PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Population-based cross-sectional study on the hearing threshold levels and hearing loss among people in Zhejiang, China
AUTHORS	Wang, Dahui; Zhang, Huai; Ma, Haiyan; Zhang, Long; Yang, Lei; Xu, Liangwen

VERSION 1 - REVIEW

REVIEWER	Justin S. Golub, MD, MS Columbia University Vagelos College of Physicians and Surgeons NewYork-Presbyterian/Columbia University Irving Medical Center United States
REVIEW RETURNED	16-Nov-2018

GENERAL COMMENTS	1. REVIEWER SUMMARY: This is a large cross-sectional population-based epidemiological study of hearing loss prevalence in a particular province in China. The data collection must have been a large and expensive effort. Several potential predictors of hearing loss are studied with logistic regression. This is a straightforward study and appears to be well performed. The analysis is understandable. The significance of the paper seems to be the simple reporting of basic epidemiological hearing loss statistics in an area of China. The associations are not surprising and confirm what is already known (e.g., males have more hearing loss, hearing loss is worse with cardiovascular disease.) Similar prevalence and association studies have been done in other countries (e.g., in the United State using NHANES data.) China is the largest country in the world and rapidly developing. Thus the findings are of interest. However, it is unclear how this paper fits in to other similar studies already performed in China: this needs to be clarified. It is also a regional and not national study. 2. UNIQUE ASPECTS: This needs to be clarified. Why is this paper unique? In other words, how does it compare to other similar studies in other provinces (or nationally) in China? Have there been national studies? Can you explain more about other regional studies? On line 51-53 you state Zhejiang has not been studied. But then you need to explain (in the discussion) more about other regional studies and the context of this study. This will influence the paper's impact, particularly since the methods and findings are not that surprising. 3. STUDY DESIGN: Cross-sectional population-based epidemiological study in a single Chinese province 4. WRITING STYLE: Nearly fluent English. Very understandable. Only minor language errors. 5. SPECIFIC COMMENTS:

	This is a large study and so almost everything reaches statistical significance. Briefly define hearing loss in the abstract in parentheses. I.e., (> 25 dB HL threshold) Page 3 - The "Strengths and limitations of this study" section does not discuss limitations. I'm not sure the purpose of this section. Will it be published? You do explain limitations in the discussion. Page 4 Line 22 - Can you explain here in parentheses what wide band of frequencies means? Wide is a relative term, it could mean anything. Page 4 Line 46-55. To those unfamiliar with the geography of China, can you please explain why Zhejiang is important? Is it one of the larger provinces? Is it changing more rapidly than other provinces? Page 5 Line 29. Please explain that +/- is standard deviation at the first instance. It is explained later in the methods, but it appears first here. Page 7 Line 7-9. Can you explain what loud noise in the workplace was defined as? Some loud noises may be bothersome, but not nearly loud enough to cause noise induced hearing loss. Loud is a relative term. Page 7 Line 44. It is good that the authors used a Bonferroni correction for multiple comparisons. Figures 1 and 2. It is good that the datapoints with the error bars are shifted slightly so you can see which error bar belongs to each data point. (In other words, the error bars do not over overlap.) That is very professional. Page 8. In a few instances in the results, you stated "There were significance differences between...." two groups and then a P value is presented. What is more important is the mean value of each group and the magnitude of difference. For example, you should state what the PTA was for the left and the right ear. There could be a difference of 23.1 dB versus 23.2 dB: while this may be a statistically significant difference, it is a not a very meaningful difference. Figure 3. It is hard to tell the difference between young, middle, and old based on the markers. Can you make the lines more different? Maybe one can be gray. Or one marker can be open instead of closed? Figures 3 and 4. Should there be error bars here? Page 12 Lines 79. Since you have $p<0.05$ as the significance cutpoint, you can not say that education was associated with speech-frequency hearing loss. Technically, it was not associated. However it was close. You used logistic regression where the hearing loss out was binary: yes or no. Since you had continuous hearing data, can you explain why you chose to use logistic regression (for binary

	hearing loss) instead of linear regression (for continuous hearing loss). When you take a continuous variable and make it binary, you lose data. If you have a justification, this is fine. You do not need to redo the analysis. However, I think it should be explained, perhaps briefly in the methods. Maybe for simplicity of interpretation? Likewise, in table 3, you used age (a covariate in the model) as a categorical variable. If you had access to the continuous age, why would you make it categorical? I would think using the continuous age would be better as it contains a finer level of information. If you can justify this, it is fine, I just don't undestand the reasoning. Page 15. Line 18-20. "The difference probably resulted from the geographic distribution of the population surveyed." Yes, but why? Can you try to explain more? Page 15. Lines 27-29. "suggesting that the hearing threshold increases with age, both in males and females." I think you can say a stronger word than "suggesting that". For example, "confirming that". You have basically confirmed the existence of presbycusis in your study, which is one of the most established disorders in humans. Page 17. Line 37-39. "we found evidence that hypertension may accelerate the occurrence of hearing loss via a different pathophysiological mechanism". What different pathophysiological mechanism? Was a mechanism explained somewhere? Page 17. Lines 52-55. "Evidently, our country attaches lesser importance to hearing loss than other developed countries." This is not evident to me. Can you explain? Why specifically is this the case?

REVIEWER	Shaun Scholes Epidemiology & Public Health, University College London, United Kingdom
REVIEW RETURNED	19-Dec-2018

GENERAL COMMENTS	The authors examined hearing loss among participants aged 18-98 years living in Zhejiang Province, China. I found the paper easy to follow and interesting. I have a number of minor comments which the authors may want to consider to strengthen their paper. Abstract I recommend presenting the sex-specific prevalence estimates (abstract and results section). The authors should specify the definition of hearing loss in the outcome measures section as outlined on page 6 and in the 1st paragraph of the discussion. Methods The authors should specify the number (and proportion) of adults who were excluded from the study due to having an ear disease or an abnormal ear structure. Results The authors say that hearing of the right ear was better than that of the left. It would be better if the authors wrote that hearing loss

	was more prevalent in the left ear (as reported in the abstract). The estimates in Table 1 should be accompanied by confidence intervals. A limitation of the manuscript is that the authors did not consider stratifying their analyses by gender, age or both. The authors should consider this in addition to the results they already show. Could the correlates of hearing loss be different for men and women? Could the correlates of hearing loss be different for the younger and older adults (the age-range for the study is wide at 18-98 years)? Would an analysis among younger adults help identify some factors for “early intervention”? Although the sample sizes will be smaller than for the overall analysis this information could be of public health relevance. At the very least, the authors did not justify their decision to simply adjust for age and gender. It might also be informative for the authors to report on the levels of exposure to occupational and recreational noise: and how these vary by age, sex, and education level. Discussion The authors state that education and personal income were protective factors: but income was not significantly associated with high-frequency hearing loss in the logistic regression analysis (P=0.129). The authors should mention in their discussion of limitations that the questions on occupational and noise exposure seem to refer to exposure at the time of data collection: and so they did not have any data on exposure over a longer period (say the last 5 years). The authors should also remind readers that their analyses excluded participants with an ear disease: and therefore underestimate the burden of hearing loss. Finally, the authors state that the difference between their prevalence estimates and those of Bu and Gong et al (2018) “probably resulted from the geographical distribution of the population surveyed”. Clearly, there is another explanation for the lower levels of hearing loss reported in this study: the study by Gong et al was conducted among older adults (60+ years). Perhaps the authors could compute the prevalence of hearing loss amongst those aged 60+ to compare with the study by Gong et al. Furthermore, the estimates for this study are higher (not lower) than those reported by Bu et al (2011: 11.7%) which surveyed people of all ages. I encourage the authors to be very exact in the comparisons they make with other studies.

VERSION 1 – AUTHOR RESPONSE

Part B (Reviewer 1)

SPECIFIC COMMENTS

1. Comment: Briefly define hearing loss in the abstract in parentheses. I.e., (> 25 dB HL threshold).

Answer: Briefly define hearing loss has been added to the abstract.

2. Comment: Page 3 - The "Strengths and limitations of this study" section does not discuss limitations. I'm not sure the purpose of this section. Will it be published? You do explain limitations in the discussion.

Answer: BMJ Open journal requires a section called ‘Article Summary’ in the manuscript, placed after the abstract, consisting of the heading ‘Strengths and limitations of this study’. So we have added the

section, in addition, the third bullet point discuss limitations. We have amended this sentence so that it can be more clearly stated.

3. Comment: Page 4 Line 22 - Can you explain here in parentheses what wide band of frequencies means? Wide is a relative term, it could mean anything.

Answer: Thanks for the reviewer's kind advice. In our study, each subject was measured for hearing threshold between 0.125 and 8 kHz (0.125, 0.25, 0.5, 1, 2, 3, 4, 6, and 8 kHz) with a total of 9 frequency points per ear. However, in other studies, for example in Reference #6, participants were only tested for hearing thresholds between 0.5 and 4 kHz (0.5, 1, 2 and 4 kHz) with a total 4 frequency points per ear.

4. Comment: Page 4 Line 46-55. To those unfamiliar with the geography of China, can you please explain why Zhejiang is important? Is it one of the larger provinces? Is it changing more rapidly than other provinces?

Answer: Zhejiang is a typical representative of the eastern coastal provinces of China. It has a relatively developed economy, a large population, and is one of the larger provinces in China.

5. Comment: Page 5 Line 29. Please explain that +/- is standard deviation at the first instance. It is explained later in the methods, but it appears first here.

Answer: Thanks, explanation has been added at the first instance.

6. Comment: Page 7 Line 7-9. Can you explain what loud noise in the workplace was defined as? Some loud noises may be bothersome, but not nearly loud enough to cause noise induced hearing loss. Loud is a relative term.

Answer: Whether exposure to noise is based on self-reports of participants, the volume of the noise is the subjective feeling of the participants. If a participant felt that the sound was too loud to feel uncomfortable, then he/she was considered to be exposed to loud noise.

7. Comment: Page 7 Line 44. It is good that the authors used a Bonferroni correction for multiple comparisons.

Figures 1 and 2. It is good that the data points with the error bars are shifted slightly so you can see which error bar belongs to each data point. (In other words, the error bars do not over overlap.) That is very professional.

Answer: Thank you for your encouragement.

8. Comment: Page 8. In a few instances in the results, you stated "There were significance differences between...." two groups and then a P value is presented. What is more important is the mean value of each group and the magnitude of difference. For example, you should state what the PTA was for the left and the right ear. There could be a difference of 23.1 dB versus 23.2 dB: while this may be a statistically significant difference, it is a not a very meaningful difference.

Answer: We added the mean hearing thresholds value of the left and right eras of all participants to more clearly show the difference between the ears.

9. Comment: Figure 3. It is hard to tell the difference between young, middle, and old based on the markers. Can you make the lines more different? Maybe one can be gray. Or one marker can be open instead of closed?

Answer: Thanks for the suggestion. We have redone the figure to make the lines more different.

10. Comment: Figures 3 and 4. Should there be error bars here?

Answer: Error bars are not added to figures 3 and 4. On the one hand, the differences in hearing threshold between different groups are obvious in both figures. On the other hand, we had drawn figures 3 and 4 with error bars, but the figures would be complicated and cumbersome.

11. Comment: Page 12 Lines 79. Since you have $p<0.05$ as the significance cutpoint, you can not say that education was associated with speech-frequency hearing loss. Technically, it was not associated. However it was close.

Answer: Thanks for the advice. We have deleted and modified the relevant content in the manuscript.

12. Comment: You used logistic regression where the hearing loss out was binary: yes or no. Since you had continuous hearing data, can you explain why you chose to use logistic regression (for binary hearing loss) instead of linear regression (for continuous hearing loss). When you take a continuous variable and make it binary, you lose data. If you have a justification, this is fine. You do not need to redo the analysis. However, I think it should be explained, perhaps briefly in the methods. Maybe for simplicity of interpretation?

Answer: One of the focuses of this paper is to study the risk factors for hearing loss, which is obtained by analysing the distribution of different factors in the two populations. Besides, what we want to emphasize is that there are two types of people (hearing loss and no hearing loss). Briefly explanation has been added to the methods.

13. Comment: Likewise, in table 3, you used age (a covariate in the model) as a categorical variable. If you had access to the continuous age, why would you make it categorical? I would think using the continuous age would be better as it contains a finer level of information. If you can justify this, it is fine, I just don't understand the reasoning.

Answer: It makes a little sense to study the probability that the risk of hearing loss with each additional year of age. Meanwhile, the risk of hearing loss for each additional year of age may be small. Hence, we studied the effects of three age groups on hearing loss.

14. Comment: Page 15. Line 18-20. "The difference probably resulted from the geographic distribution of the population surveyed." Yes, but why? Can you try to explain more?

Answer: Differences in education, economics, and industrialization level due to geographical distribution of the population surveyed may be one of the reasons. Coincidentally, education, income, noise exposure, etc. were found to be risk (or protective) factors. Furthermore, differences in the subjects may also be one of the reasons. The explanation has been added to the manuscript.

15. Comment: Page 15. Lines 27-29. "suggesting that the hearing threshold increases with age, both in males and females." I think you can say a stronger word than "suggesting that". For example, "confirming that". You have basically confirmed the existence of presbycusis in your study, which is one of the most established disorders in humans.

Answer: Thanks for the reviewer’s advice. Has replaced the relevant word.

16. Comment: Page 17. Line 37-39. "we found evidence that hypertension may accelerate the occurrence of hearing loss via a different pathophysiological mechanism". What different pathophysiological mechanism? Was a mechanism explained somewhere?

Answer: We just found that among several common chronic diseases, hypertension is the most closely related to hearing loss, so we suggest that patients with hypertension should pay special attention to their hearing. The pathophysiological mechanism of hypertension has not been further explored. Related content has been modified in the manuscript.

17. Comment: Page 17. Lines 52-55. "Evidently, our country attaches lesser importance to hearing loss than other developed countries." This is not evident to me. Can you explain? Why specifically is this the case?

Answer: As a developing country, society is more concerned about various fatal diseases, economy and ecology, so that our country attaches lesser importance to hearing loss than other developed countries. This phenomenon has been significantly improved with the progress of Chinese society, but we still feel that it is not enough.

Part C (Reviewer 2)

1. Comment: I recommend presenting the sex-specific prevalence estimates (abstract and results section). The authors should specify the definition of hearing loss in the outcome measures section as outlined on page 6 and in the 1st paragraph of the discussion.

Answer: Thanks for the suggestion. Sex-specific prevalence and definition of hearing loss have been added to the manuscript.

2. Comment: The authors should specify the number (and proportion) of adults who were excluded from the study due to having an ear disease or an abnormal ear structure.

Answer: The missing data have been added.

3. Comment: The authors say that hearing of the right ear was better than that of the left. It would be better if the authors wrote that hearing loss was more prevalent in the left ear (as reported in the abstract). The estimates in Table 1 should be accompanied by confidence intervals. A limitation of the manuscript is that the authors did not consider stratifying their analyses by gender, age or both. The authors should consider this in addition to the results they already show. Could the correlates of hearing loss be different for men and women? Could the correlates of hearing loss be different for the younger and older adults (the age-range for the study is wide at 18-98 years)? Would an analysis among younger adults help identify some factors for “early intervention”? Although the sample sizes will be smaller than for the overall analysis this information could be of public health relevance. At the very least, the authors did not justify their decision to simply adjust for age and gender.

Answer: Thanks for the reviewer’s kind advice. We have replaced the original sentence in the results section with ‘hearing loss was more prevalent in the left ear’. Chi-square test analysis method was conducted in table 1 to compare the prevalence distribution among different regions and genders. Table 1 has been redrawn and stratified by gender and age for further exploration. Age and gender were confounding factors for unhuman intervention, so the two were adjusted when studying the relationship between hearing loss and other factors (Table 3). Thanks again for the suggestion. Due to your suggestions, we have found some shortcomings in current work. We will improve research level and get more achievements in accordance with the suggestions in future work.

4. Comment: It might also be informative for the authors to report on the levels of exposure to occupational and recreational noise: and how these vary by age, sex, and education level.

Answer: Thanks for the suggestion. We have added Table S2 to provide noise exposure information by age, sex, education and income level.

5. Comment: The authors state that education and personal income were protective factors: but income was not significantly associated with high-frequency hearing loss in the logistic regression analysis (P=0.129). The authors should mention in their discussion of limitations that the questions on occupational and noise exposure seem to refer to exposure at the time of data collection: and so they

did not have any data on exposure over a longer period (say the last 5 years). The authors should also remind readers that their analyses excluded participants with an ear disease: and therefore underestimate the burden of hearing loss.

Answer: Thanks for the reviewer's kind advice. We have replaced 'education and personal income were protective factors' with 'education (for high-frequency hearing loss) and personal income (for speech-frequency hearing loss) were protective factors'. Two limitations mentioned by the reviewer have been added to the discussion.

6. Comment: Finally, the authors state that the difference between their prevalence estimates and those of Bu and Gong et al (2018) "probably resulted from the geographical distribution of the population surveyed". Clearly, there is another explanation for the lower levels of hearing loss reported in this study: the study by Gong et al was conducted among older adults (60+ years). Perhaps the authors could compute the prevalence of hearing loss amongst those aged 60+ to compare with the study by Gong et al. Furthermore, the estimates for this study are higher (not lower) than those reported by Bu et al (2011: 11.7%) which surveyed people of all ages. I encourage the authors to be very exact in the comparisons they make with other studies.

Answer: Thanks for the reviewer's note. Two possible explanations have been added to the manuscript. In addition, we also computed the prevalence of hearing loss among those aged 60+ in the discussion section.

We acknowledge the reviewers and editor for their comments and suggestions, which are valuable in improving the quality of our manuscript.

VERSION 2 – REVIEW

REVIEWER	Justin S. Golub Columbia University USA
REVIEW RETURNED	31-Jan-2019

GENERAL COMMENTS	Thank you for the revision and the responses to my comments. The responses are adequate. From my experience, when a reviewer makes a comment, a response should almost always appear inside the actual paper and not just in the response to reviewer comments document. I did not see changes in the manuscript for the following two comments. 4. You clarified to me about the significance of Zhejiang, i.e., that it is a typical/representative province. However, if I didn't know the significance of this, then other non-Chinese or non-Asian readers may also not know. 6. Explaining what loud noise in the workplace was defined as. Additional comments I accept your decision to studying hearing loss as a binary variable and age as a categorical variable. Personally, I would have kept both continuous because it doesn't discard data, but this may be a difference of preference.

REVIEWER	Shaun Scholes University College London, United Kingdom
REVIEW RETURNED	22-Jan-2019

GENERAL COMMENTS	The authors have improved the manuscript in part by taking on my board my comments to the first version: in particular the presentation of hearing loss prevalence by age and gender. Since reviewing this paper I was contacted by researchers in the US to provide a revised set of hearing loss estimates by age and sex: so providing age- and sex-specific estimates helps the hearing loss research community. I have just a couple of minor points which the authors might like to address prior to any publication: 1. The abstract would be improved by mentioning the study date and that loss refers to loss in the better ear. 2. The first sentence of the strengths and limitations section requires rewriting: perhaps the authors meant to say: to our knowledge, this is the FIRST study to... 3. The tables would be improved by having a footnote specifying what the p-values indicate and how they were calculated (e.g. a test for gender or ear differences) and whether they were adjusted for multiple comparisons.

VERSION 2 – AUTHOR RESPONSE

Part A (Reviewer 2)

1. Comment: The abstract would be improved by mentioning the study date and that loss refers to loss in the better ear.

Answer: Thanks for the reviewer's kind advice. The content mentioned has been added.

2. Comment: The first sentence of the strengths and limitations section requires rewriting: perhaps the authors meant to say: to our knowledge, this is the FIRST study to...

Answer: Thanks for the note. This sentence has been rewritten.

3. Comment: The tables would be improved by having a footnote specifying what the p-values indicate and how they were calculated (e.g. a test for gender or ear differences) and whether they were adjusted for multiple comparisons.

Answer: Appropriated footnotes have been added to the tables.

Part B (Reviewer 1)

1. Comment: From my experience, when a reviewer makes a comment, a response should almost always appear inside the actual paper and not just in the response to reviewer comments document. I did not see changes in the manuscript for the following two comments.

a) You clarified to me about the significance of Zhejiang, i.e., that it is a typical/representative province. However, if I didn't know the significance of this, then other non-Chinese or non-Asian readers may also not know.

b) Explaining what loud noise in the workplace was defined as.

Answer: Thank you very much for the reminder. Related explanations have been added.

We acknowledge the reviewers and editor for their comments and suggestions, which are valuable in improving the quality of our manuscript.