Author's response to reviews

**Title:** Prevalence and correlates of hyperglycemia in a rural population, Vietnam: implications from a cross-sectional study

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**Author's response to reviews:** see over
September 24, 2012

To: Professor Natalie Pafitis  
Editor-in-Chief, BMC Public Health  
Email: Natalie.Pafitis@biomedcentral.com

Re: Rely of reviewer’s comments

Dear Professor Natalie Pafitis,

We are grateful for the distinguished reviewers for critically reading our manuscript and also for forwarding important suggestions to improve our manuscript. We have addressed the reviewers’ comments in our revised manuscript and give a point-by-point response to your concerns in this cover letter. The revised manuscript document contains green highlighting indicating pieces that were edited. The following are the replies to the reviewers’ comments.

Your consideration of our revised version is appreciated.

Best regards,

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Reviewer #1:

**Reviewer's report:** In this study, authors conducted a cross-sectional study to identify the prevalence of impaired fasting glucose, impaired glucose tolerance, type 2 diabetes and related risk factors in rural Vietnamese population. I have only minor concerns.

**Q1.** It will be helpful to add which were the years of study and the prevalence of diabetes in the Ho Chi Minh and Hanoi.

**Q2.** Report by Quoc PS et al., Am J Epidemiol 1994;139(7):713-22, about prevalence of diabetes in Hanoi should be added.

**Author reply:** Thank you for this suggestion. We have added the years of study and the prevalence of diabetes in Hanoi and Ho Chi Minh City in the revised manuscript, page 3, lines 6-9. The report of Quoc PS et al. is listed in the References.

“In Vietnam, the prevalence of type 2 diabetes in Hanoi increased from 1.4% in 1990 to 4.4% in 2002 in residents aged 30–64 years [2,3]. In Ho Chi Minh City, the residents aged 15 years or over had a 6.6% prevalence rate of type 2 diabetes in 2001; a significant increase from 2.5% in 1993; and the prevalence of the disease in residents aged 30–72 years reached 11.4% in 2009 [4–6].”

**Q3.** How was determined the sample size?

**Author reply:** The sample size of the cross-sectional study was calculated to estimate prevalence of 5.5% of diabetes within 0.012 with 95% confidence interval, \( \alpha = 0.05, \beta = 0.2 \):

\[
n = \frac{Z_{1-\alpha/2}^2 p(1-p)}{d^2} \ DE
\]

- \( \alpha = 0.05, \beta = 0.2, Z_{1-0.2/2} = 1.96 \),
- \( p \) is estimated prevalence of type 2 diabetes: 0.055, \( q = 1 - p = 0.955 \)
- \( d \) is acceptable margin of error for proportion being estimated = 0.012,
- \( DE \) is design effect. Since it is a multistage stratified random study, a design effect of 2 was taken to reduce any inherent variation.
- Non-responce rate is about 8%.
- Estimated sample size \( \approx 3.000 \) subjects.

This sample size can also estimate the prevalence of more than 5.5% of prediabetes.

* We have added the text “The sample size was calculated to estimate the prevalence of type 2 diabetes of 5.5% within 0.012 with 95% confidence interval, considering the following parameters: \( \alpha = 0.05, \beta = 0.2, \) a design effect \( \beta = 2 \) for multistage stratified random study, and non-response rate = 8%” in the revised manuscript, page 4, line 10-12.
Q4. It should be clearly stated in the Methods section that all participants underwent an OGTT.

**Author reply:** We have added “All participants, except for those having previous diagnosis of diabetes and current use of drug for its treatment, underwent an OGTT test” in page 5 line 11-13 of the revised manuscript.

Q5. Data about age are unnecessarily repeated in Results section and Table 1.

**Author reply:** Thank you for your comment. We have deleted the sentence “Age mean and median (interquartile range) of subjects were 51.3 and 51 (46–56) years, respectively.” in the page 8 line 10.

