Author's response to reviews

Title: Judging the quality of evidence in reviews of prognostic factor research: Adapting the GRADE's framework

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Author's response to reviews:

Re: Manuscript revisions of Judging the quality of evidence in reviews of prognostic factor research: Adapting the GRADE's framework (MS ID: 1807494844977408)

Dear editors and reviewers,

Thank you so much for your feedback on our revised manuscript. We have addressed each of the reviewers’ concerns. Below we explain what we have done to approach of each concern and indicate where changes have been made in the manuscript.

Editorial requests:

We understand the need for a structured abstract adhering to the journal guidelines. Following the editorial request, we have modified the abstract into separate sections of Background, Methods, Results, and Conclusions. Please note, that due to the format of our manuscript and process taken for this work, the sections do not concisely fit with our research. Please review for appropriate clarity (see Abstract, page 2).

As requested by the editors in the Contributions section we have included each of the authors specific contributions (see Contributions, page 18).

Reviewer: Nick Meader

Minor Essential Revisions:

1) p5, paragraph 2: 'We think that most of factors taken into consideration by the GRADE framework...' This should be modified to something like: 'We think most of the factors taken into consideration by the GRADE framework....'
Thank you for catching this wording issue. We have modified the sentence appropriately (see page 5, paragraph 2).

2) p15: ‘...whether publication bias is evidence potential problem.’
   This should read something like ‘whether there is evidence that publication bias is a potential problem.’

Thank you for this suggestion, this sentence has been revised (page 14, paragraph 1)

3) p16, paragraph 4: ‘...developing a systematically way to evaluate the quality of evidence...' could modify to say ‘...developing a systematic approach to evaluate the quality of evidence...’

We appreciate you suggesting these revisions. We have followed your suggestion (page 16, paragraph 4)

Reviewer: Rob J Scholten

Reviewer's report:
I congratulate the authors with their very thoughtful amendments and I'm happy with all revisions, except one. The item 'imprecision' continues to confuse me. Page 12: “Second, if the number of participants included in the meta-analysis is appropriate, based on their best judgment, reviewers can consider the results precise when the confidence interval around the estimated effect size does not overlap the value of no effect and the interval is not excessively wide and does not contain values implying that the prognostic factor is associated with protection or increased risk.” What if there’s a very tight confidence interval that crosses the value of no effect but doesn’t include relevant values for a protective effect or increased risk? To me, that seems to be very precise (a very precise indication of no effect). Shouldn’t this line be rephrased as follows? “Second, if the number of participants included in the meta-analysis is appropriate, based on their best judgment, reviewers can consider the results precise when the confidence interval around the estimated effect size does not contain values implying that the prognostic factor is associated with protection or increased risk. In addition, what if there’s a very tight confidence interval with an upper limit that doesn’t include irrelevant values for a protective effect or a lower limit that doesn’t include irrelevant values for an increased risk? To me, that’s also very precise. Maybe the challenge here is that this second rule is phrased for assigning the label ‘precise’ instead of assigning the label ‘imprecise’? I leave it to the judgment of the editors whether they share my confusion and whether or not this rule should be adapted.

We appreciate your suggestions for clarity regarding our presentation of imprecision. When writing this manuscript we have struggled with clearly representing this concept. We agree with your comments and to reduce confusion for the second requirement of precision (in addition to sample size), we
recommend authors to focus on the width of the confidence interval (rather than considering whether or not it overlaps the value of no effect). We specify that, “reviewers can consider the results precise when the confidence interval around the estimated effect size is not excessively wide while containing values implying that the prognostic factor is associated with protection or increased risk” (see page 12, paragraph 4). We hope that this modification addresses your concerns. If you feel additional explanation is needed, please advise.

Comments regarding Tables 4 and 5 (apologies for not having mentioned this in my previous report):

1. These Tables don’t seem to be self-explanatory. E.g. ‘N’ stands for number of included patients; ‘Univariate + 0 –’ stands for? Idem ‘Multivariate’? ‘Phase’ and ‘Mod-LgES’ may require footnotes.

Thank you for this suggestion, we want the tables to be as clear as possible. We have added in footnotes explaining all abbreviations in Tables 4 & 5.

2. Table 4: my comments in my previous report regarding including examples also applied to this Table. I had hoped that the authors could have populated this Table as well with some examples of their own.

We understand that having an example in Table 4 is ideal. However, we did not conduct a meta-analysis in our review, we only provide a narrative summary. Therefore, we do not have available examples that we can report in Table 4.

3. Table 5: please, explain the abbreviation HA in the legend (or write in full). A strange ‘Beta’ appears in the scores, the explanation of which in the footnote is confusing to me.

Thank you for pointing out the ‘Beta’ in the scores of Table 5. In our .docx document we present check (✓) and x (✗) marks. These did not transfer when the .pdf of the manuscript was built. We have resaved these as images in the tables and hope that with this submission they will translate appropriately. We have explained the abbreviation of HA in the footnote of Table 5, thank you.