Association of Hearing Loss With Total and Cause-specific Mortality in US Adults

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Abstract

Objectives

We expected to explore the associations of hearing loss and hearing thresholds at different frequencies with total and cause-specific mortality.

Methods

11,732 individuals derived from the National Health and Nutrition Examination Survey (NHANES) 1999-2012 were included in this study. Data of death was extracted from the NHANES Public-Use Linked Mortality File through December 31, 2015. Cox proportional hazards models were used to explore the associations between hearing loss, hearing thresholds at different frequencies and total or cause-specific mortality.

Results

A total of 1,253 deaths occurred with a median follow-up of 12.15 years. A significant positive dose-response relationship between hearing loss in speech frequency and total mortality was observed, and the HRs and 95% CIs were 1.16 (0.91, 1.47), 1.54 (1.19, 2.00) and 1.85 (1.36, 2.50), respectively for mild, moderate and severe speech-frequency hearing loss (SFHL) with a P_{trend} of 0.0003. In addition, moderate (HR: 1.90, 95%CI: 1.20-3.00) and greater (3.50, 1.38-8.86) SFHL significantly elevated risk of heart disease mortality. Moreover, hearing thresholds of >25 dB at 500, 1000, or 2000 Hz were significantly associated with elevated mortality from all causes (1.40, 1.17-1.68; 1.44, 1.20-1.73; and 1.33, 1.10-1.62, respectively) and heart disease (1.89, 1.08-3.34; 1.95, 1.21-3.16; and 1.89, 1.16-3.09, respectively).

Conclusion

Hearing loss is associated with increased risks of total mortality and heart disease mortality, especially for hearing loss at speech frequency. Preventing or inhibiting the pathogenic factors of hearing loss is important for reducing the risk of death.

Introduction

Hearing loss has become an increasingly prevalent disability and has been the fourth leading cause of disability globally (Cunningham & Tucci 2017). As a major concern for global health, hearing loss mainly results from congenital or acquired causes, including genetic mutations, aging, chronic middle ear infections, noise exposure, and ototoxic drugs (WHO 2020, Cunningham & Tucci 2017). The reach of hearing loss extends far beyond sensory impairment (Lancet 2016). As a result of communication disorder, hearing loss may bring series of profound effects on independence, wellbeing, quality of life, and daily function (Lancet 2016), which further result in various adverse health effects such as depression (Scinicariello et al. 2019), dementia (Gallacher et al. 2012), falls (Viljanen et al. 2009), metabolic syndrome (Han et al. 2018), and cardiovascular diseases (Fang et al. 2018). Apart from such effects, previous literature also explored the association between hearing loss and mortality (Engdahl et al. 2019, Genther et al. 2015, Schubert et al. 2017). The Health, Aging, and Body Composition Study revealed that hearing loss was associated with a 20% increased mortality risk among 1,958 adults aged 70-79 years (Genther et al. 2015). Self-reported hearing loss was also reported to be associated with an increased risk of total mortality among 9,522 Japanese community residents aged 40-69 years with 10-year follow-up (Miyawaki et al. 2020). Although the above epidemiologic studies showed a positive association between hearing loss and total mortality, it was not a universal finding (Karpa et al. 2010, Schubert et al. 2017). No significant association between hearing loss and total mortality was observed in the Epidemiology of Hearing Loss Study with 2,418 participants aged 53–97 years (Schubert et al. 2017). In addition, Karpa *et al.* (2010) also obtained similar non-significant results after multivariable adjustment. Thus, more studies are warranted to explicit and verify such association based on the large size and long follow-up cohorts.

To our knowledge, the effect of noise on hearing often begins at high frequency, and the influence of hearing levels at speech frequency is lower than that at high frequency in early noise-induced hearing loss (Anonymous 2003). It was estimated that the prevalence of hearing loss was 31.1% for high-frequency hearing loss (HFHL) and 14.1% for speech-frequency hearing loss (SFHL) in US adults (Hoffman et al. 2017). However, as initial hearing impairment, HFHL is rarely studied, especially for relevant unhealthy effects. In addition, few researches have focused on the relationships between hearing levels at different frequencies and total and

cause-specific mortality. Hence, we conducted this prospective study to investigate the associations of HFHL, SFHL, and hearing levels at different frequencies with total and cause-specific mortality among 11,732 representative US residents in the NHANES 1999-2012.

Methods

Study Population

Participants were originated from the NHANES, which was administered by the National Center for Health Statistics (NCHS) and was described in details elsewhere (CDC 2017). In short, the NHANES is an ongoing health-related program conducted with a complex, multistage, probability sampling design for representative sample of the US residents. The continuous NHANES was started in 1999 and was implemented in 2-year cycles. Questionnaire survey, standardized physical examinations and laboratory tests were carried out to collect data. In this study, we enrolled individuals with audiometric testing ($n=16,854$) at the baseline survey in the continuous NHANES 1999-2012 with 7 cycles. After excluded participants with uncompleted audiometric information ($n=1,774$) and those aged under 18 years or without mortality data ($n=3,348$), 11,732 individuals were finally included for analysis. The NHANES protocol was approved by the NCHS Ethics Review Board and written informed consent was obtained from all participants.

Audiometric Measurement

Audiometry measurement was performed by a trained examiner using an audiometer (AD226; Interacoustics AS, Assens, Denmark) with standard headphones (TDH-39; Telephonics Corporation, Farmingdale, New York) and insert earphones (EarTone 3A; Etymotic Research, Elk Grove Village, Illinois) in a dedicated, sound-isolating room. Hearing threshold testing was conducted on both ears of participants at seven frequencies (500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz) across an intensity range of -10 to 120 dB. The 1000 Hz frequency was tested twice in each ear to keep the reliability of the measurement. More details of the audiometric measurement are available online (NHANES 2001).

Pure-tone average (PTA) of hearing thresholds at 500, 1000, 2000 and 4000 Hz (>25 dB) was calculated to define SFHL and the PTA of hearing thresholds at 3000, 4000 and 6000 Hz (>25 dB) was applied to define HFHL (Scinicariello et al. 2019). Based on the PTA, grades of SFHL and HFHL were categorized according to the World Health Organization classifications (WHO 2021): normal (≤ 25 dB), mild ($25 - \leq 40$ dB), moderate ($40 - \leq 60$ dB) and severe (> 60 dB).

Ascertainment of Mortality Outcomes

The data including cause and date of death was extracted from the NHANES Public-Use Linked Mortality File through December 31, 2015, which was from death certificate records from the National Death Index (Statistics 2019). Causes of death were ascertained according to the International Statistical Classification of Diseases, 10th Revision (ICD-10) (Brämer 1988). The outcomes in our study mainly included mortality from all causes, heart disease (codes I00-I09, I11, I13, and I20-I51), cancer (codes C00-C97), and other causes. Follow-up time was counted as the interval from baseline to the date of death, loss to follow-up or December 31, 2015 for those who were censored.

Assessments of covariates

Covariates were collected from the questionnaire survey and physical examination, which covered information on demographic (age, gender, race/ethnicity, education level, family income-poverty ratio (PIR) and marital status), lifestyles (smoking status, drinking status, physical activity and dietary intake), occupational noise exposure, history of diseases (diabetes, cardiovascular disease, hypertension and cancer) and so on. Multiple imputations were used for all missing values with MI procedure (Yuan 2011). Body mass index (BMI) was calculated as weight (kg) divided square of height (m)², and was classified into three groups: <25 , 25-30 and ≥ 30 kg/m². The race/ethnicity was mainly including Mexican American, non-Hispanic white, non-Hispanic black and others. Education level was categorized as less than high school, high school or equivalent, and college or above. PIR was divided into three categories: 0-1.0, 1.1-3.0, >3.0 (Chen et al. 2019). Marital status was grouped as married, separated (including widowed and divorced), and never married. We divided smoking status into never smokers (smoked less than 100 cigarettes in life), former smokers (smoked more than 100 cigarettes but not smoked at the time of the survey) and current smokers (smoked at least 100 cigarettes and smoked at the time of the survey). And we categorized drinking status into three groups: never drinker (0), low to moderate drinker (<2 drinks/day), and heavy drinker (≥ 2 drinks/day) (Chen et al. 2019). Physical activity was also categorized into three groups according to the frequency of exercise: 0, 1-2 and ≥ 3 times/week (Chen et al. 2019). The overall quality of dietary was assessed by Healthy Eating Index-2015 (HEI-

2015), which was calculated as previously reported and categorized in quartiles for analysis (Krebs-Smith et al. 2018). Besides, general health condition was mainly grouped into three categories: very good to excellent, good and poor to fair.

Statistical analysis

Based on the complex, multistage, probability sampling design in the NHANES, we accounted for sampling weights, cluster and strata in our analysis according to the NHANES Tutorials (NCHS 2020). Categorical variables were expressed as number (proportion) and compared by the Rao-Scott χ^2 test, while continuous variables were presented as mean/median (95% confidence interval (CI)) and compared by analysis of variance/Kruskal-Wallis test. We used the Kaplan-Meier method to plot the survival curves associated with high-frequency and speech-frequency PTA. Cox proportional hazards models were used to estimate the hazard ratios (HRs) with 95% CIs for total and cause-specific mortality for the mild ($25 \leq 40$ dB), moderate ($40 \leq 60$ dB) and severe (>60 dB) hearing loss at different frequencies, with comparison to normal hearing level (≤ 25 dB). P for trend was calculated by including the median of PTA in each grade of hearing loss as a continuous variable in the models. Restricted cubic splines were furtherly used to examine the dose-response relationships between high-frequency/speech-frequency PTA and total/cause-specific mortality. Stratified analyses were conducted by baseline gender, age, BMI, smoking status, drinking status, physical activity, occupational noise exposure and general health condition. Moreover, we also explored the associations between hearing thresholds at different frequencies (500, 1000, 2000, 3000, 4000, and 6000 Hz) and total or cause-specific mortality. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and R version 4.0.2 (R Core Team 2020) with a 2-sided $P < 0.05$ considered statistically significant.

Results

Baseline characteristics

The baseline characteristics of the 11,732 participants were analyzed by categories of high-frequency and speech-frequency PTA (**Table 1**). Among the total participants, 14.67% (1,721/11,732), 12.33% (1,447/11,732) and 10.97% (1,287/11,732) showed mild, moderate and severe HFHL, respectively. Meanwhile, 13.41% (1,573/11,732), 7.05% (827/11,732) and 2.57% (302/11,732) had mild, moderate and severe SFHL, respectively. There were significant differences in BMI, PIR, Married status, smoking status, drinking status, and HEI across the different hearing status. In addition, compared with individuals with normal high-frequency and speech-frequency hearing level, those with hearing loss were more likely to be men, older, non-Hispanic white, less educated, physically inactive, exposed to occupational noise and with a history of diabetes, cardiovascular diseases, hypertension, or cancer.

Association between hearing loss and total or cause-specific mortality

Among 11,732 participants, a total of 1,253 deaths occurred during a median follow-up of 12.15 years, including 218 deaths from heart disease and 286 deaths from cancer. **Table 2** shows the associations of HFHL and SFHL with total and cause-specific mortality. Significant dose-response relationships were observed between HFHL or SFHL with total mortality. Compared with individuals with normal high-frequency hearing level, those with mild, moderate, and severe HFHL were significantly associated with 20% (HR: 1.20, 95%CI: 0.86-1.68), 27% (1.27, 0.94-1.72), and 42% (1.42, 1.05-1.92) increased risk of total mortality ($P_{\text{trend}} = 0.0207$). However, the HR was elevated without statistically significant for heart disease [0.84 (0.36-1.98), 1.28 (0.60, 2.73), and 1.50 (0.62, 3.60) for mild, moderate and severe HFHL, respectively] and cancer mortality [1.28 (0.73, 2.22), 1.21 (0.71, 2.04), and 1.37 (0.74, 2.52) for mild, moderate and severe HFHL, respectively], after adjusting for potential confounders. When compared with those with normal speech frequency hearing, the HRs and 95% CIs of mild, moderate, and severe SFHL were 1.16 (0.91, 1.47), 1.54 (1.19, 2.00), and 1.85 (1.36, 2.50), respectively for total mortality ($P_{\text{trend}} = 0.0003$). Different from total mortality, no significant associations were discovered between HFHL and heart disease mortality while significant associations were observed between SFHL and heart disease mortality. The HRs and 95% CIs of heart disease mortality were 1.90 (1.20, 3.00) and 3.50 (1.38, 8.86) for moderate and severe/greater SFHL.

