**Author’s response to reviews**

**Title:** The product of fasting plasma glucose and triglycerides improves risk prediction of type 2 diabetes in middle-aged Koreans

**Authors:**
Joung-Won Lee (joungwon@korea.kr)
Nam-Kyoo Lim (namkyoo.lim@gmail.com)
Hyun-Young Park (mdhypark@gmail.com)

**Version:** 2  **Date:** 01 Apr 2018

**Author’s response to reviews:**

Detailed Response to Reviewers

April 1, 2018

Reviewer

BMC Endocrine Disorders

Manuscript ID: BEND-D-17-00165R2

Title: The product of fasting plasma glucose and triglycerides improves risk prediction of type 2 diabetes in middle-aged Koreans

Dear Reviewers:

We would like to thank you and the reviewers of the BMC Endocrine Disorders for taking the time to review our article. We have made some corrections and clarifications in the manuscript after going over the reviewers’ comments.
We revised the manuscript and blue highlighted lines were marked in revised text. Here we have addressed the concerns of the reviewers on separate pages, as well as our response to the specific comments.

We hope that the revised manuscript will better meet the requirements of your journal for publication. We thank the editor and the reviewers for the BMC Endocrine Disorders once again for the constructive review of our paper.

Sincerely,

1) We found a typing error in TG. TG value was calculated in mmol/L, but we expressed the unit as mg/dl. However, considering other sample units, it was decided to express TG in mg/dl as well. Therefore, we converted the unit of TG to mg/dl in the manuscript and the table.

2) Abstract: conclusions: “Adding TyG index into the basic risk model for T2DM increases its prediction and reclassification ability in both sexes.” was changed to “Adding either TyG index or FPG into the basic risk model for T2DM increases its prediction and reclassification ability. Compared to FPG, TyG index was a more robust T2DM predictor in the stratified sex and fasting glucose level.”

3) Background Line 19:

“Also, the increase of FPG in the normal range is associated with increased incident T2DM [17].” was added.

4) Methods: Measurements and surveys Line 14:

We have changed

“LAP for men=(WC-65cm)×TG,LAP for women=(WC-58cm)×TG"
TyG index=\ln(TG\times FPG/2)'' to

“LAP for men=[WC(cm)-65]×TG(mmol/L)
LAP for women=[WC(cm)-58]×TG(mmol/L)
TyG index=\ln \left[ \left( \frac{TG(mg/dl)\times FPG(mg/dl)}{2} \right) \right] “

5) Results:

a) The subtitle “Cut-off points of TG-related indices, and WC for predicting T2DM” was changed to “Cut-off points of each index for predicting T2DM”.

b) The subtitle “Effects of the addition of TG-related indices to the basic model of T2DM on cNRI, IDI, and AROC” was changed to “Effects of the addition of each index to the basic model of T2DM on cNRI, IDI, and AROC”

6) Discussion Line 50:

The previous sentence “ However, Janghorbani et al. reported that TyG index is not superior to FPG or the Oral Glucose Tolerance Test (OGTT) as a diabetes predictor.” was changed to “For predicting T2DM risk, TyG index was not better than FPG or OGTT in Isfahan Diabetes Prevention Study [38]” and relocated.

7) Conclusions Line 1:

The previous sentence “ In conclusion, TG-related indices are more accurate than WC in the prediction of incident T2DM. Considering the prediction ability of TyG index and national health care of Korea, TyG index can be a useful screening tool for incident T2DM in middle-aged Koreans.” was changed to “In conclusion, TG-related indices and FPG were more accurate than WC in the prediction of incident T2DM. In the subgroup categorized by sex and fasting glucose level, TyG index was a more robust predictor for onset T2DM than other indexes.
Therefore, TyG index can be a useful screening tool for incident T2DM in middle-aged Koreans.”

Editor-in-Chief:

1. Your models should also include fasting plasma glucose alone as a predictor of incident diabetes.

2. You should further discuss why it is worth to screen using an additional blood measurement (TG), when non-invasive parameters or even BG alone can predict incident diabetes with equal or slightly lower accuracy.

3. In light of the above comments your conclusions should be toned down.

Authors’ response

As the editor pointed out, we tested whether TyG index was better than fasting plasma glucose alone (FPG) as a predictor of incident diabetes. We have added a detailed description of the results.

“Although TyG index predicts incident T2DM well, its usefulness is questionable, when compared to fasting glucose [38, 44]. For predicting T2DM risk, TyG index was not better than FPG or OGTT in Isfahan Diabetes Prevention Study [38]. Wang et al. reported that TyG index, LAP, and visceral adiposity were not superior to FPG or WC alone as diabetes predictors among Chinese [44]. In the Vascular-Metabolic CUN cohort, Navarro-Gonzalez et al. compared the prediction ability of TyG index and FPG for onset T2DM [35]. Association between indexes and their discrimination for onset T2DM were different depending on the fasting glucose subgroup. When the highest quartile for each index was compared to the lowest, the hazard ratios (HRs) of TyG index and FPG were 3.0 and 7.3 in the impaired fasting glucose group. On the other hand, TyG index showed stronger association with onset DM than FPG in the normal fasting glucose group (HRs: 6.8 vs. 4.6). On the other hand, TyG index showed stronger association with onset DM than FPG in the normal fasting glucose group (HRs: 6.8 vs. 4.6). The discrimination of TyG
index for onset T2DM was also better than that of FPG in the normal fasting glucose group (AROC: 0.75 vs. 0.66). In the present study, we found the association between some metabolic syndrome (MetS) components and incident T2DM (Appendix table 2). Therefore, we compared the discrimination of each index for incident T2DM in the stratified MetS components (Appendix table 3). In the elevated FPG group, the discrimination of FPG (AROC: 0.506) for incident T2DM was inferior to that of other indices. On the other hand, TyG index was a more robust discrimination index than other indices in the group stratified by sex and MetS components. Our findings indicate that TyG index is not only a better predictor for incident diabetes than WC, LAP, and TG, but it also has a better reclassification ability. On the other hand, association between FPG and its (their) reclassification ability for incident T2DM were different depending on sex.” and “It was also noted that association between FPG and its reclassification ability for incident T2DM were different depending on sex.” were added to discussion line 48-71, 75-76.