Reviewer's report

Title: STREAM: The Evaluation of a Standardised Treatment Regimen of anti-Tuberculosis Drugs for Patients with MDR-TB

Version: Date: 8 July 2014

Reviewer: Erik Cobo

Reviewer's report:

I read the protocol trial paper from Andrew J Nunn et al. about a shorter treatment for resistant TB patients, and I think that it deserves publication in Trials.

I may answer positively to 3 of the 4 questions Trials Journal has posed. (1. Will the study design adequately test the hypothesis? 2. Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing? 3. Is the planned statistical analysis appropriate? 4. Is the writing acceptable?). But, there is no mention of the planned statistical analysis, which has to be added.

Additionally, I would like to make some suggestions to the authors in order to improve the potential influence of the trial in the treatment of TB-resistant patients.

- Major Compulsory Revisions

Please, specify the planned statistical analysis, at least for the main variable and analysis, together with imputation criteria for missing values and definition of populations.

Please, note that the long follow-up is probably the greatest challenge in this trial. The final credibility of the results would rely on the proportion of enrolled patients having an evaluation at 27 months. Please, note that a non-inferiority trial has to show that it is “sensitive” to differences, that is, “in case there was a differential effect between compared treatments, the study would have shown it”. How would you face the challenge of patients not achieving the final evaluation? If, for example, there is a difference of 10% of patients evaluated at 27 months, or the overall proportion is not very high, the interpretation of the trial would heavily rely on assumptions about those patients. Please, consider specifying how you would address this point. For example, would concordant secondary sensitivity analysis restart some credibility? To prevent and treat missing values, please see very useful advice at http://www.nap.edu/catalog.php?record_id=12955 or http://www.nejm.org/doi/full/10.1056/NEJMsr1203730

Please, specify the blinding status for researchers, committees, caregivers and participants (see SPIRIT advice to report masking). If the trial is open, please, discuss the implications for it and the way you will keep the main risks of bias (performance, evaluation, attrition, etc.) controlled.

Please, describe the recruitment and randomization processes (see SPIRIT
advice).
In general, consider checking that all items from the SPIRIT reporting guideline have been addressed.

- Minor essential Revisions

From my point of view, the important outcome is to have negative bacteriological status. The change of drugs (page 13) is just some part of the process, not of the outcome. Please, consider limiting the definition of the main variable to health outcomes. (Same for “success rate … defined as cure or treatment completion”, page 5.)

This trial is addressing a top health problem. To improve STREAM influence in future care, for the reasons already stated, please consider specifying that your final report will be written in accordance with the Consort 2010 statement, as well as its extension to non-inferiority trials. Please, note that you already have to be ready to follow their advice.

Following Spirit 2013, please consider specifying your dissemination policy (item 31).

- Discretionary revisions

Please, consider changing the last keyword “short duration” to “shorter duration” or “shorter treatment duration” or just dropping it.

Please, consider specifying the month in “trial opened”, page 8.

My best wishes for the next phases of your meritorious work.

Erik Cobo

**Level of interest:** An exceptional article

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests