Author’s response to reviews

Title: The increasing need for systematic reviews of prognosis studies: strategies to facilitate review production and improve quality of primary research

Authors:

Johanna Damen (J.A.A.Damen@umcutrecht.nl)

Lotty Hooft (l.hooft@umcutrecht.nl)

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Author’s response to reviews:

Dear Dr Halabi,

We would like to thank you and the reviewers for your consideration and assessment of our manuscript "The increasing need for systematic reviews of prognosis studies: strategies to facilitate review production" (DAPR-D-18-00019).

We have addressed the comments and suggestions provided by the reviewers. We have extensively revised our manuscript to make sure our aims are more clear and to reduce focus on Cochrane. Below you will find our responses to the comments and the changes we made accordingly. Alongside this letter we submit a revised manuscript, in which changes are indicated by using track changes, as requested.

We hope to have replied and amended the manuscript to your satisfaction, and we would again like to thank you for the suggested revisions.

With kind regards,

Also on behalf of Lotty Hooft,

Johanna Damen

Cochrane Netherlands
Julius Center for Health Sciences and Primary Care
University Medical Center Utrecht, Utrecht University
The Netherlands
j.a.a.damen@umcutrecht.nl
+31 88 75 693 77
Responses to reviewers

Reviewer #1: This manuscript is well written. However, I don't quite see the point of the editorial. It announces that Cochrane now handles systematic reviews of prognostic studies. But, as a researcher who does mostly prognosis research, I'm not sure why I need to know this. Perhaps there is a better way to motivate the authors' message. I've read the manuscript, but I will just keep on publishing my prognostic studies. Would I do a better job or something if I visited the Cochrane site? Am I doing my studies poorly (I follow Tripod)? I suppose I'm just looking for a little more "so what" to this editorial, if that could be motivated further.

AUTHOR RESPONSE: We thank the reviewer for this comment. We think it is very important that our message is clear to the readers and have therefore extensively revised the editorial. We now clearly formulated the aims of our editorial, both for researchers of primary prognosis studies and for researchers of reviews of prognosis studies. Furthermore, we added more specific guidance on what researchers should do with all the tools we are describing. For researchers of primary prognosis studies, we specifically added the following:

“In addition, reviews identify gaps and redundant or unnecessary studies in the scientific literature, highlight flaws in conduct and reporting of primary studies, and identify and indicate which further studies are needed [1-5]. Therefore, reviews should serve as the essential starting point for clinical researchers of primary studies when designing a new prognosis study. The aim of this editorial is to provide an overview of the improvements in methods to perform systematic reviews of prognosis studies and freely available tools and templates. In addition, we want to raise awareness amongst clinical researchers of primary prognosis studies that those reviews and tools (e.g. reporting guidelines) are essential to use when a new study is designed, conducted and reported. Our ultimate goal is to facilitate the production of only necessary, highly relevant, and unbiased reviews, which provide an overview of high quality and useful primary prognosis studies.”

Reviewer #2: This is a commentary highlighting a growing need for systematic reviews of prognosis studies. I have no disagreement with the message that there is a growing need. The commentary also aims to discuss strategies to facilitate review production. I think this aim is not as well served. My fundamental critique of the reviewed facilitators are that they are all Cochrane tools. It is possible that no such tools exist and if this is what the authors think they should probably state so and also call for development of similar facilitators outside Cochrane. If there are other tools they should be included in the commentary as well.

One consequence of the Cochrane-centric style is that the manuscript oscillates between scholarly work and an advertisement for Cochrane’s added capabilities and interest for prognostic reviews. Half of the abstract and about one-third of the article is focused on Cochrane. While Cochrane may be the best umbrella we have for systematic reviews, it is not the only source of high-quality reviews. Hence a more balanced style of presentation is likely to benefit a larger number of reviewers.
AUTHOR RESPONSE: We thank the reviewer for this comment and we understand that this commentary looks like a big advertisement for Cochrane’s work.

