Reviewer’s report

Title: Application of GRADE: Making Evidence-Based Recommendations about Diagnostic Tests in Clinical Practice Guidelines

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Reviewer: Atle Fretheim

Reviewer’s report:

This is a manuscript that describes a group’s experiences with a particularly challenging area in guideline-development (as well as in clinical practice): the understanding and use of diagnostic tests.

By describing and discussing the approach they used in their practical application of the GRADE-framework, the authors provide potentially very useful guidance for others who will be involved in developing guidelines on the use of diagnostic tests.

The traditional format of a scientific paper is not perfectly suited for this type of report, but I find that the authors have dealt with this in a good way. The manuscript is brief, and given the difficulties many have with understanding diagnostic tests (accuracy, pre-test probability etc), I propose expanding some parts of the text in order to make it easier for readers who are not experts on diagnostics to follow the text.

Comments to the specific points the editors routinely ask reviewers to address:

1. Is the question posed by the authors new and well defined?
   The report is not directly answering a research question, so this is not fully applicable. The authors describe a process and the approach to addressing various challenges faced when developing clinical practice guidelines on the use of diagnostic tools.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
   Not fully applicable as this is a case-study.

3. Are the data sound and well controlled?
   Not applicable.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   Only partly applicable – to the extent that this applies, the answer is yes.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
Yes.

6. Do the title and abstract accurately convey what has been found?
Yes.

7. Is the writing acceptable?
Yes, although the authors should expand the text slightly to ease the understanding of non-expert readers.

Specific comments:

Introduction, para 1:
The point about patient-important outcomes is key, but I think the current wording (3rd sentence) is a bit awkward. I would re-phrase – perhaps use a couple of sentences, if necessary.

In the last sentence, I would add "MAY BE" due to the lack of….

Introduction para 2:
The claim that health care practitioners “often feel compelled to implement guidelines recommendations” is also awkward to me – for two reasons: 1) I’m not sure if this is true, and 2) The line of reasoning from describing a lack of transparent frameworks to claiming that practitioners feel compelled to use the guidelines doesn’t make perfect sense to me – I fail to see the logical link in the argument (there is a need for transparent frameworks, independent of what practitioners feel – no?)

Methods, sub-section “Formulating questions…”, para 3:
I would think that a new test could also be introduced simply because it represents a likely improvement relative to an “existing diagnostic pathway” – this is not even mentioned as a possibility (assuming, of course, that the gold-standard test is not the standard test in practice).

Methods, sub-section “Formulating questions…”, Para 4:
I found the last sentence (“For instance, if the benefits of being correctly…. very hard to understand – I had to read it a dozen times, think for 20 minutes, and write several 2x2 tables before I understood. When I finally understood the sentence, I thought it was clear and simple and felt embarrassed over having struggled for so long with it. I suspect that I am representative for many potential readers who are not readily accustomed to thinking about diagnostic tests – assessing such tests is an intellectual challenge (which is the main reason for publishing this paper in the first place!). I propose that the authors expand this sentence to a few more, in order to make it easier for readers to grasp their point - which I think is key.

Methods, sub-section “Test & Treatment…”, para 2:
I would like to learn more about how the exercise that was carried out in order to estimate treatment- and testing-thresholds. This is – at least to me – an
innovative approach that deserves more space and detail.

Results.
I feel that the first para is more naturally placed in the Methods-section.

I propose adding one sentence about how the various pre-test probabilities were selected (I assume more or less out of the air, and that’s OK – but should be reported, still).

Box 1: Was difficult to read in the version I received, so I have not reviewed that properly. It’s an important element, though, as I expect guideline developer may use what’s in the box as a practical guide. I therfore urge the authors to carefully review the Box to ensure that it includes all important elements in the process – in my mind this includes the need to specify pre-test probabilities, treatment/test thresholds etc.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests.