Author's response to reviews

Title: High prevalence of multi-drug-resistant tuberculosis in an HIV prevalent setting in Johannesburg, South Africa: a cross-sectional study

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Dear Editor
Dr Robert Wallis
BMC Infectious Diseases

Please note the following changes to manuscript MS 1655627184428250 High prevalence of multi-drug resistant tuberculosis in African children in a setting of high HIV prevalence.

Thank you for considering these changes made at the suggestion of Reviewer 1 and 2.

Reviewer 1

No correlation between WAZ scores and MDR outcome: Sentence added to last line of paragraph “Outcome of children with MDR-TB” (page 16).
No WAZ information on “non-MDR” group as data was laboratory based.
Table 3 retained as important baseline information recorded. Table 4 shortened to baseline and 12 month outcomes. Text deleted from results section (“Outcome of children with MDR-TB): page 17.
“HIV prevalence in the cohort”, clarity on role of ART: Details added to last 2 sentences of the paragraph. As study was retrospective, and drug sensitive tuberculosis data laboratory-based, no detailed information on ART available for these cases.
Contact tracing: Additional comment and reference added in discussion lines 8 through 13, second paragraph
MDR-TB episodes: Age correlation query highlighted in text “MDR-TB episodes” line 3 (page 13).
Figure 1: boxes added as suggested.
Reviewer 2

Title change as suggested to “High prevalence of multidrug-resistant tuberculosis in an HIV prevalent setting in Johannesburg, South Africa: a cross sectional study”

Multi-drug resistant changed to multidrug-resistant in title.

Abstract

Methods: Age and population of children included (line 1) and outcomes data clarified “clinical and radiological” added (line 3)
2nd sentence, clarification on methods added.

Results: Clarification on “episodes of childhood TB” line 2
Total number of children treated for TB in 2008 at both hospitals added line 1 and 2.

Conclusions: Line 2 and 3 additional text added to address concern about misleading statement.

Background

Mycobacterium tuberculosis and MTB added to text where appropriate. When describing disease and not microbiology of organism, “tuberculosis” has been retained.

3rd sentence, 2nd paragraph eliminated.

Methodology

Study population and design: 2nd paragraph: clarification on which specimens had DST performed
3rd paragraph: Clarification on methods of culture and DST revised as an error was made in original text.

Clarification on distinguishing non-tuberculous mycobacteria added to text.

4th paragraph on page 7 deleted as incorrect.

5th paragraph, clarification regarding drug testing added 2nd line.

Question re: capreomycin use: In our context capreomycin is reserved for XDR treatment, and occasionally is used for MDR cases not responding to standard treatment.

Statistical analysis: reworded to clarify denominator, line 1 and 2.
Line 1 drug-resistant hyphenated.

Ethics number eliminated line 2 “Ethics approval”

Results

Query regarding BCG cases: The authors would like to defend the decision to exclude these children as they introduce bias into the analysis for the following reasons:

1) 7/36 specimens had drug resistance (5 INH- mono resistance; 1 MDR and 1 INH polyresistance- INH and pyrazinamide). Overall drug resistance would
increase slightly including these children to 16.3%
2) The data was laboratory based and lymph node location was not recorded in all cases.
3) Age data was missing from some of the drug sensitive aspirates.
   Above information has been added to the text.
Information regarding number of tuberculosis cases treated in 2008 added (1st sentence).
Line 21-22: clarification on number and site of specimens added to text.
Line 23: clarification on DST added
Line 24-25: comparison between RMMCH and CHBH removed.
   “HIV prevalence in the cohort”: IQR’s replace range when median data represented, lines 6-9.
   “Drug susceptibility testing”: comparison between RMMCH and CHBH removed, last sentence.
   “MDR-episodes” line 2 (p=0.771) added.
   “Outcome of children with MDR-TB: 2nd paragraph eliminated and condensed to 12 month follow-up only.
MDR-TB episodes: 2nd paragraph eliminated
Table 4 (now table 3) also condensed to baseline and 12 month follow-up.
Discussion
Lines 8-13 added to enrich contact tracing discussion and reference 10 added.
Data not available to explore possibility of nosocomial MDR-TB transmission.
Table 2 (now table 1) amended to include INH resistant cases. Discussion amended accordingly line 3 and 4 2nd paragraph
3rd paragraph: Lines 8-15 revised to address questions regarding DST in South Africa.
4th paragraph, line 4-7 ammended to further describe whether time to treat affected outcomes.
3rd last paragraph: limitations expanded lines 6-8, 13-15
2nd last paragraph: primacy statement removed.
Table 1 eliminated.
Table 2 (becomes Table 1) INH-resistant (excluding suspected BCG cases) and Rifampicin mono- resistant cases added to analysis.
Table 4 (becomes table 3) condensed to include baseline and 12 month follow-up only.
References changed to [X].
Other changes:
MDR-TB episodes: Lines 9 and 10 age of children with TB contacts added.
Thank you for considering these revisions

Kind Regards
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