Q6. The post hoc analysis in Table 1, should indicate differences between all groups and not solely between NGT and “hyperglycemic groups” (IFG+IGT+IFG-IGT).

**Author reply:** The reviewer are right. The post hoc analysis can indicate the differences between all groups. In this study, we focused on analysing risk factors of IFG, IGT, IFG-IGT, and diabetes, in which NGT group was used as a reference. Thus, we marked only the differences of characteristics of subjects between NGT group and each of the IFG, IGT, IFG-IGT, and diabetes groups. It can make Table 1 uncomplicated, and help readers easy to understand the differences.

Q7. The 95%CI of the crude prevalence of diabetes should be added.

**Author reply:** Thank you for useful comment. We have added the 95%CI of the crude prevalence of diabetes and pre-diabetes in the revised manuscript in page 8, line 21-23, as follows:

“The crude prevalences of isolated IFG, isolated IGT, combined IFG-IGT, and diabetes were 9.2 (8.1–10.2), 4.4 (3.7–5.2), 1.6 (1.1–2.1), and 3.7% (3.0–4.4%), respectively.”

Q8. How can be explained that the crude and the age- and sex-adjusted prevalence of combined IFG-IGT and diabetes are the same?

**Author reply:** According to your previous comment, we have calculated the 95%CI of the crude prevalence of diabetes and pre-diabetes, and presented in the revised manuscript. As a result, the revised paragraph on page 8 shows that the crude and the age- and sex-adjusted prevalence of combined IFG-IGT and diabetes are not the same. The revised paragraph is shown as follows:

“The crude prevalences (95% CI) of isolated IFG, isolated IGT, combined IFG-IGT, and diabetes were 9.2 (8.1–10.2), 4.4 (3.7–5.2), 1.6 (1.1–2.1), and 3.7% (3.0–4.4%), respectively. The total age and sex–adjusted prevalences (95% CI) of isolated IFG, isolated IGT, combined IFG–IGT, and diabetes were 8.7 (7.0–10.5), 4.3 (3.2–5.4), 1.6 (0.9–2.3), and 3.7% (2.7–4.7%), respectively. In the present study, using the single FPG test could detect 60% of the total diabetic cases. The number of newly diagnosed cases occupied 73% of the total diabetic patients.”
Q9. A paragraph to discuss the physiological mechanism that involves the elevated blood pressure with the increase of diabetes is necessary.

Author reply: Thank you very much for the comment to improve the quality of our manuscript. We have presented the paragraph in page 12 line 8-19, as follows:

“With regard to the relationship between the elevated blood pressure and diabetes, both disorders commonly occur together and tend to share many predisposing factors including obesity, physical inactivity, and high-fat diets [21,22]. Each disease tends to affect patients who are already at risk for the other. Recent studies suggest that the elevated blood pressure may also precede the type 2 diabetes [23,24]. The elevated blood sugar has many consequences, including slow but serious damage to sensitive capillaries in the kidneys. This damage impairs the kidney’s blood pressure regulating abilities, leading to higher blood pressure [25]. This increased blood pressure causes small changes in blood flow, which exposes other sensitive capillaries to additional damage. The elevated blood pressure can also affect the delicate insulin secreting areas of the pancreas, leading to higher blood sugar [26]. In this way, the combination of elevated blood pressure and high blood sugar is a self-reinforcing loop in which both diseases tend to worsen over time.”

References


Q10. The combined IFG/IGT group should be indicated as IFG-IGT; the term IFG/IGT indicates a proportion.

Author reply:

* We have changed it in the following pages:
  - page 2: line 11,
  - page 5: line 18,
Prevalence of IFG, IGT, and combined IFG-IGT do not show age effect (Table 2). This finding should be discussed.

