Author's response to reviews

Title: Prevalence of diabetes and predictions of its risks using anthropometric measures in southwest rural area of China

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Author's response to reviews: see over
Dear editor:
Thank you very much for your great reviewing job on our manuscript. And we have revised our manuscript according to reviewer’s comments. The following responses have been prepared to address the reviewers’ comments in a point-by-point fashion.
With best wishes,

Yiming Li

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Replies to Referee 1:
Thank you very much for your great reviewing job on our manuscript. We are sending the revised manuscript according to your comments.

- Discretionary Revisions

**Question:** It would be of interest to specify how poor the population of this area of China is and its level of physical activity.

**Response:** Thank you very much for your question. Per capita disposable incomes in Songming country were 2230 yuan in 2001, and 5162 yuan in 2010. (In 2010, 6.7695 yuan equaled U.S. $1.00.). And we have added these information in the “Study area and population” of our manuscript. In this mountainous rural area, local residents are mainly engaged in agricultural industries and processing industries. It belongs to mild or moderate physical activity. And I am very sorry for not collecting data on physical activity in this study.

- Minor Essential Revisions

**Question:** Footnotes are missing in Tables and Figures (specify abbreviations).

**Response:** We appreciated your suggestion, we have added footnotes to specify abbreviations in Table 1, 3 and 4.

- Major Compulsory Revisions

**Question:** Material & Methods, Data collection by questionnaire: Please, provide details on the conditions in which data were collected, particularly regarding anthropometric data and blood pressure. How the occupation and physical activity were different between genders?

**Response:** Thank you very much for your question. We have added some details on data collection in revised manuscript. The survey was conducted in a given site of each village. Physicians completed questionnaires and blood pressure measurements, and trained nurses measured anthropometric variables including height, weight, waist circumference and hip circumference.

1. **Blood pressure measurements**

Physicians performed blood pressure measurements using an American Heart Association protocol [1]. After 5 minutes of rest in a sitting position, systolic and diastolic pressures were measured
from the participant’s right arm using standard mercury sphygmomanometer. And then two successive measurements were performed with at least a 1 minute time interval between measurements.

2. Anthropometric measurements

Anthropometric measurements included height, weight, waist circumference and hip circumference. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m²). WHtR was calculated as height (cm) divided by waist circumference (cm). WHR was calculated as hip circumference (cm) divided by waist circumference (cm). Each of these measurements was completed by two nurses; one took the measurements, and the other recorded the readings. The height and body weight were measured simultaneously with the participants standing on a balance beam scale with the participants wearing light clothing and no shoes. And hip circumference was measured at the level of maximal gluteal protrusion [2]. Waist circumference was measured with subjects standing relaxed and in underclothes only. waist circumference were obtained at the midpoint between the anterior superior iliac crest and the lowest rib. The upper border of the iliac crest and lowest rib were located, and a plastic anthropometric tape was wrapped around above this point, ensuring that it is adjusted without compressing the skin. And the reading was taken at the end of a normal breath [2].

3. I am very sorry for not collecting data on physical activity in this study. This is a limitation of this study.

Reference


• Material & Methods, Laboratory:

Question: Abbreviation ‘OGTT’ should be defined, as well as the amount of oral glucose ingested (75g).

Response: The abbreviation ‘OGTT’ refers to oral glucose tolerance test. It have been defined in revised manuscript. And a 75-gram oral glucose was given before OGTT. And we have revised our manuscript as follows: After an overnight fasting for at least 10 hours, a standard 75-g glucose solution was given. And venous blood samples were drawn at 0 minutes and 120 minutes to identify diabetes and pre-diabetes (IFG and/or IGT).

Question: It is not clear if glucose was determined in capillary and/or venous blood for diagnosis. In this chapter, ‘venous’ plasma glucose is mentioned but not in Results section.

Response: Thank you very much. Venous plasma glucose was used for diagnosing diabetes mellitus. During OGTT, venous blood samples were drawn at 0 minutes and 2 hour.

To evaluate the efficiency of capillary blood glucose measurement as compared with venous plasma glucose measurement in screening diabetes, fingertip capillary blood glucose
was also tested at 0 minutes and 2 hour. But those data was not related to this study. So we have deleted data on fingertip capillary blood glucose in revised manuscript.

And because venous blood glucose were used to diagnosed diabetes refer to diagnostic criteria, venous plasma glucose was not listed in results section.

**Question:** In Table 1, both capillary (fingertip for screening purposes only?) and venous results are provided. Please, clarify. The authors informed that another OGTT might have been done in the hospital if undiagnosed diabetes was suspected. Is there any information about the concordance between the two procedures?

**Response:** Thank you. We collected venous blood sample during OGTT at 0 minute and 2 hour. And samples of venous blood glucose were used to diagnose diabetes. And fingertip capillary blood glucose was also tested at 0 minutes and 2 hour.

