Reviewer’s report

Title: Dynamic models to predict health outcomes: Current status and methodological challenges

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Reviewer: Ewout Steyerberg

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This is an interesting manuscript on an important topic. I like the separation in 3 categories of updating approaches.

The main point suggested is 'validation'. Another point of attention is the tuning of a forgetting factor / decay? The latter seems very reasonable for a continuous in time approach; other methods are more relevant for discrete data collections? Please sharpen your view here a bit.

Other comments:

1. Calibration drift: The focus in the Abstract seems to be on calibration drift; the more general aspect is 'accurate predictions', which I would suggest can be attributed to temporal or geographic differences in baseline risk and / or predictor effects. The latter can be summarized in a calibration slope, which may also reflect some overfitting, more than a true external validity issue. Calibration drift suggests a focus on baseline risk differences. This is indeed a frequent problem with external validation, but not necessarily so.

2. In line with these more general issues with accurate predictions we recently proposed a test for updating (Vergouwe et al: https://www.ncbi.nlm.nih.gov/pubmed/27891652 ). Also, updating may be with an extra predictor / biomarker: https://www.ncbi.nlm.nih.gov/pubmed/27678479

3. The term 'dynamic modeling' might not be used in the current context, although I see that many papers did so before. See e.g. Putter's book: dynamic prediction, which takes as a time axis: follow-up per patient. Here calendar time may be considered, and 'updating' may be a far easier term, perhaps less sexy, but more appropriate? Updating applies not only to calendar time, but also to geography, which is advantageous.

4. Some references may have been missed; please consider searching with the term 'updating'. If the claim is 'extends the findings by conducting an up to date literature search', then the search needs to be comprehensive.

   a) The work by Van Houwelingen should be cited (https://www.ncbi.nlm.nih.gov/pubmed/8677400 ); my 2004 paper followed his thinking; and I put the sequence 'development, validation and updating' in the
b) If I look at my own work (simply search in PubMed with 'updating') I find some studies that may be relevant (among 26: http://www.ncbi.nlm.nih.gov/pubmed/?term=steyerberg+updating) that consider temporal impact and model adaptations:

https://www.ncbi.nlm.nih.gov/pubmed/17162015: more recent patients + difference setting (screen vs clinic)

Also, an example is the development of a diagnostic model for Lynch syndrome, where the testing procedure was modernized after some point in time:


Cardiology: https://www.ncbi.nlm.nih.gov/pubmed/21367834


Asthma: https://www.ncbi.nlm.nih.gov/pubmed/23987795

5. The formulation 'stream across real time' is ugly, and seems to refer to computer science?

6. The term 0() may confuse some as relating to baseline hazard in survival?

7. Validation: the description as "This is typically done for static CPMs by split sample, bootstrapping or external sample validation" is a bit awkward; cross-validation (e.g. 10-fold) or bootstrap validation are to be recommended; a single, random split sample validation should never be done; dominated by cross-validation / bootstrap validation.

8. Step change: this could easily be modeled with a specific factor, see e.g. for the introduction of cardioplegy: https://www.ncbi.nlm.nih.gov/pubmed/9243151

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