Reviewer’s report

Title: Predicting Diabetes Clinical Outcomes Using Longitudinal Risk Factor Trajectories

Version: 0 Date: 24 Jan 2019

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?
Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?
Yes - the approach is appropriate

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?
Yes - experiments and analyses were performed appropriately

Statistics - Is the use of statistics in the manuscript appropriate?
Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?
Yes - the author's interpretation is reasonable

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?
Yes - current version is technically sound

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: Everything is fine
ADDITIONAL REQUESTS/SUGGESTIONS:

This is a very interesting paper incorporating long term data in an attempt to evaluate subsequent DM emergence risk. However, this paper suffers from some limitations, which should be discussed by the authors.

1. The great advantage of these models is their superiority against FDR score. Nevertheless, FDR score is usually to be calculated on an outpatient clinic and applicable on every day practice.
These indexes have not been presented in the manuscript in order to provide the reader with their availability to use them in everyday practice. Of note, several patients carry an extended database with previous lab tests as well as the implementation of electronic records make data collection feasible.

2. The number of subjects who participated in the study is not clearly stated. Additionally, a graph showing the development of DM through years in this cohort would be elusive.

3. It is not clear if these FPG values analyzed in this work have been obtained during a random, regular check-up or they were obtained during a hospital visit due to any illness that may affect fasting glucose values. If the latter is the case, then the percentage of subjects with hyperglycemia who returned to normal values through years does not have to deal with the "metabolic memory" concept. Can you please clarify?

4. The fact that FPG values in the majority of labs have a great variance between 5-10%, I think you have to provide CV's of the assays employed during this study. Furthermore, since this variation may misclassify one subject from normal to prediabetic, which approach do you consider better to avoid this problem? The definition of extreme values, although reasonably made, may be less than the CV of assays and therefore it's prognostic value should be neglected. A similar methodological bias could be hypothesized for blood pressure and lipid measurements.

Note: This reviewer report can be downloaded - see attached pdf file.

**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.

Yes

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

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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

Acceptable

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