Reviewer’s report

Title: Socially isolated individuals are more prone to have newly diagnosed and prevalent type 2 diabetes mellitus - The Maastricht Study -

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Reviewer: Sara Pedron

Reviewer’s report:

General comments

The article shows the results of a study concerning the association of a large spectrum of social network variables with different stages of diabetes progression, represented by different patient groups in the cross-sectional dataset available.

Results showed significant associations of lower structural and functional support variables with newly diagnosed and previously diagnosed T2DM, albeit with different patterns for men and women, rightly considered in separate analyses by the authors. The authors conclude that social isolation and a lack of participation could contribute to the development of prediabetes into T2DM.

The aim of the study is clearly represented by the authors. Relevant studies in the literature are cited and generally appropriate methods are used. The results are also very interesting and highlight possible further research and intervention possibilities. However in some points they are not carefully interpreted, relevant actual strengths are not highlighted or imprecisely generalized.

Major Revisions

1. The authors should avoid any expression which implies causality: they are well aware that they cannot estimate it, nonetheless in some points this is not clear (examples: First sentence of the abstract, hypothesis in the background section).

2. The authors should consistently rename the group "T2DM" (sometimes also addressed as "prevalent T2DM") as "previously diagnosed T2DM" throughout the whole manuscript (only by manually adding the number of individuals in each group in Table 1 one can understand that the group T2DM is actually the group "previously diagnosed T2DM" without the newly diagnosed).

3. The authors should include a more detailed description of the study (when did it start? Is it still ongoing? How many participants involved?) and why did they choose exactly that time period. Reference 21 should be placed at the end of this block as further information for the reader.
4. The differences between the groups were assessed using appropriate statistical tests. The authors should include the results of these tests in the text or in Table 1. This should be of major concern for the authors: in the discussion section they are often referring to these results as "significant" (text lines: 243, 255, 276-280) but the reader cannot find any confirmation from the data reported.

5. The main analysis was carried out using a multinomial logistic regression, regressing diabetes status (comparison group for each outcome: NGM) with each social network variable and a set of confounders (age, BMI, educational level, employment status), stratifying by sex. Other typical confounders, which are commonly used are only included in the sensitivity analysis (hypertension, previous CVD, SF36) or reported in the descriptive statistics and in the text, but not included at all (smoking status, alcohol consumption, diabetes duration). Furthermore, income should be also considered as an additional confounder. These variables are essential moderators and should be included, not just in the sensitivity analysis or in the descriptive statistics. This means that further attention must be paid to these variables, either by including them in the main model or by extensively justifying their exclusion in the main model and explaining relevant differences in the results of the sensitivity analysis. I warmly recommend taking all control variables into account also in the main analysis.

6. The results of the analysis are very interesting. Nonetheless the most interesting results are not always fully highlighted or they are sometimes unnecessarily generalized. Authors should also add some degree of uncertainty and should be more cautious with the results interpretation. Furthermore, "socially isolated individuals" and "lack of social participation" are general terms (discussion section): what do the authors exactly mean with these terms? Where can I spot the results at a glance? The authors should either name the variables they are looking at or define these terms here or in a previous paragraph. Furthermore, if with "lack of participation" the authors are looking at the variables for contact frequency, proximity and type of relationship, the results are rather unclear, with some significant associations different for men/women and not always backed by the sensitivity analysis. In light of these and previous considerations, authors should revise their implications and conclusions. The main result is not that "the promotion of social integration and participation is a promising target in T2DM" (already known from previous literature cited in the background section) but the association with the single aspects they found, especially the type of relationship in women, the emotional support for important decisions and the practical support for sickness in both sexes.

Minor Essential Revisions

1. The authors should position their study in a more accurate way in the previously available literature: several good key studies (refs. 6-13, 8 studies) are cited in the background section, described in the following paragraph and are extensively cited in the discussion section in order to corroborate almost all of the results. Reporting that "the role of social network characteristics in the development of T2DM has hardly been studied" is in my opinion not fully accurate. The authors should consider a reformulation of this point, in
the background and in the discussion sections, by highlighting the rising interest in the last years and the relevance of this topic. Given the results of previous literature a more detailed and conjoint investigation of a larger spectrum of social factors is essential, and that is exactly what has been done in this study.

2. The authors should include a detailed account of how the different variables were computed, for example in an additional table. For example the division in levels of education is not fully understandable for the international reader: is the categorization similar to the ISCED education categorization? What is the difference between family and household? Including the variables definitions in an additional table would also help to make the text reading more fluid in paragraph 2.2.5, where authors should avoid using double parenthesis in the text.

3. An interesting point in the article is the division in different stages of the disease. The authors often highlight this point interpreting also differences between the groups as possible mechanisms with which the variables affect the "development" of the illness. In order to assess this, the correct control group for previously diagnosed/newly diagnosed T2DM should be prediabetes, and not the NGM group. Be careful in interpreting your results or add this point in the analysis.

4. The authors should include in the text a reference to the scale in which the functional support variables are computed (only available in the footnotes of the tables). Authors should also complete the results description of the same variables by adding "one additional unit of emotional support" "…was associated with 32% higher odds…", they should quantify this "less".

5. Figure 2: authors should add proper labeling of the axis and of the graphs described. "Less emotional support(…)" should be quantified also in this case (see previous point).

6. Paragraph 4.2: the authors should consider adding a reference to a possible reverse causality also in this paragraph: it is very likely that patients suffering from a chronic disease need a higher/broader functional support from their social network. By looking at the cross section, lower self-reported levels of functional support do not necessarily imply that their social network offers them a generally and absolutely lower functional support, but rather that they perceive it as less adequate to their needs (that means relatively lower). Also in this case a longitudinal analysis could help to shed some light on this very interesting point. Furthermore, Jones et al. (2015) use cross sectional data: no causal effect is shown (line 329).

7. Table 2: given the possibility of reverse causality, it would be helpful for the reader to include titles in the table to distinguish outcome variables/explanatory variables. Also explicitly state (in the text or in the table) that you are controlling for each of the social support variables separately and not in the same regression.

Discretionary Revisions
1. An additional contribution of the paper could have been the joint evaluation of some of the included aspects (structural AND functional support). The authors should also consider the inclusion of some interactions between the social inclusion/participation/support variables.

2. Concerning the main analysis, the division in "newly diagnosed" and "previously diagnosed" T2DM should be used as further sub-analysis, while the outcome "overall T2DM" (newly diagnosed + previously diagnosed cases) should be included in the main analysis for completeness (see ref. 12).

3. Figure 1 is in my opinion not necessary since it does not add any information nor does it facilitate the understanding. What about substituting this figure with a detailed account of the results of the chi-squared/ANOVA/Kruskal-Wallis tests for the significance of differences among the considered groups? (see Major Revisions nr. 4)

4. Paragraph 2.2.4.: please consider writing in italics/in quotation marks the single variables (e.g.: emotional support(discomfort), emotional support(important decisions)…). Not differentiating these elements from the text causes some problems in the text fluency.

5. Table 1: please consider restructuring of the first part of the table, adding italics titles (like the subsequent parts) for lines with multiple values.

6. Please check the list of references according to the requirements of the journal (e.g. proper citation of books; ref. 19 and ref. 22 wrongly cited).

7. Please avoid using semicolon in the text body. In the conclusion section a full stop is missing (line 380).

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

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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