Author’s response to reviews

Title: The shape of the glucose response curve during an OGTT heralds β-cell function in a large Chinese population

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Author’s response to reviews:

August 30, 2019

Nerys Astbury, PhD
Associate Editor
BMC Endocrine Disorders

Re: BEND-D-19-00268
Dear Dr. Astbury:

We would like to thank you and the reviewers for your detailed and very helpful comments on our manuscript entitled “The shape of the glucose response curve during an oral glucose tolerance test heralds β–cell function in a large Chinese population” (BEND-D-19-00268). We appreciate the opportunity to re-submit it for review. We have amended the manuscript according to your recommendations. All changes to the manuscript are indicated in the text by highlighting. Below, we detail, item-by-item, our responses to the specific suggestions.

Reviewer #1 Comments:

Comment 1

The manuscript describes the association of glucose response curve shape during oral glucose tolerance test with beta cell function and insulin resistance. Authors are highly appreciated for a valid research design.

However, revise the introduction section by adding the some more information regarding the diabetes mellitus. Authors are advised to look into the following references: Journal of Cellular Biochemistry. 2017;118(1):3577-85, Journal of Biomedical Sciences. 2016;23(1):87

<Response>

Thank you for this comment. We have added more information about diabetes mellitus in the Background section.

Background: line 38-41, page 2
Reviewer #2 Comments:

Comment 1


<Response>

Thank you for this observation. We have elaborated on the pathogenesis of type 2 diabetes in our article based on your recommendations.

Background: line 38-41, page 2

Comment 2

Background: lines 26-29: The OGTT is used to diagnose diabetes mellitus, not type 2 diabetes mellitus.

<Response>

We agree with the reviewer and have fixed this error in the original text.

Background: line 44, page 2

Comment 3

Material and methods: Subjects: the selection criteria of subjects included in the study are not clear. Were these individuals with or without DM, or both? The exclusion criteria c) suggests that patients with diabetes were also included. In this case, the study population should be restricted to subjects without previously diagnosed diabetes for various reasons, the main one being that the antihyperglycemic medication influence significantly the evaluated parameters (see for example: DeFronzo RA et al. J Clin Endocrinol Metab. 2014 Oct;99(10):3774-81.)

<Response>
We thank you for pointing this out. We have now excluded subjects with previously diagnosed diabetes and recalculated all the data.

Methods, Subjects: line 75, page 4
Tables 1-7, Figure 1-2

Comment 4
Material and methods: Blood sampling and OGTT: The standard OGTT for adults is performed with 75 g glucose. Were children included? If not, I suggest that only individuals receiving 75 g glucose be included in the analysis.

<Response>
We thank you for the thoughtful review. We have now excluded children and adults who receiving 75 g glucose. All OGTT in the analysis were therefore performed with 75 g. After changing the exclusion criteria, we recalculated the data.

Methods, Subjects: line 74-75, page 4
Methods, Blood sampling and OGTT: line 82-83, page 4
Tables 1-7, Figure 1-2
Comment 5

Material and methods: Blood sampling and OGTT: In order to evaluate the response curve after glucose loading, a more frequent sampling is necessary (at least 0, 15, 30, 60, 90, 120, 150, 180).

<Response>

We sincerely thank you for this thoughtful comment. Unfortunately, our research only included samples at 0, 30, 60, 120, and 180 minutes, because in China, OGTT experiments usually collect samples at these points to provide better guidance to Chinese doctors and decrease the burden on the participants. Thus, our research follows the standard methods used in China. We have noted this as a limitation of our study.

Discussion: line 255-259, page 11

Comment 6

Material and methods: Classification of glucose tolerance status: The normal fasting blood glucose value is < 100 mg/dl (see ADA Standards of medical care in Diabetes 2019)

<Response>

We greatly appreciate your comment. But China's latest diabetes guidelines on the classification of glucose tolerance status are based on the World Health Organization definition (Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation, 2006[M]. Geneva: WHO Document Production Services, 2006). In order to provide better guidance to Chinese clinicians, our research follows the standard criteria outlined in China.

Comment 7

Material and methods: Classification of glucose curve shapes: "This was done with a plasma glucose threshold of 0.25mmol/L to minimize fluctuations in glucose concentrations" should be rephrased - is not clear what authors describe.

<Response>

We thank you for pointing this out. We have added an explanation of this.
Methods, Classification of glucose curve shapes: line 99-104 page 5

Comment 8

Results: Table 1. The abbreviation used in the table are not explained. The same for the rest. I suggest that the tables 1 and 2 could be presented as one.

<Response>

Thank you for pointing this out. We have explained the abbreviations in all the tables and combined Tables 1 and 2 as you recommend.

Tables 1-7, abbreviations

We combined original tables 1 and 2 as the new Table 1

Comment 9

Results: A figure with monophasic and multiphasic curves are missing. This is the most important information in the paper.

<Response>

Thank you for this most helpful comment. We have added a figure showing monophasic and multiphasic curves.

Figure 2

Comment 10

Results: Figures 2 and 3 should be presents together - in fact, data from figure 2 may be presented in the text.

<Response>

We thank the reviewer for this observation. We have combined Figures 2 and 3 as recommended and presented data from Figure 2 in the text.
Results, Comparison of the glucose curve shapes among different age groups: line 158-160, page 7

We combined original figures 2 and 3 as the new Figure 3

Comment 11

Results: Data should be analyzed according to the time to peak glucose and insulin levels as well.

<Response>

Thank you for this advice. We have analyzed the data according to the time to peak glucose and insulin levels and presented this information in Tables 4-5.

Tables 4-5

Results, OGTT glucose peak time, nadir time, and insulin peak time in relation to insulin resistant and ß-cell function: line 167-168 and line 174-175, page 8

Discussion: page 10 line 233-235

Comment 12

Results: I suggest adding results for the first 30 minutes (which actually approximates the first phase insulin secretion, in the absence of 15-min sample).

<Response>

We agree with your comment. We have added results for the first 30 minutes in the tables.
Tables 1-6

Comment 13
Results: tables 3 and 5 should be re-arranged, so that data would fit in raw

<Response>
Thank you for your suggestion. We have re-arranged Tables 3 and 5.

Original Table 3 (Demographic and metabolic characteristics of 10,670 participants with monophasic versus multiphasic OGTT glucose response curve in different glycemic status) was changed to Table 2, and original Table 5 (Demographic and metabolic characteristics of 502 participants with stable versus unstable OGTT glucose response curve) was changed to Table 6.

Comment 14
Results: The way data is presented should be improved.

< Response>
Thank you for pointing this out. We have added important data in the Results section and changed the typesetting of the tables to make them clearer.

Results, Baseline characteristics according to glucose curve shapes: line 138-142, page 6

Comparison of the glucose curve shapes among different age groups section: line 150-151, page 7
Comment 15

1. English language should be substantially improved

< Response>

We have had the manuscript reviewed by a native English speaker and the attachment is our certification of English editing.

We would like to thank you again for your consideration and the opportunity to revise our manuscript. Please do not hesitate to contact us should you require any further information.

Sincerely,

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