PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Self-Reported Hearing Loss in Russians. The population-based Ural Eye and Medical Study
AUTHORS	Bikbov, Mukharram; Fayzrakhmanov, Rinat; Kazakbaeva, Gyulli; Zainullin, Rinat; Salavatova, Venera; Gilmanshin, Timur; Arslangareeva, INga; Nikitin, Nikolai; Panda-Jonas, Songhomitra; Mukhamadieva, Svetlana; Yakupova, Dilya; Khikmatullin, Renat; Aminev, Said; Nuriev, Ildar; Zaynetdinov, Artur; Uzianbaeva, Yulia; Jonas, Jost

VERSION 1 – REVIEW

REVIEWER	Prof.Dr. Abdulbari Bener Prof. Abdulbari Bener Advisor to WHO Professor of Public Health Dept. of Biostatistics & Medical Informatics Cerrahpaşa Faculty of Medicine Istanbul University and Istanbul Medipol University, International School of Medicine 34098 Cerrahpasa-Istanbul, TURKEY Mobile:+90-535 663 9090 Tel: +90-212-414 3041 Fax:+ 90-212-632 0033 e-mail: abdulbari.bener@istanbul.edu.tr email:abener99@yahoo.com
REVIEW RETURNED	28-Jul-2018

GENERAL COMMENTS	Overall, the methods section is grossly deficient from epidemiological and Medical screening point view. Especially, very important issue can be considered such as Limitation of this study were that hearing loss was assessed in a series of 11 standardized 83 questions without performing an audiometric examination. This is not scientifically acceptable at all. The current study addresses an important issues concerning public health and can be adopted in other countries. Although, the study does not contribute novel knowledge or new information, but, it would help local policy makers, therefore, the manuscript can be considered after major revision for the publication" in the local Journal in Russia.

REVIEWER	Jonathan Gelfond UT Health San Antonio San Antonio, TX, USA
REVIEW RETURNED	01-Aug-2018

GENERAL COMMENTS	This is a well-written article on a survey of the prevalence and risk factors for self-reported hearing loss in Russian adults. The study methods and statistical analyses are appropriate. There was a concern about the detail given regarding how the study was conducted. It is not clear how the participants were contacted. For example, was there a phone call, letter, or a sweep of neighborhoods? Relatedly, how was the number of eligible people determined? There are some minor concerns below.

	1. In the abstract, age units should be listed alongside the odds ratio. Likewise, it is hard to interpret the effect size of depression score. 2. Line 102: “population in a Russian population” is awkward. 3. Line 143: In describing the statistical analysis, it may have better flow to list the statistical software last instead of first. 4. Lines 236 to 242: Comparisons to other articles should state which country the statistics refer to. 5. Line 204: “both gender[s]” the ‘s’ could be added here.

REVIEWER	Silvia Ferrite Associate Professor, Federal University of Bahia, Brazil
REVIEW RETURNED	13-Aug-2018

GENERAL COMMENTS	Comments 1 and 2 are major concerns. 1) Noise exposure at work is the main modifiable risk factor for hearing loss (HL), however it was not included in the (multivariate) analysis of HL associated factors. Introducing this variable would be naturally expected in studies with this objective. Where “noise” is mentioned in the manuscript it is only to help explain another association found. Even though noise is the major determinant of hearing loss along with aging, the lack of data on noise exposure was not mentioned among the limitations of the study. Therefore, authors should try to overcome its absence. If noise data are not available, there would be other options. For example, conducting only univariate analysis (avoiding multivariate analysis, where the lack of noise would bias the results) or to restrict the variables to the descriptive ones (sociodemographic). 2) Authors state that “Hearing loss was assessed by a series of 11 standardized questions (Table 1).” From the answers to these questions, two outcome variables were defined: hearing loss score - quantitative, and hearing loss - dichotomous. Was this set of questions previously published? (there is no citation) What are the validity measures regarding these outcome variables against pure tone audiometry (gold-standard for hearing loss)? I understood there was no a subsample validity study (what would be a good methodological choice), but sensitivity/specificity should be shown from other validity studies. 3) The modeling procedure is not clearly described in the Methods section. Also, there are data in Tables that are not in line with this statement about which variables were included in multivariate analysis “… and as independent variables all those parameters which were significantly associated with the hearing loss score in the univariate analysis”. For example, hypertension shows p=0.03 in univariate analysis (Supplementary Table) and was not included in the multivariate analysis (Table 3). In contrast, history of skin disease which shows p=0.07 in univariate analysis was included in multivariate analysis. 4) Rinne and Weber tests are not presented as a procedure in Methods section, although we find their results described (Results section). Also, it is not clear their potential contribution to the objectives of this study. 5) The manuscript - abstract, strengths and limitations, main text - can be improved, by minimising redundancy, repetitions and excess numbers, in order to more clarity in reading. Please, also check References (for example, 22 and 40 are the same).

