Author’s response to reviews

Title: Blood pressure and hypertension prevalence among oldest-old in China for 16 year: based on CLHLS

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Version: 2 Date: 24 Jul 2019

Author’s response to reviews:

Jul 24, 2019
Re: BGTC-D-19-00304R1

" Blood pressure and hypertension prevalence among oldest-old in China for 16 year: based on CLHLS”

Dear Editor-in chief and Reviewers:

Thank you very much for your positive comments on our manuscript and the opportunity to revise the paper. We are grateful for the reviewers’ constructive suggestions and our revised paper has incorporated all the suggestions. Below is our line by line response to the reviewers’ comments. We hope that the revised paper meets your approval for publication in BMC Geriatrics.

Sincerely

Miao Liu, Yao He

Institute of Geriatrics,
Chinese PLA General Hospital,
28 Fuxing Road, Beijing 100853, China.
Reviewer 1 Reviewer reports:

Chenkai Wu, PhD, MPH, MS (Reviewer 1): The authors have improved the manuscript substantially; however, some of my comments have not been adequately addressed.

1. The authors stated in their response to my first comment that they decided not to include the analyses of hypertension awareness and control rates. However, the results were still presented in Table 2 and S7.

Reply: Thanks for your careful review. We have deleted accordingly.

2. Although the authors considered not having information on use of anti-hypertensive medication is a limitation, I would encourage the authors to elaborate on this more. At least, the authors could discuss approximately how large the bias could be for the estimate of hypertension prevalence in the absence of information on medication use.

Reply: Thanks for your careful review. Although this kind of definition had been adopted in quite a number of epidemiological investigations, the resulting bias cannot be ignored.

In this study, hypertension was defined as those who had SBP≥140mmHg or DBP≥90 mmHg or self-reported being diagnosed as hypertension by II&III grade hospital before. Compared with the method used in the guideline, we didn’t have the medication information. This would cause a certain proportion of participants with normal BP levels, to be classified as “hypertension” rather than “no hypertension” (Overestimating hypertension prevalence). Detailed calculations can be based on the classification and number from the table 1 below. Number B usually has a very low proportion since nobody would take medicine under the absence of a doctor's diagnosis. Number D has nothing to do with the calculation since it didn’t count in either method. Number A has nothing to do with the calculation since it count in both methods. So, the evaluation of this bias was calculated as: C/total population.

Table 1. The distribution of misclassification

<table>
<thead>
<tr>
<th>Mediation status</th>
<th>Preciously diagnosed</th>
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<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>A</td>
</tr>
<tr>
<td>No</td>
<td>C</td>
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<td></td>
<td>D</td>
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</table>

Take the 2014 survey (n=4587) as an example. There were a total of 2294 participants who had SBP≥140 mmHg or DBP≥90mmHg, and those 2294 were classified as hypertension. Among those 2293 participants with lower BP levels, there were a total of 299 participants were classified as previously diagnosed. Assuming the treatment rate was 33.3% among the oldest-old,
the detailed number should be: 299-299*33.3%=200. So the overestimated part of the prevalence was calculated as: 200/4587=4.4%. The crude prevalence would change from 56.5% to 52.1%.

The above calculation process and results show that in the definition of hypertension prevalence, the use of past history rather than medication history can result in an overestimation of about 4%.

3. The authors defined isolated systolic hypertension as SBP >=140 mmHg and DBP<90 mmHg. I was wondering how did the authors deal with persons who reported a physician diagnosed hypertension but having a measured SBP <140 mmHg.

Reply: Thanks for the question. We defined those who reported a physician diagnosed hypertension but having a measured SBP <140 mmHg as hypertension. Only those whose SBP≥140 mmHg and DBP<90 mmHg were defined as isolated systolic hypertension according to the guideline [1].

4. The authors did a sensitivity analysis focusing the first measurement of BP of the CLHLS participants. I have two additional comments on this. First, I think it is more appropriate to focus on these persons in the main analysis instead in the sensitivity analysis. Typically, multiple cross-sectional survey does not include the same person more than once. Second, there were appreciable differences between the results of the sensitivity analysis and those of the main analysis. For example, the prevalence of hypertension is 62.3% in 2014 in the sensitivity analysis, while the prevalence is between 55.3% and 57.4% in the main analysis.

Reply: Thanks for your careful review. Indeed, as you mentioned, the results for those who were first included in each survey wave were slightly higher than those based on the whole population. This was also in line with our expectation of sensitivity analysis, that hypertension participants may be more likely to be excluded from multiple inclusions due to death or hospitalization events.

Considering that the main purpose of this study is to describe the trend of hypertension prevalence based on the results of multiple cross-sectional studies, Therefore, after discussion by the authors, the sensitivity analysis would still be presented as appendix tables. And we made corresponding modifications in the result section. Accordingly.

5. Another interesting pattern is that the prevalence was lower 1998 than in 2005 (Table 1) while the mean SBP was substantially higher in 1998 than 2005 (Figure 1). Similar seemingly conflicting results were observed in the sensitivity analysis: the average SBP and DBP were both higher in 1998 than in 2005 (148.5 vs. 130.6 & 84.4 vs. 82.1), while the prevalence of hypertension was lower in 1998 than in 2005 (43.1% vs. 47.1%). Any explanations?

Reply: Thanks for your careful review. This may be related to the characteristics of the subjects and the process of each survey. Besides, this may also be attributed to the increase of treatment and control rates of hypertension for the past years. In 1998, although the prevalence of
hypertension was low, its treatment and control rates were at relatively lower level, so the SBP levels were higher. In 2005, the treatment and control rates of hypertension had increased, so although the prevalence of hypertension was high, the SBP levels were lower than that in 1998.

The results about control rates previously reported were listed below. As we can see, the control rate increased from 1.1% in 1998 to 4.3% in 2005.

Table 1. The control rates (%) of hypertension by seven waves

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<tbody>
<tr>
<td>Male</td>
<td>1.5(1.0-2.1)</td>
<td>2.7(2.0-3.5)</td>
<td>4.7(3.7-5.6)</td>
<td>5.0(4.0-6.0)</td>
<td>10.1(8.8-11.4)</td>
<td>12.0(10.1-14.0)</td>
<td>14.6(12.7-16.5)</td>
<td>&lt;0.001</td>
</tr>
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<td>Female</td>
<td>1.0(0.5-1.2)</td>
<td>3.3(2.7-4.0)</td>
<td>4.0(3.7-4.7)</td>
<td>3.8(3.1-4.5)</td>
<td>9.3(8.3-10.3)</td>
<td>11.2(9.6-10.8)</td>
<td>10.8(9.5-12.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>p</td>
<td>0.065</td>
<td>0.240</td>
<td>0.287</td>
<td>0.041</td>
<td>0.336</td>
<td>0.552</td>
<td>0.001</td>
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<td>80-89 yrs</td>
<td>1.6(1.0-2.3)</td>
<td>3.7(2.9-4.6)</td>
<td>5.6(4.6-6.6)</td>
<td>4.9(4.0-5.9)</td>
<td>10.4(9.1-11.7)</td>
<td>14.2(12.3-16.1)</td>
<td>15.2(13.3-17.0)</td>
<td>&lt;0.001</td>
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<tr>
<td>90-99 yrs</td>
<td>0.5(0.1-0.9)</td>
<td>2.9(2.1-3.7)</td>
<td>3.8(2.9-4.7)</td>
<td>4.4(3.4-5.3)</td>
<td>10.2(8.8-11.5)</td>
<td>10.1(8.1-12.2)</td>
<td>11.4(9.7-13.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>100-yrs</td>
<td>1.0(0.4-1.6)</td>
<td>1.9(1.0-2.7)</td>
<td>2.9(2.0-3.8)</td>
<td>3.0(2.0-4.0)</td>
<td>7.3(5.9-8.8)</td>
<td>6.6(4.2-7.9)</td>
<td>7.2(5.2-9.2)</td>
<td>&lt;0.001</td>
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<tr>
<td>p for trend</td>
<td>0.021</td>
<td>0.019</td>
<td>0.001</td>
<td>0.041</td>
<td>0.009</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
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<tr>
<td>City</td>
<td>1.5(0.8-2.1)</td>
<td>4.1(3.1-5.2)</td>
<td>6.7(5.2-8.1)</td>
<td>6.6(5.2-7.9)</td>
<td>15.9(13.7-18.0)</td>
<td>20.9(16.4-25.4)</td>
<td>23.3(19.8-26.9)</td>
<td>&lt;0.001</td>
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<tr>
<td>Town</td>
<td>2.3(1.6-3.0)</td>
<td>3.2(2.5-3.8)</td>
<td>3.2(2.5-3.9)</td>
<td>3.2(2.5-4.0)</td>
<td>7.9(7.0-8.9)</td>
<td>8.5(7.1-9.9)</td>
<td>9.6(8.3-11.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rural</td>
<td>0.9(0.5-1.3)</td>
<td>3.0(2.1-3.9)</td>
<td>4.3(3.1-5.5)</td>
<td>4.1(2.9-5.3)</td>
<td>7.8(6.1-9.5)</td>
<td>13.4(11.1-15.8)</td>
<td>11.1(9.3-13.1)</td>
<td>&lt;0.001</td>
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<td>p for trend</td>
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<td>0.010</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
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<tr>
<td>East</td>
<td>1.2(0.7-1.6)</td>
<td>2.3(1.8-2.9)</td>
<td>4.2(3.5-5.0)</td>
<td>4.1(3.3-4.8)</td>
<td>12.1(10.8-13.3)</td>
<td>12.5(10.8-14.2)</td>
<td>13.0(11.5-14.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Central</td>
<td>0.8(0.2-1.5)</td>
<td>3.9(2.7-5.0)</td>
<td>4.8(3.6-6.1)</td>
<td>4.0(3.0-5.1)</td>
<td>6.6(5.3-7.8)</td>
<td>7.9(5.9-9.9)</td>
<td>9.2(7.3-11.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>West</td>
<td>1.4(0.4-2.3)</td>
<td>6.5(4.3-8.7)</td>
<td>6.1(4.3-8.0)</td>
<td>5.6(3.9-7.4)</td>
<td>7.0(5.3-8.6)</td>
<td>13.9(9.6-18.3)</td>
<td>11.7(7.8-14.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>p for trend</td>
<td>0.926</td>
<td>&lt;0.001</td>
<td>0.047</td>
<td>0.149</td>
<td>&lt;0.001</td>
<td>0.289</td>
<td>0.029</td>
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</tr>
</tbody>
</table>

| Total                 | 1.1(0.8-1.4)| 3.1(2.6-3.6)| 4.3(3.7-4.8)| 4.3(3.7-4.8)| 9.6(8.8-10.4)| 11.6(10.3-12.8)| 12.3(11.2-13.4)| <0.001   |
6. The authors did not address my third comment. They need to conduct an additional sensitivity analysis restricting the sample to those with a remaining life of at least 1 or 2 years.

Reply: Thanks for your suggestion. We have added the appendix table 7, mainly focusing on the proportion of those who can't have the BP recorded. Although there was only less than 3.5% who didn't have BP recorded were most frail oldest-old, with severe diseases or disability, and may have relatively higher hypertension prevalence. Unfortunately, we didn’t have the information of the remaining life years, so we couldn’t calculate the sensitivity analysis restricting the sample to those with a remaining life of at least 1 or 2 years. And we have added this to the limitation part.

7. The authors mentioned in the discussion that persons living in nursing homes were not included in the CLHLS. Actually, a non-negligible amount of CLHLS participants lived in nursing homes.

Reply: Thanks for your careful review. After confirmation with the staff, we agree with your proposal. And the original text has been revised.

Jane Masoli (Reviewer 2): This study provides blood pressure prevalence for the oldest old in China and would therefore provide a useful contribution to existing literature. There have been significant improvements since the previous version of the manuscript. However, there remain some major issues. There remain potential sources of bias that are essential to convey to the reader clearly to aid interpretation.

In particular, potential selection bias due to the requirement for completeness of BP/hypertension recording and the combination category of BP recording and patient reporting without medication awareness or corroboration from medical notes. It is noted that the missing data is now numerically summarised in the appendix. However, the nature of missingness and what approach was taken to overcome missing data are not addressed. Was it clear from the protocol who might not have BP recorded? Are these the most frail potentially?

Reply: Thanks for your careful review.

The main problem in this study is the lack of information about drug treatment. Therefore, according to the opinions of reviewers, there is a big bias on the control rate. So we deleted the section of control rate.

As for the impact of lack on drug treatment information on the hypertension prevalence, there would be small bias i by comparing the previous similar studies and the field survey experience.
Since hypertension was defined according to the measurement of blood pressure levels and the previously diagnosis history by II&III grade hospitals. We have both parts of the information. Therefore, we believe that the lack of detailed information on medication will not have an important impact on the hypertension prevalence.

For this question: “Was it clear from the protocol who might not have BP recorded? Are these the most frail potentially?” As we can see from appendix table 1, there were only less than 3.5% who didn’t have BP recorded. And Just as the reviewer’s opinion, those who didn’t have BP recorded, were most frail oldest-old, with severe diseases or disability. Although there was only less than 3.5% who didn’t have BP recorded were most frail oldest-old, with severe diseases or disability, and may have relatively higher hypertension prevalence. And considering this fact, we have added the corresponding content to the limitations of the study.

The language is much improved, however refinements are still required to aid clarity and interpretation. I list some of the suggested changes below, along with some other points.

P.2. line 9
Backgrounds change to Background
Reply: Thanks for your careful review. We have corrected accordingly.

P2. Line 18
Be more precise as "oldest old" is not a clearly defined term and can vary. Needs age clarifier here.
Reply: Thanks for your careful review. We have added “aged 80 and over” accordingly.

P2 line 24
There is a described decrease in systolic BP rather than increase.
Reply: Thanks for your careful review. We have corrected accordingly.

I would also suggest including more detail on those diagnosed with hypertension, given the presented reduction in SBP over time. I am unclear how there can be a reduction in SBP over time, with increased isolated systolic hypertension and an increase in overall hypertension.

Reply: Thanks for your careful review. This may be related to the characteristics of the subjects and the process of each survey. Besides, this may also be attributed to the increase of treatment and control rates of hypertension for the past years. In 1998, although the prevalence of hypertension was low, its treatment and control rates were at relatively lower level, so the SBP
levels were higher. In 2005, the treatment and control rates of hypertension had increased, so although the prevalence of hypertension was high, the SBP levels were lower than that in 1998.

The results about control rates previously reported were listed below. As we can see, the control rate increased from 1.1% in 1998 to 4.3% in 2005.

P3 line 7

Backgrounds change to Background

Reply: Thanks for your careful review. We have corrected accordingly.

P3 line 13

"coronary heart disease and stroke risks"

Reply: Thanks for your careful review. We have corrected accordingly.

P3 line 13

"However, there were age differences among the prevalence of hypertension and also its risk for related diseases."

I don't understand what this means.

Reply: Thanks for your careful review. We have corrected accordingly. Below is our revised description:

Hypertension is one of the important risk factors for cardiovascular disease. The higher the blood pressure (BP), the greater the coronary heart disease and stroke risks [1-3]. Therefore, it is particularly important to understand the epidemic trend of hypertension. The prevalence of hypertension varies greatly among different age groups, especially among elderly. And isolated systolic hypertension (ISH) (systolic blood pressure (SBP) ≥140 mmHg while diastolic blood pressure (DBP)<90 mmHg) was most existed in elderly[4-5].

P4

Please reference "definitions".

Reply: Thanks for your careful review.

P5 line 23

"The mean SBP level was 148.4±24.4 mmHg in 1998 wave for 8694 participants and there was significant difference and fluctuations over the past 16 years for SBP levels. A significant decrease was seen along with age groups (p<0.05)."
This needs refining for clarity. The reader has to guess the meaning from the results rather than being able to be guided by the text.

Reply: Thanks for your careful review. We have corrected accordingly.

Conclusions

"The results also provided evidence about the trends of prevalence of hypertension in China, which indicated that hypertension prevention was still a long and arduous task since the prevalence was high. Additionally, it suggested that specific people should be targeted for enhanced hypertension screening and management to reduce related cardiovascular disease burden."

I would suggest rewording the "long and arduous task"

The last sentence is an over-interpretation of results, given that cardiovascular outcomes are beyond the scope of this study. I would suggest removing this sentence "Additionally…burden"

Reply: Thanks for your careful review. We have corrected accordingly.

Once again, we really appreciate the reviewers’ comments and suggestions, which are valuable in improving the quality of our manuscript.

Should you have any questions, please contact us without hesitate.

With kindest regards,

Sincerely yours,

Miao Liu, Yao He

Reference