Author's response to reviews

Title: Prevalence of cardiovascular disease and risk factors in a rural district of Beijing, China: a population-based survey of 58,308 residents

Authors:

Liu He (heliu@bjmu.edu.cn)
Xun Tang (tangxun@bjmu.edu.cn)
Yan Song (yansong@ucla.edu)
Na Li (lina@fissic.org)
Jingrong Li (jingrongli@fissic.org)
Zongxin Zhang (zongxinzhang@fissic.org)
Jianjiang Liu (jianjiangliu@fissic.org)
Liping Yu (lipingyu@fissic.org)
Haitao Xu (haitaoxu@fissic.org)
Jianguo Zhang (jianguozhang@fissic.org)
Yonghua Hu (yhhu@bjmu.edu.cn)

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Author's response to reviews: see over
Dear Editor,

The revised manuscript (MS: 1915141033586087) entitled “Prevalence of cardiovascular disease and risk factors in a rural district of Beijing, China: a population-based survey of 58,308 residents” (former title: “Prevalence of cardiovascular disease and risk factors among rural Chinese in Beijing: a population-based survey of 58,308 residents”) is resubmitted to your esteemed office for your re-evaluation.

We appreciate the constructive comments made by all reviewers regarding the original version of the manuscript. The new version of this manuscript has been revised extensively according to the reviewers’ comments and we have responded to every point in the revised manuscript, as detailed in the responses below. We believe the manuscript has been substantially improved as a result of the changes, and we hope that it is now judged to be worthy of publication. If you still feel it necessary for more revision, we are pleased to do it accordingly.

We appreciate your efforts for this manuscript.

Yours sincerely,

Prof. Yonghua Hu,
Department of Epidemiology & Biostatistics,
Peking University Health Science Center,
38 Xueyuan Road, Beijing, 100191, China.
Tel. +86 10 82801189, Fax +86 10 82801518.
E-mail: yhhu@bjmu.edu.cn
Major compulsory revisions:

1) Abstract: in this study number of women is higher than number of men. Since men and women have different level of CHD and stroke risk, CHD and stroke prevalence should be reported separately for men and women.

Yes, we followed the advice and have reported CHD and stroke prevalence separately for men and women in the highlighted Abstract of revised manuscript.

2) Statistical analysis: it is not clear if the age distribution used in the age-adjustment is the same for men and for women, and for different geographic areas. In order to compare men and women, and geographic areas, avoiding age influence, means and prevalence should be age-adjusted using the same age distribution.

Yes, we’ve clarified the age distribution used in age-standardization for men and women in the revised manuscript (please refer to the Statistical Analysis and footnotes in Table 2). In order to compare between two genders and also provide data for comparison with other previous studies in Chinese population, we used the same age distribution of the entire 2000 China population (not age distribution by genders) to standardize disease prevalence for both men and women. Furthermore, we’ve changed the crude prevalence among different geographic areas into standardized prevalence (to 2000 China population) for better comparisons (please refer to the Results Para 4 and Figure 4).

3) Results: prevalence of CHD and stroke in persons over 65 years and below 65 years are reported for men and women together. Since men and women have different level of CHD and stroke risk, as well as different level of risk factors, and in this study number of women are higher than number of men, results should be reported also for men and women separately.

Yes, it is a helpful comment. We’ve added a new figure (Figure 2) in the revised manuscript to show the standardized CHD/stroke prevalence by genders in persons over 65 years and below 65 years.

4) Results: differences between men and women and among geographic areas reported in the Results paragraph, table 1 and Figure 3 could be affected by
different age distribution (from table 1 is clear for examples that mean level of age in men is higher than the mean level in women). In order to compare men and women, and geographic areas, avoiding age influence, means and prevalence should be age-adjusted using the same age distribution.

Yes, we agreed with the reviewer’s comments, and have changed the crude prevalence among different geographic areas into standardized prevalence (to 2000 China population) and also provided age-adjusted prevalence by genders (please refer to the Figure 4).

5) Results: no data are reported on mean age in the geographic areas.

Yes, we’ve added this information in the revised manuscript (please refer to the Results Para 1).

6) Results: authors declare that CHD and stroke prevalence decrease and obesity increases from mountainous, hill and plain area. In the text it is reported the p-value of the chi-squared test consider the three areas together. From figure 3 seems that CHD and obesity prevalence are not significantly different in hill area and plain area. This aspect should be reported in the text.

Yes, since crude prevalence in this part has been changed into standardized prevalence, the data could be compared directly.

7) Results: authors declare that in diabetics CHD risk is higher than stroke risk, but don’t specify that the difference is not statistically significant as shown in table 3.

Yes, it was not appropriate to make a conclusion that the diabetics CHD risk is higher than stroke risk, because the confidence intervals for diabetes association with CHD and with stroke overlapped. Therefore, we’ve modified this in Results Para 5 as highlighted.

8) Discussion: authors report data of stroke prevalence trend in China, but they don’t report data for CHD prevalence trend. Data on CHD trend should be reported if available. If not available, this should be specified in the text.

Yes, to the best of our knowledge, data for CHD prevalence in China from other studies is currently not available, we’ve discussed this in the Discussion Para 2.

9) Discussion: authors report that hypertension prevalence in mountainous area is lower than in the other two areas, but from Figure 3, prevalence seems to be similar.
After we changed the crude prevalence into standardized prevalence among different geographic areas, hypertension prevalence was presented to be lower in mountainous area than those in the other two areas (please refer to the Figure 4).

10) Discussion: since men and women have different level of CHD and stroke risk, as well as different level of risk factors, and in this study number of women is higher than number of men, authors should prefer to report, compare and interpret data for men and women separately.

Yes, we followed the advice and have made some complement report, comparison and interpretation for men and women separately in the highlighted Abstract, Result and Discussion of revised manuscript.

Minor essential revisions:
1) Tables: Definition of hypertension, diabetes, overweight and obesity should be reported as footnotes

Yes, we’ve added definition of hypertension, diabetes, overweight and obesity as footnotes of Table 1-3 in the revised manuscript.

Discretionary revisions:
1) Data collection: data collection follows standardized procedures.

Yes, we conducted this study and collected data following the WHO STEPwise approach to Surveillance (STEPS) program for stroke and adult risk factor and the STROBE checklist for cross-sectional study.

2) Data collection: International Diabetes Federation indicates that more than 50% of diabetics didn’t know to be diabetic, then using diabetes definition based on self reported current treatment could give a underestimated prevalence of diabetes. This should be more taken in consideration in the interpretation of results.

Yes, we agreed with the reviewer and have had taken the low awareness of diabetes in rural Chinese population into consideration, and also had discussed that the actual diabetes prevalence in Fangshan District might be higher than our data (please refer to the Discussion Para 4).

3) Results: comparison between InterASIA 2000-2001, Suburban Beijing 2007 and this study are presented in Figure 2 and commented in the Results paragraph. If available, it could be also interesting to know if differences are statistically significant or not.

Yes, since all data from InterASIA 2000-2001, Suburban Beijing 2007 and this study
were directly standardized to the 2000 China population, we could compare them directly. To make it clearer, we’ve clarified this in Results paragraph 3 and added a footnote to Figure 3.

4) Results: comparisons among geographic areas are reported considering men and women together. If the size of men and women samples stratified by geographic areas allow separated estimation, could be interesting to know if trends are similar in men and women.

Yes, we’ve changed the crude prevalence among different geographic areas into standardized prevalence (to 2000 China population) for better comparisons and also provided sex-specific standardized prevalence in the revised manuscript (please refer to the Results Para 4 and Figure 4).

5) Discussion: a diabetes definition based on self reported current treatment could give an underestimated prevalence of diabetes. This should be more considered for the interpretation of results, moreover in order to have a better interpretation of results, it could be interesting to report and consider the definition of diabetes used in this paper to evaluate the diabetes prevalence trend in China.

Yes, it had been taken into consideration that the actual diabetes prevalence in Fangshan District might be higher than our data due to the low awareness of diabetes in rural Chinese population in Discussion Para 4. And we also agreed that it is interesting to evaluate the diabetes prevalence trend in China. However, diabetes prevalence and prevalence trend in China has already been reported by the China National Diabetes and Metabolic Disorder Study Group recently (Wenying Yang, et al. N Engl J Med. 2010, 362: 1090-1101), as cited in our paper. Therefore, we didn’t use our regional data to evaluate the diabetes prevalence trend in China.
Point-by-point Response Report 2

Version: 1

Date: 1 October 2011

Reviewer: Perviz Asaria

Reviewer’s report:

Major compulsory revisions:
1) My major concern about this cross sectional study centers on the definition and collection of IHD and stroke prevalence data. This has not been clearly explained in the paper.
   a. Were possible ‘cases’ of IHD or stroke identified from the structured questionnaire or in other ways. I.e. were medical records/case histories only reviewed if the patient happened to mention that they had a stroke/IHD event, or were they reviewed for every single participant in the survey? Could it be that person who forgot that they had had a CVD event and did not mention this during questioning did not have their notes reviewed?

As we mentioned in the Methods section, this cross-sectional study is baseline survey for the Fangshan / Family-based Ischemic Stroke Study In China (FISSIC) program (Tang X, et al. BMC Med Genet. 2007,8:60), and this survey was initialed through the three-tier prevention and health care network (village, township and county level) in the rural area. At the village level, our trained investigators from local general practitioners (GP) and health care staff identified the possible “cases” of CHD or stroke using structured questionnaire. Most of the possible “cases” could be screened at the survey because local GPs were familiar with the health issue of patients whom they were in charge of in their serving communities, and it is unlikely for both patients and GPs to forget their CVD history simultaneously during the interview.

b. Was the case history of every participant reviewed by a neurologist and a cardiologist or were only selected cases reviewed?

Only the participants screened from the above “cases” of stroke or CHD at the village level, their CVD history would be reviewed by a study neurologist and cardiologist from the central hospital at the township and county level. Doctors will check the medical records for evaluation and confirmation, including patient history, physical examination, ECG, CT or MRI etc, to avoid potential over-estimated prevalence at the previous village level.

c. What were the criteria used to define a case of IHD or stroke?

We’ve clarified this in the Data Collection of the revised manuscript as highlighted.
According to diagnosis standardization from World Health Organization CHD / Stroke Community Registers, stroke was defined as a history of language or physical dysfunction which had been continued for more than 24 hours and diagnosed using computerized tomography (CT) or magnetic resonance imaging (MRI); and CHD was defined as a history of angina or hospitalization for myocardial infarction with electrocardiography (ECG) findings, or a surgical history of coronary balloon angioplasty, coronary artery bypass or coronary stent implantation in our study.

d. What quality control measures were employed to ensure that these criteria were adhered to?

As quality control measures in this study, confirmation of medical history by qualified doctors was an important step in the process of data collection. Furthermore, results of ECG, head CT and head MRI were recorded in the questionnaire for further study or quality control by researchers.

e. What quality control measures were instituted to ensure that every possible prevalent case of IHD or stroke was identified?

As we mentioned in Question 1) a, cases of CHD or stroke were identified through the community-based health care networks (village, township and county level) in this rural area to reduce both missed diagnosis and misdiagnosis.

f. How was prevalence defined? Was it any participant who had ever had an event at any point in time?

In this study, prevalence was defined as the proportion of cases of CHD or stroke to total amount of participants. One case of CHD or stroke referred to a participant who had ever had at least one event at any point in time.

2) The structured questionnaire should be available for review.

Yes, our questionnaire has been translated into English version and provided as an appendix file for review.

3) Secondly the wording in not always entirely clear as to whether the prevalence odds ratios are attempting to quantify the prevalence of CVD in diabetic/hypertensive/obese patients compared to those without diabetes/hypertension/obesity or whether they are trying to quantify the prevalence of diabetes in those with CVD. The two are different.

In our opinion, it might not be appropriate to interpret that the prevalence odds ratios (POR) quantified the prevalence of CVD in diabetic/hypertensive/obese patients compared to those without diabetes/hypertension/obesity or they quantified the
prevalence of diabetes in those with CVD, mainly because POR is not a ratio of prevalence in two groups. In a cross-sectional study, take CHD and diabetes for example:

<table>
<thead>
<tr>
<th>Coronary heart diseases</th>
<th>yes</th>
<th>no</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>yes</td>
<td>a</td>
</tr>
<tr>
<td></td>
<td>no</td>
<td>c</td>
</tr>
</tbody>
</table>

In this case, POR = (a/b)/(c/d) = ad/bc, and POR ≠ [a/(a+b)]/[c/(c+d)] (Mary Lou Thompson, et al. *Occup Environ Med*. 1998, 55: 272-277). Therefore, POR is not a ratio of prevalence. We’ve clarified these both in Statistical Analysis section and Results Para 5.

4) **If the CVD prevalence data have not been systematically and rigorously collected then section referring to CVD prevalence and prevalence odds ratios should be dropped.**

As we mentioned, this study was the baseline survey of the FISSIC program. It is rather difficult to collect very detailed information of each CVD event in a large population-based survey. However, in order to be more objective and accurate, each CVD case was confirmed by qualified doctors with patients’ records through medical chart review, based on ECG, CT or MRI. Thus, the CVD prevalence data were systematically and rigorously collected and the section referring to CVD prevalence and prevalence odds ratio might have some further implications.

5) **Table1/Table2:** The results of surveys like this one are often used for secondary analysis, national/international comparisons, or temporal comparisons. The main value of the current study is the primary risk factor data which have been collected on a large sample size. It would therefore be useful to have the following variables broken down by 5 year age group and sex (i.e. age and sex specific) in the results table or as a web-appendix: Sample size, SBP, DBP, Weight, BMI

We have prepared a table as a web-appendix to show sample size, SBP, DBP, Weight, BMI which were broken down by 5 year age group and sex.

6) **Title:** wording misleading to the non-Chinese implies that this is a survey of rural migrants who have moved to Beijing. Suggest: “Prevalence of cardiovascular disease and risk factors in a rural district of Beijing, China: a population based survey of 58,308 residents”

Yes, it is really a helpful suggestion. The title of this manuscript has been changed into “Prevalence of cardiovascular disease and risk factors in a rural district of Beijing,
China: a population based survey of 58,308 residents

7) Background Para 1: Where is the evidence for sentence 1? Mortality from CVD is increasing (see Global Burden of Disease). We do not have good global data for prevalence of CVD. Secondly risk factor distribution are increasing in some places and decreasing in others – please see: Dannei (glucose), Farzadfar (cholesterol), Finucaine (BMI), and Dannei (BP) in Lancet 2011 for references.

Yes, We’ve changed the first sentence in Para 1 into “Mortality and disease burden of cardiovascular disease (CVD) is increasing globally; and with demographic shifts, urbanization and changing lifestyles, the number of people with high blood pressure, diabetes, obesity or dyslipidemia may grow larger, suggesting a further increase in CVD in the future”, and added a reference (Salim Yusuf, et al. Circulation. 2001, 104: 2746-2753).

8) Method, Para 6 Statistical analysis: Unclear how confidence intervals were calculated.

Yes, we carried out the calculation for 95% confidence intervals of prevalence with PROC SURVEYFREQ from the SAS statistical package, and we’ve clarified this in the Statistical Analysis section.

9) Results Para 5: needs to be written more clearly. The confidence intervals for diabetes association with CHD and with stroke overlap – therefore not really valid to say that diabetes has stronger association with CHD than with stroke from this study, similarly with hypertension.

Yes, we agreed with the reviewer’s comments, and have revised this paragraph following the reviewer’s advice as highlighted in the Results Para 5.

10) Discussion Para 3: Not appropriate to compare the pattern of CHD: stroke in incidence study directly to that found in a prevalence study. The paragraph itself says that mortality from stroke is double that of CHD (this will undoubtedly affect prevalence). The wording of this paragraph and its concluding sentence need to be revised.

Yes, we agreed, and have revised Discussion Para 3 to be more appropriate.

11) Discussion Para 5: Is there any evidence for the explanations proposed? There are no references given here.

Because lack of published studies on the diversity in the distribution of CVD and its risk factors across different geographic areas (most studies focused on difference between urban and rural area), we didn’t find appropriate evidence to support our
discussion in this paragraph. Therefore, we could not discuss too much on this issue and we will address it in our further study.

12) Discussion Para 6: To make comprehensible international comparisons of prevalence rates, the rates would need to be standardized to a single population, or age specific rates need to be reported. The alternative would be to report absolute numbers (i.e. the actual burden) or to state that the figures reported are country prevalence rates not standardized for international comparison.

Yes, we agreed with the reviewer’s comments and have clarified the population which was used for standardization in each study mentioned in Discussion Para 6. However, in this paragraph, we were trying to point out that stroke is highly prevalent in people aged 65 and above, and did not intend to compare the prevalence between countries.

Minor revisions:
1) Method, Para 6 Statistical analysis: It looks like the prevalence data have been directly standardized to the 2000 5th China Population Census and this should be explicitly mentioned. The current wording is confusing.

Yes, we’ve reworded the sentence in Statistical Analysis Para 6 into “Prevalence data was directly standardized to the adult sample data of 2000 China 5th Population Census and 2005 China population for comparison”

2) Method, Para 6 Statistical analysis and Table 3: I think separate Prevalence Odds Ratios have been reported for each of diabetes, hypertension and obesity. Can the authors confirm this? Once again the wording is confusing. Something along the lines of “prevalence of CHD and stroke amongst those with diabetes, hypertension and obesity compared to those without are reported after adjustment for age and sex, using logistic regression.”