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1 (Reviewer Name: Prof.Dr. Abdulbari Bener)
5. Reviewer #1: Overall, the methods section is grossly deficient from epidemiological and Medical screening point view. Especially, very important issue can be considered such as Limitation of this study were that hearing loss was assessed in a series of 11 standardized questions without performing an audiometric examination. This is not scientifically acceptable at all. The current study addresses an important issues concerning public health and can be adopted in other countries. Although, the study does not contribute novel knowledge or new information, but, it would help local policy makers, therefore, the manuscript can be considered after major revision for the publication" in the local Journal in Russia.
Our response: As also pointed out in the reply to comment #12 by reviewer #3, the methodology has been described and its limitations have been discussed in greater detail in the revised manuscript:
- "Hearing loss was assessed by a series of 11 standardized questions ten of which were derived from the "Hearing Handicap Inventory for the Elderly Screening Version (HHIE-S)" (Table 1).17-19 The questions could be answered by "no" (0 points), "sometimes" (2 points) and "yes (4 points). The total hearing loss score was the sum of all points and could range between 0 points and 44 points. The amount of hearing loss was assessed by the hearing loss score. The HHIE-S had been applied in previous investigations.17-19 The diagnostic performance of the HHIE-S against five definitions of hearing loss as assessed by pure-tone audiometry had assessed in a previous investigation on 178 elderly subjects.20 The HHIE-S had sensitivities ranging from 53 to 72% and specificities ranging from 70 to 84% with the different definitions. The receiver-operating characteristics and the likelihood ratios of the HHIE-S were similar regardless of the hearing loss definitions. Another investigation had examined the reliability, validity, and associations of the HHIE-S with quality of life measures such as the subjective well-being, depressive symptoms, subjective loneliness, and physical functioning.21 It revealed that the reliability of the HHIE-S was relatively high with a Cronbach's alpha coefficient of 0.91, a Spearman-Brown coefficient of 0.90 and an intra-class correlation coefficient of 0.85. The prevalence of self-reported hearing loss as a binary variable was assessed by the single question "Do you experience a hearing loss?". Hearing loss was additionally examined performing Rinne´s test and Weber´s test. For Rinne´s test, a vibrating tuning fork (c2 512 Hz; KaWe Co., Germany; Kirchner & Wilhelm GmbH+Co. KG, Asperg, Germany) was placed initially on the mastoid process behind each ear until the sound was no longer heard. The fork was then immediately placed just outside of the ear and the participant was asked to report when the sound caused by the vibration was no longer heard. Rinne´s test was normal or positive when the sound heard outside of the ear (air conduction) was louder than the initial sound heard when the tuning fork end was placed against the skin on top of the mastoid process behind the ear (bone conduction). For Weber´s test the same vibrating tuning fork was placed in the middle of the crown and the individual was asked to report in which ear the sound was heard louder. Weber´s test was normal if the participant reported the sound heard equally in both sides." (Page 5, line 140)
- In the revised manuscript it has also been discussed that "Limitations of our study should be discussed. First, the main outcome parameter was self-reported hearing loss assessed in a series of 11 standardized questions. In previous studies, audiometry was applied to quantify the hearing impairment. Although the latter method is a more quantitative one, the degree of self-reported hearing impairment as compared to audiometrically defined hearing loss may be more important to reflect the quality of the daily life of the individual. Interestingly, a study by Hannula et al. showed that self-reported hearing difficulties were more frequent than hearing impairment defined by audiometric measurement.26 Hannula also reported that self-reported hearing difficulties predicted hearing impairment at high frequencies (4-8 kHz) rather than at frequencies of 0.5-4 kHz, which were commonly used to define the degree of hearing impairment in medical and legal issues. The test-retest reliability of the Hearing Handicap Inventory for Adults was evaluated in a study showing a correlation coefficient of r2=0.94.47 In another investigation, the HHIE-S showed a significant reduction in perceived emotional and social/situational effects of hearing impairment following the use of hearing aids.48" (Page 9, line 307)

