Reviewer's report

Title: Evidence synthesis in prognosis research

Version: 0 Date: 27 Aug 2018

Reviewer: Georgios Markozannes

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Thank you for the opportunity to review this work. Debray et al. provide a nice overview of methods that have been implemented to synthesize data from various sources in the field of prognostic research. This is a clear and well-written paper. I only have some minor comments. My specific comments are as follows:

I believe that the use of the term "meta-analysis" is somewhat insufficient to properly describe the scope of the paper as well as the breadth of methodologies presented. Although most of the methodologies presented are pertinent to meta-analysis, there are also some that are clearly not. I would suggest to use the term "evidence synthesis" instead or in addition to "meta-analysis".

The author state: "In this paper, we discuss how the data or prognostic results … can be combined quantitatively." And later "An overview of all methods is provided in Table 1." Although there are numerous methodologies presented in the paper, the list is clearly not exhaustive. In fact, what the authors present may be better described as a list of methodologies that have been implemented for synthesizing evidence in the field of prognostic research. For example, the fact that no study has performed a meta-analysis of non-linear and not similarly adjusted factor-outcome association before does not mean that it cannot be done, for example based on a multivariate meta-analysis similarly to a linear factor-outcome association. This is also the case for individual participant data (IPD) on model validation, where another possible approach would be a two-stage meta-analysis, or a network meta-analysis used for aggregate data (AD) + IPD (given sufficient details from the AD).

The authors present in a clear and concise way the AD fixed (common) and random effect meta-analysis models early in the paper. Another, less known, interpretation of the fixed effect(s) model exists that could be potentially of interest [1] (although this interpretation has not been considered in any of the presented methodologies). The three models can be seen roughly analogous to the IPD common, random or independent (fixed) effect estimate from a mixed model. It would be useful to highlight the differences (assumptions and interpretation) across these models (and possibly their implications) also for model development and validation. What difference does it make in clinical practice if a model has been validated based on a fixed or random effects model? Also, in which cases would it be prudent for the researchers to provide extra relevant information to allow for tailored predictions for certain populations?
On the concluding remarks the authors advise researches to conduct a systematic review of the literature, and to harmonize available IPD sets. While the former advice is self-evident for most researchers working on the field of systematic reviews and meta-analyses, the latter may not be so, whereas the methods used for harmonization range from simple standardization techniques to more complex statistical methods [2]. Please, expand this briefly and, if possible, provide some references.

References


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