Reviewer’s report

Title: World Health Organization (WHO) antibiotic regimen against other regimens for the treatment of leprosy: A systematic review and meta-analysis

Version: 0 Date: 31 Jul 2019

Reviewer: Emmanuelle Cambau

Reviewer's report:

Lazo-Porras et al. INFD-D19-01127

The authors performed a systematic review and meta-analysis of all therapeutical regimens for leprosy including the standard multidrug therapy (MDT) recommended by WHO as a control.

The methods were done according to standard rules and by authors with such expertise.

The choice of the studies published between 1982 and 2018 was justified by the WHO recommendations being published in 1982 but it could have been extended to papers previous 1982 since leprosy studies are scarce and the standard MDT relies on studies done before.

Among 135 papers, 24 studies were selected, mostly randomized controlled trials (RCT). The authors tried to present all the data from these studies. However the disparity of the outcome criteria and the definitions used in these studies make it very difficult to follow. This is a great work but only few relevant conclusions are obtained from it.

The authors should rely and discuss their findings with regard to the recent systematic review done under the umbrella of a WHO guideline group following GRADE recommendations (WHO guidelines for the diagnosis, treatment and prevention, 2018, details of the literature review).

Major comments:
1. There are many studies comparing the ROM regimen (rifampicin, ofloxacin and minocycline combination) to the standard MDT. The authors need to detail if the ROM combination is giving daily, monthly and how many doses in total. It is not clear in the table 1, e.g. for Kumar 2015 study, and lines 243-246.

2. The definitions of relapse and treatment failure should be discussed and referenced:
   - what does mean "presence of the disease at the completion of the treatment". In leprosy, it is very often observed that the lesions did not disappear after 6 months or 1 year treatment but the lesions cannot progress.
   - what does mean "BI positivity during any time of the treatment". It is very often observed that the BI remains positive even several months after the end of sterilizing treatment.

3. The type I and type II reactions cannot be presented as safety outcomes. They are occurring as a part of the disease and are specifically treated. They are not adverse effects of the treatment.
4. In the figure 1, a number of articles were excluded because of unobtainable: How many articles were not available, and for which reasons?

Minor comments:

- All the figures are of poor quality, difficult to read.

- The tables are difficult to read and needed to be split at least for PB and MB.

- Figure 3a could be deleted since the figure 3b is gathering the data of all studies with the endpoint at the follow up. In the text (lines 264-267, and 358-361) it is explained that at the completion time there is no difference but one study was added in the figure 3b and this is the only one with a significant benefit and a very large number of patients included. This has to be explained in the text. The sentence line 268 is not justified.

- since many studies on PB compared the standard MDT versus MDT+clofazimine, can the authors summarized the effects in a figure or a table.

Table 2: many lines need to be revised: in Fajardo 2009, the study arm does not correspond to what written in table 1; what is the CDC treatment?, In Fajardo and Jadav, is the treatment different from the standard MDT;,

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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