Reviewer: 2 (Reviewer Name: Jonathan Gelfond)
6. Reviewer #2: This is a well-written article on a survey of the prevalence and risk factors for self-reported hearing loss in Russian adults. The study methods and statistical analyses are appropriate. There was a concern about the detail given regarding how the study was conducted. It is not clear how the participants were contacted. For example, was there a phone call, letter, or a sweep of neighborhoods? Relatedly, how was the number of eligible people determined?
Our response: It has been described in greater detail in the revised manuscript that "All people residing in the study regions were officially registered, and home visits were performed according to the people registration to all homes. The eligible subjects fulfilling the inclusion criterion of an age of 40+ years were visited up to three times if they did not participate in the study after the first visit. The only inclusion criteria for the study were living in the study region and having an age of 40+ years. There were no exclusion criteria." (Page 4, line 110)
- It has also been added to the revised Methods section: "Assuming a participation rate of approximately 80% and aiming at a study population size of about 5500 to 6000 participants, the number of eligible individuals was calculated to be approximately 7000 to 7500 individuals. The number of 5500 to 6000 study participants was based on the experience gained in previous population-based investigations the study populations of which were assumed to have a similar prevalence of major diseases as the present study population." (Page 4, line 115)

7. Reviewer #2: There are some minor concerns below. 1. In the abstract, age units should be listed alongside the odds ratio. Likewise, it is hard to interpret the effect size of depression score.
Our response: It has been added to the revised Abstract: "In multivariable analysis, higher prevalence of hearing loss was associated with older age (P<0.001; odds ratio (OR) (per year of age): 1.06 [1.06, 1.07]), …" (Page 2, line 56)

8. Reviewer #2: 2. Line 102: "population in a Russian population" is awkward.
Our response: The authors would like to apologize for the fault which has been corrected: "We therefore conducted this study to assess the prevalence of hearing loss in a Russian population and to explore associations of hearing loss with other parameters such as gender, region of habitation and level of education." (Page 4, line 99)

9. Reviewer #2: 3. Line 143: In describing the statistical analysis, it may have better flow to list the statistical software last instead of first.
Our response: The description of the statistical analysis has been re-worded as recommended: "The statistical analysis was conducted in several steps. In a first step, we determined the frequency of hearing loss, presenting the results as the mean value and the 95% confidence intervals (CI). In a second step, we searched for associations in univariate analysis between the hearing loss score and other parameters. In a third step, we conducted a multivariable regression analysis with the hearing loss score as dependent variable and as independent variables all those parameters which were associated (P≤0.10) with the hearing loss score in the univariate analysis. All variables in the list of independent parameters were tested for multicollinearity. Associations of the prevalence of hearing loss as binary variable were examined in a binary regression analysis. Odds ratios (OR) and their 95% confidence intervals (CI) were calculated. All P-values were two-sided and considered statistically significant when the values were less than 0.05. We used a commercially available statistical software program (Statistical Package for Social Science, SPSS, version 25.0; IBM-SPSS Inc., Chicago, USA) for the statistical analysis." (Page 6, line 166)

10. Reviewer #2: 4. Lines 236 to 242: Comparisons to other articles should state which country the statistics refer to.
Our response: The country information has been added to the Discussion: "The prevalence of hearing

loss as found in our study population also well with figures found by Ikeda and colleagues for the United States, and with other data reported for the United States by the Health, Aging and Body Composition Study after adjusting for age differences in the study populations.24,25 The prevalence of hearing loss in our study population was lower than the figures found by Hannula and associates for Northern Finland (prevalence of self-reported hearing problems of 37.1% and of 43.3% for difficulties in following a conversation in noise),26 and it was lower than the prevalence of unilateral and bilateral speech-frequency hearing impairment in the National Health and Nutrition Examination Survey for the United States.27-29“ (Page 8, line 260)

11. Reviewer #2: 5. Line 204: “both gender[s]” the ‘s’ could be added here.
Our response: The authors apologize for the fault which has been corrected: “For the age group of less than 60 years (P=0.57) and for the age group of 80+ years (P=0.87), both genders did not differ significantly in the prevalence of hearing loss (Fig. 2).” (Page 7, line 228)

