Author's response to reviews

Title: Treatment outcomes from community-based drug resistant tuberculosis treatment programs: a systematic review and meta-analysis

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Author's response to reviews: see over
Editorial Office
BMC Infectious Diseases

To the editors and reviewers,

Thank you for reviewing our research article titled “Treatment outcomes from community-based drug resistant tuberculosis treatment programs: A systematic review and meta-analysis”. We have responded to each of your comments (in bold) below:

Referee #1
Background:
1. Paragraph 2, Sentence 2: The tenses are a bit confusing and inconsistent
   We have modified this sentence accordingly.

2. Paragraph 3, Sentence 2: The description of cb-DOTS excludes local health care workers as treatment observers though later in the paper, the authors refer to HCWs and their role in cb-MDR programs
   We have included healthcare workers in this description.

Selection of Studies:
1. Sentence 1: There seem to be a few words missing…. “Examined for eligibility beginning with the abstract, and followed by full text review”
   We modified this sentence accordingly.

Treatment Outcome Definitions:
1. Sentence 2: Missing words. “Patients that met criteria for….were classified as having unsuccessful treatment outcomes”
   We modified this sentence accordingly.

Study Characteristics:
1. Did the authors examine the impact of program “maturity” (ie number of years in practice)? One wonders if this may impact patient outcomes
   We looked at this issue based on your suggestion, but unfortunately not all papers included details of program duration and we were already quite limited in our sample size for meta-regression. In addition, treatment cohorts often spanned several years and the number of people treated in each individual year was unclear. Meaning, a program that was formed in 2000 could report on 80 patients in 2004—but the number treated in each individual year during this period would be unclear. Presumably, if program maturity influenced treatment outcomes, we would need to examine outcomes stratified by program duration in years (after controlling for calendar year, as we believe this may also influence outcomes). This would be a very interesting question to answer with individual data!
2. Sentence 2: It may be worth noting that you are referring to the HIV prevalence among the cohort described, not the HIV prevalence in the geographic area.
*Thank you, we have modified this description.*

Discussion:
1. Paragraph 2, Sentence 2: “report” should be changed to “reported”
*Thank you, we have modified this sentence.*

2. Paragraph 5: It may be worth mentioning the impact of novel POC diagnostics for DR-TB and how they may also impact the “decentralization” of MDR care and complement cb-MDR programs and their impact on waiting times, transmission dynamics, etc.
*Thank you for the suggestion. We have added a sentence to address this issue.*

3. Paragraph 6: It may be worth commenting on the “maturity” of the program (i.e. number of years in practice) as this may be a relevant factor that affects patient outcome.
*This is quite hard to assess given that the maturity of a program changes over time, and we were unable to capture the dynamics of this change in the studies. Presumably, program maturity does affect outcomes, but as programs mature they may also take on more patients which could influence outcomes. Often times programs with few patients have good outcomes despite their relative inexperience (e.g. a low incidence region), so this issue may be quite difficult to assess.*

4. It would be worth noting more explicitly the limitations of the analysis, particularly the limited sample size in some of the sub-group analyses.
*Thank you. We have added this limitation to our discussion.*

Table 1:
1. It is not clear what the asterick next to Study Type refers to. It may be worth defining PC and RC and prospective and retrospective.
*We have adjusted Table 1 accordingly.*

2. What is the purpose of the “* Resistance for MDR, XDR TB” at the bottom of the table?
*This was a typo- we have adjusted Table 1 accordingly*

Table 3:
1. The title could be “Patient Treatment Outcomes”
*For the inexperienced MDRTB reader we wanted to be very clear what ‘treatment outcome’ meant, which is why we chose this title.*

2. The “Summary” line is a little confusing. Can the 129 be labeled as the mean sample size?
*Thank you, we have added the “mean” to clarify this issue.*
Reviewer #2
Line 3 – clarify the definition of XDR “resistant to at least two or four of”
We have modified paragraph 1 accordingly.

Thank you again for your consideration,

[Signature]

Dr. James Johnston
On behalf of all authors