Reviewer's report

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

Version: 0 Date: 21 Feb 2019

Reviewer: Beverley Shields

Reviewer's report:

This paper describes landmark models and exponential decay curves to quantify the risk of developing islet autoantibody positivity at different ages and for different periods of follow up. The manuscript describes a novel and really interesting study. It is generally clear and well written, and statistical approaches appear appropriate for describing the data. There are just a couple of areas where a bit more explanation or clarification would be useful.

1) A little bit more explanation on how the exponential decay functions were derived would be helpful as it took me a while to get my head round what was done and I'm still not 100% clear. Was it purely from the values in Table 1 (although data for 1.5 and 9.5 landmark ages aren't provided)? Was this carried out using the exponential decay curve fit function in GraphPad prism? Please could this just be clarified a bit more in the paper.

2) The results for the risk by age 20 when plugging in landmark ages into the exponential decay functions seem lower than the risks reported in Table 1 from the landmark models (e.g. risk by age 20 for landmark age 6.5 = 8.8*10^(-0.19*6.5) = 0.5, whereas in Table 1 the risk is 2.7% (95% CI 1.9-3.6)). The same applies to the other functions. Is there a reason why this is? Should it be 8.8*exp(-0.190*ageX) instead (and similarly for the other equations)?

3) Results third paragraph (page 9) - the relationships between landmark age and risk of developing islet autoantibodies in those with high risk HLA genotypes - as well as saying the pattern is consistent I think it's worth stating that as expected, the risks overall were much higher. Even though this is to be expected, the fact that the figures are on different scales, means that you miss this on first look.
4) I think it might be more informative to have the exponential decay functions on the plots in Figure 3 rather than the r2, as that's the key result rather than the goodness of fit.

5) Minor comment - How was islet autoantibody positivity defined? Was it based on specific thresholds? Although this is probably the same as in the references provided, as it's the key outcome, it would be useful just to add this information in to this paper.

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?
If not, please specify which controls are required in your comments to the authors.
Not applicable

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
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