Most tools we describe here actually have not been developed specifically for Cochrane, but for a wider public. These tools have however been adopted by Cochrane and are thus now advocated by Cochrane. The researchers that developed these tools are indeed all involved with Cochrane, however for some of the tools we are referring to (e.g. the QUIPS tool) development started before the formation of the Cochrane Prognosis Methods Group. Authors of these tools were often not involved with Cochrane at the moment of writing, but later joined Cochrane to join forces. We see this as a good thing: researchers from various universities and countries are now together developing more advanced methods and tools, to make sure everyone follows the most up-to-date methods. This also creates uniformity between reviews. We have made several adjustments to the editorial to reduce focus on Cochrane and have written only one paragraph on Cochrane’s work in this field. Further, we have now added text that the tools we describe can also be used by authors not writing a Cochrane review.

“The growing attention for prognosis research and the increasing emphasis on the importance of prognostic information in clinical practice has led to the introduction of the Cochrane Prognosis Methods Group (PMG) in 2007 [28]. Over the years, a growing group of experts in the field of primary prognosis studies and evidence synthesis have joined this group to work together and develop tools and guidance necessary for facilitating reviews of prognosis studies. Since 2016 reviews of prognosis studies are formally adopted and implemented within Cochrane (via the Cochrane PMG [29]). The first two Cochrane reviews were published in 2018 [30, 31], 9 protocols are published in the Cochrane Library, and 5 titles have been registered. The implementation within Cochrane comes together with the development of tools and templates for conducting a review of prognosis studies. Trainings and webinars are organised by the Cochrane PMG, aiming to give researchers sufficient skills on how to use the tools and templates and up-to-date knowledge on performing a systematic review of prognosis studies (see [29] for available tools and templates). All tools, templates, and methods developed by researchers involved with Cochrane are also available for authors writing a non-Cochrane review.”

Beyond this main critique I have some minor points to make:

1) The four different types repeated mentioned in the manuscript (overall prognosis, prognostic factors, prognostic models and predictors of treatment effect) is not a classification I have seen beyond the papers cited (and looks like mostly co-authored by members of Cochrane Netherlands). If it is a widely accepted grouping please cite some other articles that refer to it beyond Cochrane authors. I am partly puzzled because I do not understand why we do not have a separate category of models of predictive effect.

AUTHOR RESPONSE: We have now highlighted that this classification has been developed by the PROGnosis RESearch Strategy (PROGRESS) partnership. The Cochrane PMG has adopted this classification as it is useful and review methods differ for the different types of primary prognosis studies. This classification is also being used by researchers outside Cochrane (see for example PMID: 30142609, 30231051, 30205818 and 29718407). We agree that it is strange that
predictive models are not described in this classification. This is simply because these types of models are rather new. We have added a sentence on these predictive models.

“Studies on predictors of treatment effect (4) aim to identify individuals’ factors that are associated with the effectiveness of a certain treatment, e.g. the presence of the oncogene HER2/neu is predictive of the effectivity of the monoclonal antibody trastuzumab for treating breast cancer [12]. An additional primary study type is where several predictors of treatment effect are combined, to form a predictive model that predicts treatment effect. A model like this can be used to select individuals that benefit most from a certain treatment.”

2) The authors cite numbers from PubMed (72500 in 2000 and 200000 in 2017) to back their assertion that this kind of research is on the rise. My observations agree with their assertion but this way of defending seems to ignore the fact that all literature is exploding and these numbers are conflating the "general growth in science" with "specific growth in prognostic modeling" I realize it is a commonly used tool but I also think for the empirical research community that this journal represents it is an important distinction.

AUTHOR RESPONSE: We thank the reviewer for this excellent comment and we fully agree that numbers like this are a bit misleading. As these actual numbers are not important for our main message (growing attention for prognosis research) we decided to delete this sentence.

3) Manuscript arrived without page numbers but what I could as the third page om top line ther eis a reference to "all review types" and I do not know what a review type is.

AUTHOR RESPONSE: Apologies for the lack of page and line numbers. We have now added them. With all review types we actually refer to reviews summarizing evidence on either one of the types of primary prognosis studies. We now made this more clear:

“All types of primary prognosis studies can be summarized, evaluated and interpreted in different types of systematic reviews, following the broad range of aims and objectives of the included prognosis studies.”

4) Same paragraph halfway though (~line 13) "predictive performance" do you mean prognostic performance?

AUTHOR RESPONSE: with predictive performance we indeed refer to prognostic performance. We have added this term now as different terms are being used in literature:

“the predictive (prognostic) performance of the Revised Cardiac Risk Score”