Author reply: Thank you for useful comment. We have revised and presented the discussion in page 11 line 5-13, as follows:

“The estimated prevalence of IFG and IGT increased in 50–54 age group compared to 40–49 age group, and the prevalence was not different between 50–59 age group and 60–64 age group. The prevalence of combined IFG–IGT was significantly higher in group aged 50–59 years compared to the others. The findings indicated that prevalence of pre–diabetes did not show age effect, consistent with other reports [18,19]. Our results can be explained by: i) 5–10% of people per year with pre–diabetes may progress to diabetes, with the same proportion converting back to normoglycaemia [20], and ii) people with pre–diabetes may postpone or completely avoid the onset of type 2 diabetes with three simple strategies including losing weight, increasing physical activity, and eating more healthfully [20].

References


Reviewer #2:

Reviewer's report:
This manuscript is very interesting and important, because this data show prevalence of hyperglycemia in a rural population in Vietnam and may lead to develop the diabetes mellitus prevention model in Vietnam. However, several comments are raised as below.

Q1. Blood glucose levels were measured in the central laboratory of the Ha Nam Center for Preventive Medicine after preparation of plasma, stored at 2–8°C and transported. Did you confirmed that glucose levels was not changed during this process?

Author reply: Thank you very much for your comment. The best way to measure the blood glucose is to do it immediately after taking venous blood sample. However, in the population-based study with a large representative sample, it is crucial to consider the feasible methods to minimize the reduction of glucose concentration.

In the present study, we used the process: “Blood samples were collected and centrifuged immediately in the morning after a participant had fasted for at least 8h prior to the clinic visit. Aliquots of plasma were stored at 2–8°C in iceboxes and then transported into the central laboratory of the Ha Nam Center for Preventive Medicine for analysis within 6 hours.”

We selected this process, considering several evidences including:

i) Serum separation and refrigeration within 30 min after venous sampling is recommended over NaF method, not only to minimize the preanalytical impact on detecting diabetes but also to reduce effect of NaF on blood glucose sample volume and number of tubes[1];

ii) Rapid plasma glucose separation is superior to fluoride alone for abrogating glycolytic effects on blood glucose measurements in the clinical laboratory [2]; and

iii) Plasma sample obtained within one hour after getting venous blood sample can minimize the glucolysis process. The fall in glucose concentration was minimal, on average less than 0.05 mmol/L, when stored for 48 hours at temperatures from 4°C to 22°C [3].

If we use the fall of 0.05 mmol/L in glucose concentration to recalculate the prevalence of diabetes and pre-diabetes in our survey, the prevalence of diabetes is not changed; however, the prevalence of pre-diabetes increases from 15.2% to 17.3%. Thus, our process may underestimate about 2% of pre-diabetes prevalence.

References


We have presented this limitation in the Discussion of the revised manuscript, page 14 line 16–20.

“Next, blood samples were collected and centrifuged immediately in the morning after a participant had fasted for at least 8h prior to the clinic visit. Aliquots of plasma were stored at 2–8°C in iceboxes and then transported into the central laboratory for analysis within 6 hours. However, although this process we used can minimize the preanalytical impact on detecting diabetes, it may cause about 2% underestimate of prediabetes prevalence [34].”

Q2. The explanation on lines 19-23 in page 8 is difficult to understand. Please clarify it.
Author reply: Thank you for the comment. We have clarified it in the last paragraph of page 8, line 21, 22 and page 9 line 1-4.

“The crude prevalences of isolated IFG, isolated IGT, combined IFG–IGT, and diabetes were 9.2 (8.1–10.2), 4.4 (3.7–5.2), 1.6 (1.1–2.1), and 3.7% (3.0–4.4%), respectively. The total age and sex–adjusted prevalences (95% CI) of isolated IFG, isolated IGT, combined IFG–IGT, and diabetes were 8.7 (7.0–10.5), 4.3 (3.2–5.4), 1.6 (0.9–2.3), and 3.7% (2.7–4.7%), respectively. The number of newly diagnosed cases occupied 73% of the total diabetic patients. Without relying on the OGTT test, we would have missed 40% of the total diabetic cases.”

Q3. GOTT in page 12 should be OGTT.
Author reply: Thank you. We have corrected it in page 14, line 2,4,5.