Reviewer: 3 (Reviewer Name: Silvia Ferrite)
12. Reviewer #3: 1) Noise exposure at work is the main modifiable risk factor for hearing loss (HL), however it was not included in the (multivariate) analysis of HL associated factors. Introducing this variable would be naturally expected in studies with this objective. Where “noise” is mentioned in the manuscript it is only to help explain another association found. Even though noise is the major determinant of hearing loss along with aging, the lack of data on noise exposure was not mentioned among the limitations of the study. Therefore, authors should try to overcome its absence. If noise data are not available, there would be other options. For example, conducting only univariate analysis (avoiding multivariate analysis, where the lack of noise would bias the results) or to restrict the variables to the descriptive ones (sociodemographic).
Our response: In full agreement with the reviewer, it has been added to the revised manuscript: “Limitations of our study should be discussed. First, …. . Third, although noise is a major determinant of hearing loss along with aging, the exposure to noise at the working place was not specifically assessed in the study. This lack of data on noise exposure was therefore one of the limitations of the study. The amount of physical activity at the working place however was evaluated and in the multivariable model, a higher hearing loss score was associated with a higher amount of physically vigorous activity during work (P=0.008) (Table 3). Although the amount of physical activity at the working place is not a direct measure for the noise exposure, both parameters are correlated with each other so that a higher amount of physically vigorous activity during work may be a surrogate for an increased noise exposure.” (Page 9, line 327); and:
- “The association between vigorous physical activity at work and higher prevalence of hearing loss in our study might have been due to a potentially confounding correlation between heavy work and higher noise level at work.” (Page 8, line 282)

13. Reviewer #3: 2) Authors state that “Hearing loss was assessed by a series of 11 standardized questions (Table 1).” From the answers to these questions, two outcome variables were defined: hearing loss score - quantitative, and hearing loss - dichotomous. Was this set of questions previously published? (there is no citation) What are the validity measures regarding these outcome variables against pure tone audiometry (gold-standard for hearing loss)? I understood there was no a subsample validity study (what would be a good methodological choice), but sensitivity/specificity should be shown from other validity studies.
Our response:
- It has been stated in the revised manuscript that “Hearing loss was assessed by a series of 11 standardized questions ten of which were derived from the “Hearing Handicap Inventory for the Elderly Screening Version (HHIE-S)” (Table 1).17-19 The questions could be answered by “no” (0 points), “sometimes” (2 points) and “yes (4 points). The total hearing loss score was the sum of all points and could range between 0 points and 44 points. The amount of hearing loss was assessed by

the hearing loss score. The HHIE-S had been applied in previous investigations.17-19 The diagnostic performance of the HHIE-S against five definitions of hearing loss as assessed by pure-tone audiometry had assessed in a previous investigation on 178 elderly subjects.20 The HHIE-S had sensitivities ranging from 53 to 72% and specificities ranging from 70 to 84% with the different definitions. The receiver-operating characteristics and the likelihood ratios of the HHIE-S were similar regardless of the hearing loss definitions. Another investigation had examined the reliability, validity, and associations of the HHIE-S with quality of life measures such as the subjective well-being, depressive symptoms, subjective loneliness, and physical functioning.21 It revealed that the reliability of the HHIE-S was relatively high with a Cronbach's alpha coefficient of 0.91, a Spearman-Brown coefficient of 0.90 and an intra-class correlation coefficient of 0.85." (Page 5, line 140)
- In the revised manuscript it has also been discussed that "Limitations of our study should be discussed. First, the main outcome parameter was self-reported hearing loss assessed in a series of 11 standardized questions. In previous studies, audiometry was applied to quantify the hearing impairment. Although the latter method is a more quantitative one, the degree of self-reported hearing impairment as compared to audiometrically defined hearing loss may be more important to reflect the quality of the daily life of the individual. Interestingly, a study by Hannula et al. showed that self-reported hearing difficulties were more frequent than hearing impairment defined by audiometric measurement.26 Hannula also reported that self-reported hearing difficulties predicted hearing impairment at high frequencies (4-8 kHz) rather than at frequencies of 0.5-4 kHz, which were commonly used to define the degree of hearing impairment in medical and legal issues. The test-retest reliability of the Hearing Handicap Inventory for Adults was evaluated in a study showing a correlation coefficient of r2=0.94.47 In another investigation, the HHIE-S showed a significant reduction in perceived emotional and social/situational effects of hearing impairment following the use of hearing aids.48" (Page 9, line 307)

