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RESPONSE POINT BY POINT

Manuscript # 26405

Reviewers' comments:

Reviewer #1: The review study of Update on pre-diabetes: focus on diagnostic criteria and cardiovascular risk is a very well conducted and written study. This study provides good information and I believe it could be very useful in clinical practice. I have no major comments on it just the text should be checked for the language one more time before publication.

We thank the Reviewer for these comments. The language has been re-checked from native-speaker, as requested.

Reviewer #2: A review article with good structure. Only some suggestions and some minor errors. 1. In page 4, 'normal glucose tolerance (NGT)''; page 7,'' NGT/NT''; page 7-8,'' normal fasting glucose (NFG) and normal glucose tolerance (NGT)''; page 9, "NGT/NFG we found that the NFG/NGT subjects with HbA1c 39-46 mmol/mol showed an alteration of subclinical markers of cardiovascular risk compared with NFG/NGT''; page 10, "NFG and NT''. Please use uniform term.

We thank the Reviewer for this comment. The abbreviations have been re-checked according to Reviewer's suggestion.

2. Some studies have shown that there is poor concordance between HbA1c and FPG or 2hPG during an OGTT in diagnosis of DM. Some studies recommended lower cut-off point of HbA1c for diagnosis of DM. So, the authors may add your comment on this point in diagnosis of pre-diabetes by Hba1c.

This is a good point. Like the Reviewer suggests some studies recommend different cut-off

point of HbA_{1c} for diagnosis of type 2 diabetes and this point presents controversies also for

pre-diabetes diagnosis. In particular, longitudinal epidemiological studies have reported that

demographic and ethnic factors may contribute to complications in using HbA$_{1c}$ for the diagnosis of diabetes, and the optimal diagnostic HbA$_{1c}$ cut-off of is debated and varies due to genetic and biological variations. Yan ST *et al*. [1] identified optimal HbA$_{1c}$ cut-off points for pre-diabetes in two diverse population-based cohorts with different ages. The optimal HbA$_{1c}$ cut-off point for pre-diabetes diagnosis was 38 mmol/mol (5.6%) in the young and middle-aged population, whereas, the optimal cut-off for diagnosing pre-diabetes increased to 39 mmol/mol (5.7%), in the elderly population. Furthermore, many studies have shown that racial disparities affected the performance of HbA$_{1c}$ for diagnosing pre-diabetes [2]. We added these considerations in the appropriate section (Page 9, Line 20-29).

1 - Yan ST, Xiao HY, Tian H, Li CL, Fang FS, Li XY, Cheng XL, Li N, Miao XY, Yang Y, Wang LC, Zou XM, Ma FL, He Y, Sai XY. **The cutoffs and performance of glycated hemoglobin for diagnosing diabetes and prediabetes in a young and middle-aged population and in an elderly population.** *Diab.Res.Cli.Prct.* 2015 Aug;109(2):238-45. doi: 10.1016/j.diabres.2015.05.047.

2 - Masanori Shimodaira, Shinji Okaniwa, Norinao Hanyu and Tomohiro Nakayama **Optimal Hemoglobin A1c Levels for Screening of Diabetes and Prediabetes in the Japanese Population** J Diabetes Res. 2015; 2015: 932057. doi: 10.1155/2015/932057 PMCID: PMC4465763