Reviewer's report

Title: Judging the quality of evidence in reviews of etiological and prognostic studies: Adapting the GRADE's framework

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Reviewer: Nick Meader

Reviewer's report:

This an article that seeks to adapt the GRADE approach to assessing the quality of evidence for prognostic studies. This is a good and well thought out attempt to do this.

Major Compulsory Revisions:

1) Discussion of confounding (GRADE framework for prognosis paragraph 1) – I understand the point you make by suggesting confounding should be dealt with as an issue of risk of bias rather than as an additional factor to rate up the quality of evidence. I think this seems sensible. But I think you have to justify much more clearly in your paper how this would be an improvement on the approach GRADE currently takes. My guess is that your modification reflects a critique of the role of confounding in the GRADE system as a whole – rather than just in relation to its application to evaluating prognostic studies.

So I think you need to set out what the rationale GRADE uses for their current approach regarding confounding and then provide a clearer critique of that and why your modification improves the logic of this approach both in the context of prognostic studies but also beyond.

2) Inconsistency (points 1-3) – This is pretty much as reflected in the current GRADE system. But I think some refinement of the criteria may be helpful.

Point 1 – I would probably add that the differences between point estimates should be clinically meaningful rather than just based on statistical significance. But some further rationale for either approach would be an improvement

Point 3- I’m wondering whether I2= 75% as a criterion for inconsistency is a little liberal. Granted heterogeneity tends to be much higher in prognostic studies – but I think this just reflects the inherent uncertainty of much of this literature. So I’m not sure that we should use a more liberal threshold just on this basis.

3) Publication bias – I think your discussion of publication bias is not very clear. This is particularly the case when judging if publication bias is unlikely to be present. You seem to be arguing publication bias should be judged unlikely when adequate adjustment for confounding has been undertaken. I don’t follow how this would suggest publication bias is unlikely. I may have misunderstood your argument but this seems to be referring to a different issue. So I think you need to elaborate on this section and argue it more clearly.
4) The article needs a thorough read through and edit.

Discretionary Revisions:

5) Defining serious and very serious limitations (i.e. downgrading one or two levels) for inconsistency, imprecision, indirectness. You provide some guidance for risk of bias but not for these domains – further discussion of serious or very serious limitations. I accept that this does require judgement depending on the particular situation – but I also think it is possible to develop some general rules of thumb. Some examples from the GRADE working group articles would probably be helpful.

6) Imprecision – I think you would also want to take into account number of studies as well as total number of participants particularly if you were wanting to explore and quantify heterogeneity which I would think is almost always the case in relation to prognostic studies.

7) Have you contacted the GRADE working group and received feedback from them? I would have thought this would be an important aspect of refining this approach.

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