Author’s response to reviews

Title: Evaluation and refinement of the PRESTARt tool for identifying 12-14 year olds at high lifetime risk of developing type 2 diabetes compared to a clinicians assessment of risk: a cross-sectional study

Authors:
Laura Gray (lg48@le.ac.uk)
Emer Brady (emer.brady@uhl-tr.nhs.uk)
Olatz Albania (oalbaina@kronikgune.org)
Charlotte Edwardson (ce95@leicester.ac.uk)
Deirdre Harrington (dh204@leicester.ac.uk)
Kamlesh Khunti (kk22@le.ac.uk)
Joanne Miksza (jkm42@leicester.ac.uk)
Joao Raposo (filipe.raposo@sapo.pt)
Ellesha Smith (eas24@leicester.ac.uk)
Andriani Vazeou (agerasim@gmail.com)
Itziar Vergara (itziar.vergaramitxelto@osakidetza.eus)
Susann Weihrach-Blüher (Susann.Blueher@medizin.uni-leipzig.de)
Melanie Davies (melanie.davies@uhl-tr.nhs.uk)

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We are grateful for the opportunity to revise our manuscript for publication in Endocrine Disorders. Following the first round of extensive reviewer’s comments, the first reviewer is happy to accept the manuscript as it is. The second reviewer has a number of additional comments, many of which would require the study to be conducted with a different design and collecting different data. This is not possible to do given this was an EU funded study and the funding has now come to an end. Therefore we have justified our approach and have made
additions/changes to the manuscript where possible. We have addressed each comment in turn below.

Comment 1: It is good to clarify that the prediction of T2DM was for lifetime incidence; however, the authors were not sure if the timeframe used was consistent across all clinicians who participated in the study. The authors need to revisit each clinician for their definition of T2DM incidence.

Response: This was not part of the original research. At the reviewers request we have re-contacted each of the clinical assessors by email to request additional information from them. We have only received one reply, in regards to this point the assessor stated – “Diabetes during mid-life (35-55 years)”. We do not feel adding the opinion from one of 10 assessors to the manuscript is a robust way of representing this and therefore we have not added this to our manuscript. We have added this to the limitations section.

Comment 2: Although the authors toned down their claim of developing and validating their prediction tool for lifetime risk assessment for T2DM in juveniles, the study still examined how well the questionnaire-based tool could recapture what human experts, clinicians, judged on the risk of developing T2DM. It would be probably much better to collect these clinician's judgement criteria and come up with a consensus model.

Response: We agree with the reviewer that there are many different ways this study could have been designed. We used a combination of methods to develop the tool – risk factors were identified from a systematic review and consensus study was used to refine these. Therefore consensus methods were used for this part of the study. We then collected data from over 500 adolescents and asked a pool of clinicians to assess each adolescent’s risk of developing T2DM based on the data collected. These data were then used to refine and simplify the tool. We did not collect data on how the clinical assessors made their decision. This is included as a limitation in the discussion section of the manuscript and we suggest that this is an area for further work.

Comment 3: Related to above comment, the authors confirmed that no record of rationales of clinicians' judgement was collected. Considering each clinician handled less than 100 subjects, I highly recommend the authors to work with the clinicians to reassess the same subjects and record their decision as well as their rationales. I think most clinicians probably used just a few factors in their decision making, which will be easily captured.

Response: This is an interesting point. Unfortunately, the study was not designed to collect qualitative data from the clinical assessors. We would argue that the recall of the clinicians of
their decision making processes on the 100 adolescents may not be reliable given the time that has past. Further, as funding has finished and the study closed there would be no human resource to co-ordinate this additional work or indeed backfill the clinician’s time. We also do not have relevant regulatory/ethical approvals to conduct the suggested additional work. The risk factors included in the initial tool were selected by clinical experts using a consensus study, therefore they reflect the risk factors which clinicians feel are important in the assessment of T2DM risk.

Comment 4: The author disclosed that the sequential removal of risk factors for model refinement was based on the feedback from stakeholders and PRESTARt collaborative. This is not well justified. Who determined the order of sequential removal, on what basis? The current approach does not fully explore the all possible combinations of risk factors.

Response: The reviewer is correct we do not assess all possible combinations of risk factors. The risk factors included in the initial tool were based on the findings of a consensus study. Looking at each possible combination of risk factors is a data driven process, as is best practice for developing prognostic models we wanted to use existing literature and clinical opinion to derive our initial tool and use the data only to simplify the tool. We have added a discussion of this point to the discussion. Importantly the final tool developed has a high level of performance when assessed the clinical assessment.

Comment 5: Using weight alone achieved one of the best prediction performances, which also suggests that the clinicians probably heavily used this factor in their decisions. The authors believe a more holistic assessment of risk is more important for a few reasons. However, the bottom line is none of these additional factors actually improve in terms of prediction performance within the current context of evaluation (matching clinicians' judgement). I recommend the authors to examine models, including only non-weight factors (either uni-variate or multi-variate).

Response: We agree with the reviewer – weight is highly predictive of T2DM risk. This is also the case in risk tools developed for use in adults. We have included additional risk factors to give a holistic assessment of risk and to engage adolescents/parents with their modifiable risk factors, this has also been done in the well-used adult risk scores. For example the FINDRISC includes questions on physical activity and consumption of berries for this very reason. Given weight is so predictive we can’t see the rationale for not including it in a risk assessment of T2DM risk.
Comment 6: The authors disclosed that there were eighteen participants (6.41%), who were had been deemed to be at high risk by the clinicians, even though they were overweight/obese. It would be important to understand why the clinicians determined them to be at high-risk.

Response: We presume the reviewer is referring to the 18 participants who were not overweight/obese. This would be an interesting to understand. However, as previously stated the reasons behind the decision making process for the clinical assessors were not collected.