

From:

dme_editorial@wiley.com

To:

inouek@m.u-tokyo.ac.jp

CC:

dme_editorial@wiley.com

Subject:

Diabetic Medicine DME-2009-00292

Body:

Re Should the threshold for definition of impaired fasting glucose be lowered?

Dear Professor Inoue

Thank you for submitting your paper to Diabetic Medicine.

It has been read by reviewers with an interest in the field.

As you can see from the enclosed reports all find your manuscript of interest but have raised significant concerns. As a result, we cannot accept your paper for publication as it stands.

However, if you feel able to respond to the reviewers' comments then we will give very careful consideration to the revised paper. I should emphasise that we are not guaranteeing acceptance at this stage. A decision will be based on whether you can meet the reviewers' concerns.

Your responses to each point made by the reviewers should be made at <http://mc.manuscriptcentral.com/dme> through your Author Centre by clicking the appropriate button. Please then submit your revised manuscript by clicking its title. You will be prompted to upload the file(s).

Please ensure that all changes to your paper are tracked using 'track changes' function in Word.

Any revised paper should be submitted to the Diabetic Medicine site within one month of your receipt of this letter. Failure to adhere to this deadline may lead to your manuscript being considered a new submission.

Thank you for submitting to Diabetic Medicine.

Yours sincerely,

[REDACTED]
[REDACTED]

Editor/Associate Editor comments:

Please use UK not US spelling throughout eg haemoglobin not hemoglobin

In HbA1c, please subscript the 1c throughout

Give numbers with the number of decimal places to which they are measured eg glucose 5.8 not 5.82 mmol/l

Reviewer comments:

Reviewer: 1

Comments to the Author

The manuscript by Dr. K. Inoue, et al., entitled, "Should the threshold for definition of impaired fasting glucose be lowered?" is a follow-up study of approximately 11,000 Japanese without diabetes mellitus to estimate the conversion risk for newly diagnosed diabetes mellitus, depending on fasting glucose values. Ultimately, this manuscript aims to determine if the definition of impaired fasting glucose, a predictor of diabetes mellitus, needs to be revised. Overall, the manuscript is well-written, but I have some major and minor issues to be addressed as follows:

Major issues:

1. The authors cited their previous publication for the description of the study

population. The authors should present essential information to allow readers to accurately interpret this analysis without looking for an external citation.

2. About half of the study's participants who underwent at least one check-up during the baseline period (N=21,885) did not return for a check-up during the follow-up period (N=11,129). Any biases, potentially generated from this loss of follow-up, need to be addressed along with the characteristics of the participants who were lost.

3. There are many ways to define "optimal" cut-off point for impaired fasting glucose. Please explain how they determined this point (5.72 mmol/l), including the following information: a) the definition of "accuracy"; b) the reason why the authors chose the highest accuracy as the definition of the optimal cut-off point; and c) if the cut-off point with the highest accuracy was estimated by sex or a combination of both sexes.

4. All analyses were performed according to sex. The authors need to explain their motivation for this stratification and the subsequent public health implications when they propose a threshold for screening.

5. In the Discussion, the authors concluded that the results of their study are compatible to the evidence that the ADA cited to revise the impaired fasting glucose criteria. However, the authors did not support the ADA's lowering of the threshold for a variety of reasons. This latter part of the discussion itself sounds valid in general, but I wish the authors had found ways to present their overall discussions better so that what they observed in their analysis would better support their conclusions.

Minor issues:

1. I suggest that title be more specific.

2. The authors wrote, "The three baseline FPG categories (<5.56, 5.56-6.06, and 6.11-6.94 mmol/l)," in the Abstract and Results sections. Please explain why the category for 6.06-6.11 is missing.

3. In the Introduction, the recommendations from three organizations (ADA, EDEG, and JDA) were cited. Please add the years when those recommendations were published as they change over time.

4. In the Discussion, the authors stated “Second, there was 5-7 fold difference in relative risk of diabetes incidence between the original (6.11-6.94 mmol/l) IFG and the IFG newly added by the ADA (5.56-6.06 mmol/l) both in men and women.” Is the estimate of 5-7 fold difference based on this study? The text in Results section does not state incidence or relative risk. Clearer presentation is desired.

5. In the Discussion, the authors mentioned that the study subjects participated on a voluntary basis and that they might be healthier than the general population. Are the authors implying that the optimum cut-off for this study—5.72 mmol/l—could have been even lower if they had studied the general population?

Reviewer: 2

Comments to the Author

The authors focus on the important question of whether the cut-off value of fasting plasma glucose for diagnosing impaired fasting glucose (IFG) should be lowered or not, using data from a large Japanese population.

They conducted a retrospective cohort study, and calculate the optimal cut-off FPG value to predict diabetes was 5.72 mmol/l both for men and women. They concluded that it may be reasonable to retain the conventional lower FPG limit for IFG and treat FPG values of 5.56-6.06 mmol/l as non-diabetic hyperglycemia, considering the four to five fold increase in individuals classified as IFG when the new cut-off is applied.

This paper is very interesting for following many subjects for a long term, so I would support publication after the topics below have been addressed by the authors.

Major Points:

1) (Page 6, Discussion) The authors wrote “Risk evaluation according to continuous glucose levels in various populations should be performed for diabetes and cardiovascular disease.”

It will be better to note the prevalence of cardiovascular disease of the IFG subjects, and to note whether there is a particular cut-off FPG value for estimating the risk of cardiovascular disease.

2) (Page 5, Discussion) The authors wrote “Second, there was 5-7 fold difference in relative risk of diabetes incidence between...”

It will be better to compare their study to Funagata Study in Japan (Tominaga et al. J Japan Diab Soc 2008;51: 473-475.) , which is also focused on the cut-off value of fasting

plasma glucose as concerned by JDA (Kadowaki et al. J Japan Diab Soc 2008;51: 281-283.) in the discussion.

3) (Page 2, Title, Conclusions) Although the authors mentioned the limitations of this study in the discussion, the title and the conclusions seem to suggest the whole Japanese population.

It will be better that the authors include the word taking into account the limitations in the title and the conclusions.

4) In the authors' previous study (Inoue et al. Diabetic Medicine 2008;25: 1157-1163.), they excluded 433 people with <2 years between their baseline and follow-up check-ups, but in this study, they don't.

It will be better that the authors write the reason why they included these subjects who were removed from previous study.

Minor Points:

1) (Page 2) The authors wrote "During follow-up of an average of 5.4 years, 279 (5.2%) out of 5,372 men and 98(1.9 %) out of 5,103 women developed diabetes. According to the three baseline FPG categories (<5.56, 5.56-6.06, and 6.11-6.94 mmol/l), 28/3,401 (0.8%), 91/1,456(6.3%) and 160/515 (31.1%) respectively in men and 13/4,218 (0.3%), 30/695(4.3%) and 55/177 (31.1%) respectively in women developed diabetes."

The total subjects of the three categories of women (4218+695+177=5090) are not equal to the total subjects of women (5103). The data should be corrected.

2) In this paper, the authors used the word "diabetes", which means perhaps about type 2 diabetes, but it should be noted if there is another type of diabetes or not.

Date Sent:

15-Jun-2009

Note

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The definitive version is available at www.blackwell-synergy.com.