Reviewer's report

Title: Landmark models to define the age-adjusted risk of developing Stage 1 type 1 diabetes across childhood and adolescence

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Reviewer: Hein Putter

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This paper uses landmark models to dynamically predict the probabilities of development of islet autoantibodies and diabetes at birth and at the age of 3.5, 6.5 and 12.5 years, with either 6 years (short-term), 12 years (mid-term) or 20 years (long-term) follow-up. Data from the prospective BABYDIAB and BABYDIET are used for development of the landmark models.

The idea to use this type of methodology is novel in this subject area, I think. I have a number of statistical comments.

One potential problem concerns the definition of the outcome islet autoantibody positivity, namely as being positive for at least one islet autoantibody in at least two consecutive samples. I understand where it comes from, the first positive sample might be a false positive result, but it has its consequences. One is that in case of censoring after the first positive result, this will not be confirmed in a second sample, even if that would have been positive, and the first positive result should then have been defined as the outcome islet autoantibody positivity. The second consequence is specific for the landmarking, which specifies the selection of subjects who did not have the event of interest yet. How did the authors handle the potential situation that a landmark was positioned between the two consecutive positive samples? Was the subject in or out of the landmark data in that case? Can the authors comment on possible biases occurring from wrongly in- or excluding subjects from a landmark data set?

About the exponential decay: how were the parameters (two, I think, a*exp(-b*x), correct?) fitted to the data, and how was the correlation defined? I get the impression (from the fact that the authors have calculated a correlation) that this was simply a fit of this function to the landmark prediction. Is that correct, and if so, to which predictions exactly? Or was this obtained through a proportional baselines landmark super model?
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
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Not applicable

Are the conclusions drawn adequately supported by the data shown?
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Yes

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