14. Reviewer #3: 3) The modeling procedure is not clearly described in the Methods section. Also, there are data in Tables that are not in line with this statement about which variables were included in multivariate analysis "… and as independent variables all those parameters which were significantly associated with the hearing loss score in the univariate analysis". For example, hypertension shows p=0.03 in univariate analysis (Supplementary Table) and was not included in the multivariate analysis (Table 3). In contrast, history of skin disease which shows p=0.07 in univariate analysis was included in multivariate analysis.
Our response: In the revised manuscript, the statistical analysis has been described in greater detail, namely that "In a third step, we conducted a multivariable regression analysis with the hearing loss score as dependent variable and as independent variables all those parameters which were associated (P≤0.10) with the hearing loss score in the univariate analysis." (Page 6, line 169) It explains why the parameter of "history skin disease" with a P-value of 0.07 (as well as the parameter of "arterial hypertension") was included into the primary list of independent parameters in the multivariable analysis. In the following analysis, the parameter of "arterial hypertension" lost the statistical significance in the final multivariable model, while the association between the hearing loss score and the parameter of "history skin disease" became statistically significant (P=0.01) (Table 3). It has been stated in the revised Results section: "In univariate analysis, a higher hearing loss score was correlated with parameters such as older age (P<0.001) (Table 2) (Fig. 1), male gender (P<0.001) (Fig. 1) and other variables (Supplementary Table 1). The multivariable regression analysis included the hearing loss score as dependent variable and as independent variables all those parameters which were associated (P≤0.10) with the hearing loss score in the univariate analysis. Due to collinearity, we first dropped the parameters of body weight (variance inflation factor (VIF): 6.8) and waist circumference (VIF: 4.0). We then dropped step by step those parameters, such as the prevalence of arterial hypertension, which were no longer statistically significantly associated with hearing loss in the multivariate analysis. In the resulting final model, a higher hearing loss score was associated (regression coefficient r: 0.33) with older age (P<0.001), male gender (P<0.001), a higher depression score (P<0.001), a higher prevalence of headache (P<0.001) and a higher prevalence of

history of cancer (P=0.008), cardiovascular disease including stroke (P=0.003), osteoarthritis (P=0.006) and skin disease (P=0.01), a lower number of days with intake of fruits (P=0.02), and a higher amount of physically vigorous activity during work (P=0.008) and of physically moderate activity during leisure time (P<0.001) (Table 3)." (Page 7, line 208)

15. Reviewer #3: 4) Rinne and Weber tests are not presented as a procedure in Methods section, although we find their results described (Results section). Also, it is not clear their potential contribution to the objectives of this study.
Our response: It has been added to the revised Methods section: "Hearing loss was additionally examined performing Rinne´s test and Weber´s test. For Rinne´s test, a vibrating tuning fork (c2 512 Hz; KaWe Co., Germany; Kirchner & Wilhelm GmbH+Co. KG, Asperg, Germany) was placed initially on the mastoid process behind each ear until the sound was no longer heard. The fork was then immediately placed just outside of the ear and the participant was asked to report when the sound caused by the vibration was no longer heard. Rinne´s test was normal or positive when the sound heard outside of the ear (air conduction) was louder than the initial sound heard when the tuning fork end was placed against the skin on top of the mastoid process behind the ear (bone conduction). For Weber´s test the same vibrating tuning fork was placed in the middle of the crown and the individual was asked to report in which ear the sound was heard louder. Weber´s test was normal if the participant reported the sound heard equally in both sides." (Page 5, line 155)

16. Reviewer #3: 5) The manuscript - abstract, strengths and limitations, main text - can be improved, by minimising redundancy, repetitions and excess numbers, in order to more clarity in reading. Please, also check References (for example, 22 and 40 are the same).
Our response:
- The authors apologize for listing reference #22 twice and have corrected the fault.
- The whole manuscript has been re-edited with the help of an English speaking colleague.

VERSION 2 – REVIEW

REVIEWER	Prof. Dr. Abdulbari Bener Prof. Abdulbari Bener Advisor to WHO Professor of Public Health Dept. of Biostatistics & Medical Informatics Cerrahpaşa Faculty of Medicine Istanbul University and Istanbul Medipol University, International School of Medicine 34098 Cerrahpasa-Istanbul, TURKEY
REVIEW RETURNED	03-Nov-2018

GENERAL COMMENTS	The authors have satisfactorily addressed most of my queries with clarity

REVIEWER	Jonathan Gelfond UT Health San Antonio, USA
REVIEW RETURNED	04-Nov-2018

GENERAL COMMENTS	The authors have responded fully in an acceptable manner to this reviewer's earlier critiques.