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Undiagnosed TB in adults dying at home from natural causes in a high TB burden setting: a post mortem study

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RESPONSE TO EXAMINERS COMMENTS:

EXAMINER 1:

There is a problem with Table 4.1. Also some of the results do not add up or diverge from the results in the text (HIV infection).

Several corrections have been made to Table 4.1. See detailed responses below. The HIV results in the text have been corrected – paragraph 1 Page 14, and Chapter 4.5 page 25.

Those with TB had cough more frequently. It is incorrectly stated that they had shortness of breath more frequently too, as it is 44% in those with TB and 69% in those without.

This has been amended in the text, paragraph 2, page 14. The data indicate that shortness of breath was commoner in those without a TB diagnosis. This has been added.

There are a number of errors in Table 4.1as well as the fact that the top half has characteristics which are not opposite their results i.e. the results are not opposite the characteristics but have slipped down one, as Male is on the line with study numbers.

The parameters listed in column one, Table 4.1, Page 15 have been correctly realigned .

Furthermore, the text tells of 11 HIV-infected subjects identified by next of kin while the table has 14.
The correct number is 14, as reflected in the table. The HIV results in the text have been corrected – paragraph 1 Page 14, and Chapter 4.5 page 25.

There are 24 with hypertension in all patients but 22+16=38 in the subgroups.

The numbers for deceased with a history of hypertension in Table 4.1, page 15 have been rectified.

58 of all have cough but 22+21=43 in the subgroups.

The numbers for cough in the “No TB” group have been corrected in table 4.1, page 15.

Almost a third of home deaths had infectious TB. This makes one wonder why the abstract conclusion in the report and paper state that “one quarter”of home deaths had evidence of undiagnosed TB.

By the stricter definition of TB being present(TB diagnosed on two or more laboratory tests), 21.2% had TB. When the less stringent definition was applied (TB diagnosed on at least one laboratory test), almost one third (31.8%) had TB.
The abstract conclusion (page VI) has been modified to reflect concordance with the final conclusion.

Chapter 2. Aims and objectives
The candidate uses the term “bronchiolar alveolar lavage fluid” (not found on a search and does not seem to exist) in the report but uses the correct term “bronchoalveolar” in the published paper. An alternative is “bronchial alveolar”.

“bronchiolar alveolar lavage ” has been substituted by “broncho-alveolar” - see Chapter 2.2, Page 5.

EXAMINER 2:

Page 3 – The phrase “one quarter of all global HIV/TB co-infections occur in South Africa” is not quite correct. What is correct is that just over one quarter of all HIV - associated TB cases (i.e. active TB with HIV co-infection) occur in SA. This is different to “HIV/TB co-infection” which also includes people with HIV infection and latent TB.

The sentence has been corrected to reflect HIV associated TB cases.

Page 4 – last paragraph should read “two endemic diseases”

This has been corrected as recommended.

Page 5, 9 and at other places in the thesis: the correct term is “MGIT” not “MIGIT”

This has been corrected on the stated pages and at all places in the text where it appears.

Page 11 – “TB infection diagnosed…” should rather read “ TB disease diagnosed…”

This has been corrected - see paragraph 3.7.2 Data analysis, Page 11.

Page 13 – Participants should have a small”p”.

This has been corrected – Chapter 4.2 page 13.

Page 15 – The rows in this table have been mixed up. For example, there is an IQR for Male!

The parameters listed in column one, Table 4.1, Page 15 have been correctly realigned .

Page 23 – The figure 86.67%...its unclear what the denominator here was. Was it the 14 with histology suggestive of TB?

Yes, the denominator is the 14 histologically diagnosed cases. This has been clarified in the text – paragraph one page 23.

Page 28 – It is surprising that Xpert performed better than MGIT culture in BAL. Is it possible that the post-mortem delay in obtaining samples for culture (median 5 days) could have intefered with yield of culture? This may be worth discussing with a microbiologist about.

Discussions with a microbiologist at the National Institute of Communicable Diseases, Dr. Kerrigan McCarthy, confirmed the examiner's explanation for the poorer performance of the MGIT culture when compared to Xpert.
Time delay is likely to increase the possibility of bacterial contamination, and a consequent negative result. A comment in this regard has been added to the discussion – see page 28.

Page 29 – It is stated that these patients did not access healthcare before death. The study excluded patients who had been hospitalised, but do you have data to show these patients did not access health care at all? Do you know that they were not visiting ambulatory health care services such as clinics and GPs prior to death? This statement suggests that you have the history from family that they did not visit ambulatory services.

The examiner is correct. The study has no definitive data that the deceased did not attend ambulatory services. Clinical data was drawn from next-of-kin interviews after death and suffers from recall and knowledge bias. This is stated in the limitation sections.
The relevant section on page 29 has been amended to reflect that the information is drawn from family interviews.