Reviewer’s report

Title: Distinction of cardiometabolic profiles among people ≥ 75 years with type 2 diabetes: A latent profile analysis

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Reviewer: John Hughes

Reviewer's report:

The authors performed a latent profile analysis (LPA) to classify patients using age at diabetes diagnosis, insulin sensitivity (HOMA2%-S), beta-cell-function (HOMA2%-β), and the product between both (HOMA2%-βxS) as a measure of residual beta-cell function.

Latent Profile Analysis (LPA) tries to identify latent profiles (sub-groups) based on responses to a series of continuous variables or indicators within the observed data.

One hundred and forty seven patients from the 3600 patients followed up were selected. These patients were aged ≥75, Caucasian and had had a Homeostasis Model Assessment (HOMA2) after the diagnosis of their diabetes. All participants were GAD-antibodies-negative.

The analysis identified six clinically different cardio-metabolic profiles within this group. The authors recommend that these should be used to guide the intensity and choice of GLT.

I do not think that this article is suitable for publication for the following reasons.

1. Statistical Analysis

The continuous discriminant variables (indicators) within the observed dataset were insulin sensitivity (HOMA2%-S), BCF (HOMA2%-β), hyperbolic product βxS (HOMA2%-βxS) and age at diabetes diagnosis.

The authors found six sub-groups within this observed dataset but then assumed that other variables or indicators not included in the analysis and therefore outside the observed dataset, could be partitioned in the same way.

This is scientifically unsound.

If these other variables had been included in the analysis, as they could have been, this would inevitably produce different sub-groups.

2. Conclusion
The conclusion is not supported by the results of the analysis.

The sentence that "This study identified 6 clinically different cardio-metabolic profiles in features among older patients ≥75" in the first sentence of the Conclusion is not correct. The six profiles were identified from age, HOMA2%-S and HOMA2%-β and HOMA2%-βxS. No other variables were included in the analysis (see Point 1 above).

3. Figure 1 and Table 1

Figure 1 clearly shows that LPA can identify distinct sub-groups. In Table 1 the significant p-values are found for age at diabetes diagnosis and HOMA2%-S, HOMA2%-β and HOMA2%-βxS. But this is exactly what latent profile analysis is designed to do.

In contrast differences or similarities between variables that were not included in the analysis have arisen by chance and cannot be used to support any of the authors' arguments.

4. Discussion

The authors acknowledge that their sample "may not de facto be representative of other populations of older patients with type 2 diabetes of various ethnicities".

This is an understatement. The pool of 3600 patients was already unrepresentative and the reduction of these to 147 makes generalising the results practically impossible.

5. HOMA

HOMA2%-S, HOMA2%-β and HOMA2%-βxS are related via the HOMA calculator (https://www.dtu.ox.ac.uk/homacalculator/). This means there must be conditional dependence between these indicators. Have the authors adjusted for this?

6. Presentation of Results

The results of the latent profile analysis are lost in Table 1. The HOMA results are presented together but the Age at Diagnosis is several lines above. The results of the analysis deserve to be presented by themselves in one table.

**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?  
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No

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