1, HIV-2 and HIV-Dual infection, including risk factors associated with disease progression and mortality unique to this region. While the current study utilizing only archived samples and data and was not the main reason for the establishment of the main cohort for which subjects originally consented to, the actual consent form used in obtaining the consent of these subjects was included as part of the ethical review by the three committees in The Gambia (Joint Gambia Government/MRC Ethical Review Committee), the UK (London School of Hygiene & Tropical Medicine) and USA (Cornell University). All committees deemed it ethically acceptable research.

Further text has been added to the document to provide additional clarification.

- “...we would like to know whether there were any missing data or information and how did it affect the analysis.”

Text has been added to inform the reader that missing data was present in this retrospective analysis and that this could influence the ability to detect statistical differences in regression models.

Results

- “There are some variables where the sum of the category percentages is more than or less than 100%. These need to be reviewed.” Linking with “Additional File 2: Categories percentage either greater of less than 100%...You can present percentages to one decimal....”

Percentages were modified to include one decimal place that reduces the rounding error in Additional File 2. Furthermore, table 1 now also includes a footnote specifying totals may not equal 100% as diagnosis of EPTB and PTB were not mutually exclusive.

References

- “...they used the Vancouver Style of referencing but stating up to 10 authors before et al instead of six.”

Reference style guidelines for the journal were consulted, these specify that the first 30 authors should be listed followed by et al. thereafter. References have been changed to reflect this journal requirement.
Acknowledgements

• “The project was funded in part...”
  Changed wording as suggested.

Referee 2:

There were no additional comments or concerns specified by this Referee.