Prevalence Odds Ratios of diabetes, hypertension and obesity with CHD/stroke were calculated in one multivariate logistic regression model, adjusted by age and sex. To make it clearer, we’ve added “Prevalence odds ratios were calculated with the use of multivariate logistic regression models. All variables listed were included in the model simultaneously, adjusted by age and sex.” under Table 3 as a footnote.

3) Results Para 3 and Figure 2: Were data from the current study, from the 2007-2008 China National Diabetes Study and from the 2001 InterASIA study all directly standardized to the 2005 China population to allow comparison? If so please state this clearly.

All the data were directly standardized to the 2000 China population to allow comparison. We’ve clarified this in Results Para 3 and added a footnote to Figure 3.
Language and spelling:
4) Abstract Para 2 and 3 need to be re-worded in light of above comments.

Yes, we’ve reworded Abstract Para 2 and 3 in light of above comments.

5) Data collection sentence 2 should be “using a structured questionnaire”.

Data Collection sentence 2: we’ve changed “by structured questionnaire” into “using a structured questionnaire”.

6) Data collection: remove “with antidiabetes medication” and just say “with insulin or oral hypoglycaemic agents”

Data collection: we’ve changed “with antidiabetes medication (insulin or oral hypoglycaemic agents)” into “with insulin or oral hypoglycaemic agents”.

7) Data collection – was an average of the three BP measurements used? How long was the rest period between measurements?

Yes, we’ve clarified this in the paragraph of Physical Examination. The participant has been resting a seated position for 5 minutes.

8) Criteria for data interpretation: “(BMI) was calculated as the ratio of weight to height squared”

Criteria for data interpretation: we’ve changed “(BMI) was calculated as weight to height squared” into “(BMI) was calculated as the ratio of weight to height squared”.

9) Results: “participants were classified into 10 year age bands”

Results: we’ve changed “participants were categorized into five age groups in every 10 years” into “participants were classified into 10 year age bands”.

10) Results Para 2: English needs adjusting

Yes, we’ve adjusted the English in Results Para 2.

11) Discussion Para 2: “in spite” not “in spide”

Discussion Para 2: we’ve corrected “in spide” into “in spite”.

12) Discussion Para 6: “Korea” not “Korean”

Discussion Para 6: we’ve corrected “Korean” into “Korea”.
13) Discussion Para 6: could be worded more politely eg. “World population is aging and this has already made a considerable impact on the CVD burden in developed countries in recent decades. It is reasonable to suppose, that as the age structure of the Chinese population increases, the CVD burden in China will be aggravated.”

Yes, we followed the reviewer’s suggestion, and changed the last sentence of Discussion Para 6 into “World population is aging and this has already made a considerable impact on the CVD burden in developed countries in recent decades. It is reasonable to suppose that, as the age structure of the Chinese population increases, the CVD burden in China will be aggravated”.

14) Discussion Para 8: “cardiologists and neurologists were joined to confirm the diagnosis”?? Does not make sense.

Yes, we’ve clarified this in Discussion Para 8, changing “cardiologists and neurologists were joined to confirm the diagnosis” into “qualified cardiologists and neurologists were joined to confirm the diagnosis of these diseases with patients’ records through medical chart review, based on ECG, CT or MRI”.

15) Table 2 appears to show age and sex specific rates except for top and bottom lines – the heading therefore needs to be reworded.

Yes, we’ve changed the heading of Table 2 into “Age- and sex-specific prevalence of cardiovascular diseases and risk factors among participants (% and its 95% confidence interval)”

16) Figure 3a legend: need “h” on hypertension.

Figure 4a legend: we’ve corrected “ypertension” into “hypertension”.

Discretionary revisions:
1) Discussion: a comment on why twice as many women as men participated would be helpful. Were the same number of men and women invited?

All people who were aged 40 years and above and living in towns we sampled were invited in our study. To explain the sex ratio, we would like to take the InterASIA study as an example. The InterASIA study was well designed (Jiang He, et al. Ethnicity & Disease. 2004, 14: 260-268) with nationally representative samples of China, and Fangshan district of Beijing was chosen as a representative north and rural area. In this study, they finally enrolled 272 men and 562 women from Fangshan district (APCSC. J Epidemiol Community Health. 2007, 61: 115-121). That was twice as many women as men, which was similar to our study. It is probably because a
proportion of male labor force living in Fangshan district went out for work to cities (such as downtown Beijing) for more money, and therefore, more women (i.e. their wives) than men were left in this area. It is a common problem in rural China. We’ve added a discussion on this in Discussion Para 8.

2) Discussion: age in the elderly – how easy was it to ascertain in the over 85s? We recorded all the participants’ birthday from ID cards, and could calculate their ages.