As mentioned above, fingertip capillary blood glucose was not related to this study, so we deleted this data. And venous blood glucose were used to diagnosed diabetes, it was not listed in results section. And another referee also suggested that comparison of fingertip capillary and venous blood glucose in Table 1 were insignificant, as it is a main diagnostic criteria in this paper. And the concordance between fasting capillary blood glucose and fasting venous blood glucose were highly positive ($r=0.75$, $P<0.000$). And the concordance between 2h capillary blood glucose and 2h venous blood glucose were also positive ($r=0.91$, $P<0.000$). Detailed information about the concordance between the two procedures have been published recently [1].

**Reference**

**• Material & Methods, Statistics:**

**Question:** Consider informing 95% confidence intervals of the prevalence rates. Intervals are useful to compare differences in rates according to subgroups (for instance by genders).

**Response:** Thank you for your advice. We have add the 95% confidence intervals in Table 2.

**• Results:**

**Question:** Second paragraph: Probably, the third sentence needs to be modified in order to correct its meaning (Suggestion: Among the diabetic subjects, 59.2% were women and 40.8% were men).

**Response:** Thank you very much for your suggestion, we have followed your advice and have revised our manuscript in the last sentence of the first paragraph (Results, Page 5).

**• Discussion:**

**Question:** Which would be the main explanation for different efficiency of anthropometric measurements in identifying risk for diabetes in men (WHtR) and women WHR?

**Response:** Thank you very much. WHR and WHtR were used as indices of central obesity or abdominal obesity. Abdominal obesity was closely correlated with both insulin resistance and
diabetes. Central obesity is an excess accumulation of fat in the abdominal area. Abdominal fat is especially active hormonally, secreting adipokines that may possibly impair glucose tolerance[1]. such as tumor necrosis factor α, interleukin-6, or resistin [2]. Those cytokines and low grade Chronic inflammation in fat led to insulin resistance and pancreatic β cell damage and aggravated the development and progression of diabetes.

Obese men tend to be "apple-shaped" with the increasing of waist circumference. But obese women tend to be "pear-shaped". The female had big pelvis designed for childbirth And estrogens affected body fat distribution [3] causing fat to be stored in the buttocks in women. In the same WHtR values, an increasing WHR was more correlated to the increasing abdominal fat accumulation in women than in men, and increased the risk of insulin resistance and diabetes. And muscular men also had high BMI, but had low body fat. So WHtR in men was closed related to central obesity.

In addition, we have added table 4 in revised manuscript. In man, we found that venous blood glucose (fasting and 2h) and WHtR had a correlation stronger than that with WHR when waist circumference was adjusted for (Table 4). And in woman, WHtR was not found to have any significant association with both fasting (r=0.031, P=0.473) and 2h (r=0.036, P=0.44) venous blood glucose when waist circumference was adjusted for. These data are in accordance with what we have speculated.

Reference
Replies to Referee 2:

General comments

Question: English needs improvement throughout the text. In some occasions, it is even difficult to understand clearly what the authors meant.

Response: Dear reviewer, thank you very much for giving me a chance to improve my manuscript. I am sorry for my poor English level, I have expressed my idea exactly in Chinese and ask the native English speaker to translate it. Hope getting an significant improvement.

Introduction ---- Major compulsory reviews

Question: The introduction section is informative and succinct. However, authors state that anthropometric measures are necessary for diabetes screening. It is not true. Actually, this kind of work is important to establish association and possible causality.

Response: Thank you very much for your advice. In this study, we unexpectedly found different efficiency of anthropometric measurements in identifying risk for diabetes in men and women. In this rural area site, we thought that anthropometric measures may be useful to screen diabetes candidate in rural countryside. And this was a conclusion of this study, this statement was inappropriately placed in the introduction. And we have deleted this wrong expression in revised manuscript.

Methods ---- Major compulsory reviews

Question: Which was the rationality to include only residents for at least 5 years? A population-based study supposedly would include every inhabitant (only selected by age) in a given moment.

Response: To select a sample of homogeneous lifestyles and genetic background for specific area, we enrolled only persons who had lived in their current residences for 5 years or longer. And also in the process of study design, We have refered to some big studies [1,2] in China published in NJEM using this criteria. Local resident registration system can best discriminate locals and the outsiders in China. Because 5 years were need to obtain a local resident registration. Truly speaking, very few people moved into this poor and mountainous area.

Reference


Question: How was sample selection done?
Response: We have added this information in the “Sampling technique” of revised manuscript (Line6, Page2.).

A multistage stratified sampling method was used to select a representative sample of persons 30 years of age or older. Firstly, all townships were divided into three groups including county, industry town and agriculture town according to geographic regions and economic development status. And secondly, three villages were randomly selected from each group. In each selected village, individuals aged ≥30 years were recruited and all subjects were Han Chinese and homogeneous lifestyles.

Question: Anthropometric measures were effectively measured? The text suggests it was only informed by participants.
Response: Thank you very much. We have added some details on anthropometric measures in the “Anthropometric measurements” of revised manuscript (Last paragraph, Page3).

Anthropometric measurements included height, weight, waist circumference and hip circumference. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m²). WHtR was calculated as height (cm) divided by waist circumference (cm). WHR was calculated as hip circumference (cm) divided by waist circumference (cm). Each of these measurements was completed by two nurses; one took the measurements, and the other recorded the readings. The height and body weight were measured simultaneously with the participants standing on a balance beam scale with the participants wearing light clothing and no shoes. And hip circumference was measured at the level of maximal gluteal protrusion [1]. Waist circumference was measured with subjects standing relaxed and in underclothes only. waist circumference were obtained at the midpoint between the anterior superior iliac crest and the lowest rib. The upper border of the iliac crest and lowest rib were located, and a plastic anthropometric tape was wrapped around above this point, ensuring that it is adjusted without compressing the skin. And the reading was taken at the end of a normal breath [1].

Reference

Question: Definition of diabetes mellitus exclusively by the use of medications may include individuals for whom metformina was prescribed preventively, as well as other medications that could be prescribed for weight loss. This group should be analyzed separately or excluded from the diabetic subgroup.
Response: Thank you. We have taken this into consideration. The inclusion criteria and study process of our study refered to the study by yang et al [1]. The interview included questions related to the diagnosis and treatment of diabetes. If subjects have a history of diabetes or take any diabetic drug to treat diabetes, steamed bread meal test was performed to verify the participator’s
diabetes. In this study, the criteria for excluding persons who prescribed drugs (for example Sibutramine and Orlistat) for weight loss was not included in this study. And in the studying process, we actually have not found any people who prescribed drugs (for example Sibutramine Orlistat) for weight loss. This may be due to the fact that it was difficult to have access to health care and get those drugs in this underdeveloped rural area. And also we had not found people who prescribed metformina preventively in confirmed prediabetes patient. And we have re-analyzed undiagnosed diabetes and diagnosed diabetes separately in Table 1.

Reference

Results ---- Major compulsory reviews

Question: First paragraph of results is redundant. Unless the authors want to reinforce information deliberately, it must be rewritten. Other redundancies are present in the text.

Response: Thank you very much, the first paragraph of results have been rewritten. And Other redundancies in the text have been rewritten.

Question: Table 1 has some comparisons that do not lead to objective/practical conclusions, as the fact that glucose levels are higher in diabetic individuals, as it is a main diagnostic criteria in this paper.

Response: Thank you for your useful suggestion. We have deleted the comparision of capillary and venous blood glucose, we have modified Table 1 to make it more relevant to objective/practical conclusions.

Question: Proportions should be presented as percentages. As well, “mean” age or BMI is much less informative than proportions in (clinically relevant) stratified groups

Response: Thank you, We appreciate your suggestion. Proportions in sub-groups which were clinically stratified were informative. We have re-analyzed Table 1. Some variables in table 1 have been stratified according to the cut-offs as suggested by literature [1] and WHO [2-3].

Reference

   [http://www.wpro.who.int/nutrition/documents/Redefining_obesity/en/index.html]


Discussion ---- Major compulsory reviews
**Question:** Discussion is sometimes confusing and some numbers (as diabetes prevalence) are inaccurate and need to be reassessed.

**Response:** Thank you, we have rewritten discussion to give a clear expression and reassessed the figure referenced in discussion. And the outline of the discussion in our manuscript was organized as following:

Firstly, compared our results with total prevalence of diabetes in China and with underdeveloped rural regions of China. And discussed on reasons of high prevalence of diabetes and prediabetes.

Secondly, discussed on reasons of high prevalence of undiagnosed diabetes in this rural area, and compared with other studies on prevalence of undiagnosed diabetes.

Thirdly, abdominal obesity is common in this area. It is correlated with both insulin resistance and diabetes. And WHtR and WHR are better anthropometric indices in identifying risk of diabetes. And some reasons contributed to different efficiency of anthropometric measurements in identifying risk for diabetes in men (WHtR) and women (WHR)

**Question:** Information that people in Yunnan share SEAR risk factors must be referenced, as well information on their diet and habits.

**Response:** Thank you very much. Yunnan is adjacent to SEAR area and we could speculate therefore that they may share common risk factors, such as genetic determinants [1], food habit [2-4], Climate and Environment [4].


**Question:** It is a mathematically obvious statement that diabetes prevalence is equal to or higher than diagnosed diabetes, once it is the sum of diagnosed diabetes and undiagnosed diabetes. Please review authors’ intention.

**Response:** Thank you very much. There was an error in English expression. And we have revised our manuscript as follows: “Several studies have showed that the prevalence of undiagnosed diabetes was equal to or higher than diagnosed diabetes”

**Question:** Description of reference 33 shows an AUC comparison with equal values (0.726) and p<0.01. Please clarify.

**Response:** I am very sorry. Because of our carelessness, there was a mistake in writing. This sentence have been corrected as follows: “And also a meta-analysis [29] containing 25 studies from nine countries (six countries were from Asia, and one of each from the Caribbean, Europe,
and the Middle East) analysing the data of AUCs in predicting type 2 diabetes showed significant differences between WHtR and BMI in only men (0.672 vs. 0.726, P<0.01). ”