Reviewer's report

Title: A systematic review of the diagnostic accuracy of Loop-mediated-isothermal AMPlification (LAMP) in diagnosis of invasive meningococcal disease in children.

Version: 0 Date: 31 Oct 2018

Reviewer: Merryn Voysey

Reviewer's report:

This systematic review and meta-analysis appears to be well conducted, however, suffers from a paucity of relevant studies that could be included. This is, of course, not the fault of the authors and not something that can be amended.

Some minor comments:

1. The statistical methods appear to be appropriate however there are some obvious errors that need amending.

For instance In Table 2 the specificity is reported as 100% for the Lee study yet there are false positive results so this is impossible. Similarly for the Bourke study, 100% sensitivity is reported for Swabs even though there are 4 false negs. The McKenna results don't look right either.

The results in table 2 don't appear to be the ones in the meta-analysis as figure 3 reports different sens and spec so I think these are just typos in table 2.

2. The Stata package used for the meta-analysis should be cited in the methods section and the authors of the package appropriately referenced.

3. It would be helpful to have the references for the three studies included in Tables 1 & 2 reported in the tables so that these paper can be easily found. There are two Lee 2015 papers so name and year alone is not sufficient to point the reader to the correct paper if they want to read it.

4. CSF results for the Bourke study have not been included. Can the authors provide an explanation/justification for this exclusion?

5. McKenna study: the Blood EDTA and the serum results have been combined under one heading 'blood'. This may not be the best approach as these may be replicates of multiple samples on the same participants. In Bourke it is Blood-EDTA only so for consistency EDTA and serum should probably be reported separately as they are in the paper. In addition the tables should have footnotes to give details of all acronyms and definitions.
6. McKenna report 139 throat swabs in Table 3 of their paper yet there are 255 in the review - I can't see where the numbers are coming from

For the discussion some additional thoughts:

Can the authors make it more clear that this review compares the diagnostic accuracy of the LAMP test to conventional RT-PCR +/- blood culture tests. Not the accuracy of LAMP in diagnosing MD. The gold standard for diagnosing MD is RT-PCR +/- BC however this gold standard is an imperfect gold standard and may not detect all true cases of MD. Those isolates classified as false positives by LAMP may in fact be true disease cases that were not detected by PCR and the authors could include some discussion of this possibility. What are the implications of having false positive LAMP samples and are they really 'false’?

In addition, what are the implications of having false negative samples by LAMP? Presumably this is a much more worrying possibility and as the confidences intervals for the sensitivity of LAMP is as low as 71% (or 24% for blood and CSF only), this means potentially 29% (or up to 76%) of cases may be missed by LAMP compared with PCR.

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?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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