Reviewer’s report

Title: Untapped potential of multicenter studies: a review of cardiovascular risk prediction models revealed inappropriate analyses and wide variation in reporting.

Version: 0 Date: 22 Oct 2018

Reviewer: Jan van den Brand

Reviewer's report:

The manuscript by Wynants et al details a systematic review of clinical prediction models in the field of cardiology. The aim of the study was to determine how authors commonly deal with clustering by center in the development of prediction models in multi-center studies. The authors found that of the included studies published after the year 2000, 65% were multi-center studies. From 390 eligible studies, the authors randomly selected 50 for full text review and data extraction.

They showed that out of these 50 studies, clustering was ignored in 39 (78%). Moreover, sample size imbalances between centers were common. However, in only 22 of the 50 studies sample size imbalance was reported and 9 out of 50 studies reported sample sizes by center. The authors go on to highlight the possible consequences of ignoring clustering and center level differences during the development of a clinical prediction model. Importantly, generalizability may be lacking due to mis-calibration and non-transportability of the models.

Finally, the author make a series of recommendations on study design, model development, validation, and reporting.

I found this an interesting and education manuscript on an important but often overlooked topic. Standard textbooks (such a Steyerberg Clinical Prediction Models) make little mention of the impact of clustered data. Hence, the manuscript may be of interest to the readership of BMC-DAPR. The manuscript was generally well written in appropriate English, barring a few minor mistakes (e.g. the use of a contraction in line 189).

I only have several minor comments/questions.

* How was the sample size of 50 arrived at?

* The models were selected from cardiology, where there is a relatively long standing tradition of prediction modeling and research. For the purpose of their discussion and the generalizability of their findings, have the authors considered the state-of-the-art in other fields. For example, by checking a few reviews?

* The figures were vague. May be the dpi was set too low. Exporting from R in a vector format (pdf or eps) should avoid this issue.
**Level of interest**
Please indicate how interesting you found the manuscript:

An article of importance in its field

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal