

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Association between Low Bone Mineral Density and Hearing Impairment in Postmenopausal Women: the Korean National Health and Nutrition Examination Survey
<b>AUTHORS</b>	Lee, Seong-Su; Han, Kyungdo; Joo, Young-Hoon

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Zhi-feng Sheng M.D. Ph.D. Associate professor of Medicine Institute of Metabolism and Endocrinology, the Second Xiang-Ya Hospital, Central South University, National Clinical Research Center for Metabolic Disease. No. 139, Renmin Road, Changsha Hunan, 410011, China
<b>REVIEW RETURNED</b>	27-Aug-2017

<b>GENERAL COMMENTS</b>	<p>This is a study focusing on the association between bone mineral density (BMD) and hearing impairment in a nationally representative sample of Korean female adults. The study is designed very well and sample size is good enough. However, there were several questions should be further addressed.</p> <ol style="list-style-type: none"><li>1. According to the WHO recommendations, hearing loss is divided into 5 grades: 26~40db is mild, 41~55db is moderate, 56~70db is moderate and severe, 71~90db is severe, more than 90dB is extremely severe. The author should further clarify how is reasonable to define hearing impairment as pure-tone averages (PTA) of frequencies at 0.5, 1.0, 2.0, and 3.0 kHz at a threshold of <math>\geq 40</math> decibel hearing level (dBHL) in the ear with better hearing. It possible, all the subjects should be regrouped before data is used for further analysis.</li><li>2. The same condition is as the definition of “drinkers”. WHO recommends that alcohol consumption should be classified into three categories: low risk (female 1-20g/d, male 1-40g/d), moderate risk (female 21-40g/d, male 41-60g/d) and high risk (female &gt;40g/d, male &gt;60g/d); heavy drinking is defined as the past 30 days at least once a day to drink more than 5 cups of standard. This factor should also be re-stratified clearly.</li><li>3. Table 1, the prevalence of hearing impairment in each group should be presented and compared.</li><li>4. Figure 1 A-C should be marked clearly and presented into one picture.</li></ol>
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	5. Page 6 line 13. "The final sample included 8,773 8,773 adults aged 19 years and over men, premenopausal, and postmenopausal women were 3,885, 2,622, and 2,266, respectively", should be restated.
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<b>REVIEWER</b>	Stephanie C. Rigters Erasmus MC Rotterdam, the Netherlands
<b>REVIEW RETURNED</b>	14-Sep-2017

<b>GENERAL COMMENTS</b>	<p>Introduction</p> <ol style="list-style-type: none"> <li>1. Suggestion: describe prevalence of osteoporosis rather than exact number of diseased.</li> <li>2. Minor grammatical mistakes; e.g. osteoporosis sometimes is used as singular / plural.</li> <li>3. You describe a contradiction. Is BMD associated with hearing impairment in Caucasian women or is it not? It was confusing to me.</li> <li>4. Although you describe why osteoporosis and why hearing impairment are relevant for research, you don't describe why we need to know about the relation between the two. In the future; will we conduct a hearing test when we want to know about osteoporosis? Or vice versa?</li> </ol> <p>Methods</p> <p>Good description of the study population.</p> <ol style="list-style-type: none"> <li>1. Two times 8.773 in main text</li> <li>2. Again spelling / grammar: "Testing was conducted", rather say: "The test was ..."</li> </ol> <p>Discussion</p> <ol style="list-style-type: none"> <li>1. Please add to the limitations that you only measured air thresholds. Theoretically you do not know whether a person has conductive or sensoneurinal hearing loss.</li> </ol>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Zhi-feng Sheng

Institution and Country: Institute of Metabolism and Endocrinology, the Second Xiang-Ya Hospital, Central South University, China

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

This is a study focusing on the association between bone mineral density (BMD) and hearing impairment in a nationally representative sample of Korean female adults. The study is designed very well and sample size is good enough. However, there were several questions should be further addressed.

1. According to the WHO recommendations, hearing loss is divided into 5 grades: 26~40db is mild, 41~55db is moderate, 56~70db is moderate and severe, 71~90db is severe, more than 90dB is extremely severe. The author should further clarify how is reasonable to define hearing impairment as pure-tone averages (PTA) of frequencies at 0.5, 1.0, 2.0, and 3.0 kHz at a threshold of  $\geq 40$  decibel hearing level (dBHL) in the ear with better hearing. If possible, all the subjects should be regrouped before data is used for further analysis.

© Response : I really appreciate your comments. In this study the PTA of both ears at each frequency was obtained for frequency analysis. As you mentioned before, the degree of hearing loss was categorized as mild (26~40 dB), moderate (41~55 dB), moderately severe (56~70 dB) and severe (71~90 dB) based on the standard of the International Organization for Standardization (ISO). Disabling hearing loss refers to hearing loss greater than 40 dB in the better hearing ear in adults and greater than 30 dB in the better hearing ear in children from the definition of WHO. So we defined hearing loss at a threshold of a  $\geq 40$  decibel hearing level in the ear with better hearing.

2. The same condition is as the definition of "drinkers". WHO recommends that alcohol consumption should be classified into three categories: low risk (female 1-20g/d, male 1-40g/d), moderate risk (female 21-40g/d, male 41-60g/d) and high risk (female >40g/d, male >60g/d); heavy drinking is defined as the past 30 days at least once a day to drink more than 5 cups of standard. This factor should also be re-stratified clearly.

© Response: Our research was based on the KNHANES, a big data, performed by the government. The KNHANES is a nationwide survey conducted by the Division of Chronic Disease Surveillance under the Korea Centers for Disease Control and Prevention since 1998. The questionnaire and measurements could not be chosen by any other researchers because the researchers could only access and evaluate the results of big data without intervening in the national survey. However, the questionnaires regarding alcohol consumption in this survey have been used as nationwide survey tools for about ten years by the government by and these measurements have been validated by a lot of previous publications. (BMJ Open. 2015 Oct 26;5(10):e008224., PLoS One. 2016 Feb 9;11(2):e0148813., Obes Facts. 2015;8(4):252-60., Clin Hypertens. 2015 Jun 11;21:8., Korean J Fam Med. 2016 Jan;37(1):51-6.)

3. Table 1, the prevalence of hearing impairment in each group should be presented and compared.

© Response : We have added the prevalence of hearing impairment in men, premenopausal women, and postmenopausal women.

4. Figure 1 A-C should be marked clearly and presented into one picture.

© Response: According to your comment, we have changed the figure 1A-C.

5. Page 6 line 13. "The final sample included 8,773 8,773 adults aged 19 years and over men, premenopausal, and postmenopausal women were 3,885, 2,622, and 2,266, respectively", should be restated.

© Response: I have a mistake. I have changed this sentence.

"The final sample included 8,773 adults aged 19 years and men, premenopausal, and postmenopausal women were 3,885, 2,622, and 2,266, respectively."

Reviewer: 2

Reviewer Name: Stephanie C. Rigters

Institution and Country: Erasmus MC Rotterdam, the Netherlands

Please state any competing interests or state 'None declared': None declared.

Please leave your comments for the authors below

Introduction

1. Suggestion: describe prevalence of osteoporosis rather than exact number of diseased.

© Response: According to reviewer's comment, I have changed this sentence.

"Osteoporosis prevalence at the total hip or hip/spine ranged from 9 to 38 % for women and 1 to 8 % for men in nine industrialized countries in North America, Europe, Japan, and Australia."

2. Minor grammatical mistakes; e.g. osteoporosis sometimes is used as singular / plural.

© Response: I have a mistake. I have changed those sentences.

3. You describe a contradiction. Is BMD associated with hearing impairment in Caucasian women or is it not? It was confusing to me.

© Response: According to reviewer's comment, I have changed this sentence.

"Clark et al reported that 369 white women aged 60 to 85 years with femoral neck bone mass values below the mean value of 0.696 g/cm<sup>2</sup> had a 1.9 greater odds of having a hearing loss. 5 In contrast, Helzner et al. showed no association between hearing and any of the bone measurements in white and black women. 13"

4. Although you describe why osteoporosis and why hearing impairment are relevant for research, you don't describe why we need to know about the relation between the two. In the future; will we conduct a hearing test when we want to know about osteoporosis? Or vice versa?

© Response: According to reviewer's comment, I have added this sentence.

"Understanding and identifying the associations between BMD and hearing impairment in a large-scale study would greatly contribute to patient care and relief of social burden for these conditions."

#### Methods

Good description of the study population.

1. Two times 8.773 in main text

© Response: I have a mistake. I have changed this sentence.

"The final sample included 8,773 adults aged 19 years and men, premenopausal, and postmenopausal women were 3,885, 2,622, and 2,266, respectively."

2. Again spelling / grammar: "Testing was conducted", rather say: "The test was ..."

© Response: I have changed this sentence.

#### Discussion

1. Please add to the limitations that you only measured air thresholds. Theoretically you do not know whether a person has conductive or sensorineural hearing loss.

© Response: According to reviewer's comment, I have added this sentence.

"The final limitation of the present study was the absence of bone-conduction pure tone testing. This audiometric assessment could not entirely exclude conductive hearing losses."

I hope the revised manuscript will better meet the requirements of the 'BMJ open' for publication. I thank you again for the constructive review by the reviewers.

### VERSION 2 – REVIEW

<b>REVIEWER</b>	zhifeng sheng Institute of Metabolism and Endocrinology, the Second Xiang-Ya Hospital, Central South University, National Clinical Research Center for Metabolic Disease. No. 139, Renmin Road, Changsha Hunan, 410011, China
<b>REVIEW RETURNED</b>	06-Nov-2017
<b>GENERAL COMMENTS</b>	No any other comments.