The dose-response relationships between high-frequency and speech-frequency PTA with total and cause-specific mortality were further intuitively showed by the spline curve in **Figure 1**. A significantly monotonic increasing dose-response relationship was found between high-frequency PTA and total mortality. Similarly, significant linear dose-response relationships were also observed among speech-frequency PTA and total and heart disease mortality. In addition, **Figure 2** showed that the survival probability gradually decreased as the high-frequency and speech-frequency PTA increased during the follow-up time.

In the stratified analyses, significant associations between HFHL and total mortality were mainly observed among female, current smokers and those with inactive physical activity (**Table S1**). Likewise, the association between SFHL and total mortality were more

significant among females, obese individuals, heavy drinkers and those with poor to fair general health condition (Table S2).

Associations between hearing thresholds at different frequencies and total or cause-specific mortality

We furtherly evaluate the associations between hearing thresholds at different frequencies and total or cause-specific mortality (Figure 3). Compared with hearing thresholds of ≤ 25 dB at 500, 1000, or 2000 Hz, hearing thresholds of > 25 dB were significantly associated with increased total [(1.40 (1.17, 1.68); 1.44 (1.20, 1.73); and 1.33 (1.10, 1.62), respectively] and heart disease mortality [1.89 (1.08, 3.34); 1.95 (1.21, 3.16); and 1.89 (1.16, 3.09), respectively]. In addition, the risk for total and heart disease mortality also showed increasing trends as hearing thresholds at 3000, 4000 and 6000 Hz increased, though they were not statistically significant. The dose-response relationships between hearing thresholds at different frequencies and total or cause-specific mortality were presented in Figure S1, which further yielded significant associations between hearing thresholds of > 25 dB at low frequencies (500, 1000, or 2000 Hz) and total/heart disease mortality.

Discussion

In this study, we observed positive dose-response associations of total mortality with SFHL and HFHL in US adults. Also, SFHL was associated with heart disease mortality in a positive dose-dependent manner. Moreover, we found that hearing thresholds at speech frequencies (500, 1000, and 2000 Hz) were positively associated with total and heart disease mortality.

Although several epidemiological studies have explored the association between hearing loss and mortality, the results from these researches are not entirely consistent (Engdahl et al. 2019, Genther et al. 2015, Karpa et al. 2010, Miyawaki et al. 2020, Schubert et al. 2017). Genther *et al.* (2015) reported that hearing loss was associated with an increased risk of mortality among 1,958 older adults in the US, whereas Schubert *et al.* (2017) failed to discover significant association between hearing loss and total mortality in the Epidemiology of Hearing Loss Study. The discrepancy might due to different race/ethnicity, different sample sizes, and follow-up time. In addition, most studies except Karpa *et al.* (2010) and Gopinath *et al.* just explored the association of SFHL or self-reported hearing loss with total mortality (Gopinath et al. 2013, Karpa et al. 2010). Different from previous studies, the present study documented the associations of HFHL and hearing thresholds at different frequencies with total and cause-specific mortality with a large sample size and long follow-up time (12.15 years). As hearing loss is widely prevalent and greatly threatens people's health (Blackwell et al. 2014, Strawbridge et al. 2000), the findings of our study have important public health implications that more effective measurements are needed to be taken for preventing the occurrence and development of hearing loss.

Although the underlying mechanisms of the associations between hearing loss and mortality are unclear, several reasons might be considered. Firstly, as described in the study, individuals with hearing loss were more likely to be smokers, physical inactive, exposed to occupational noise, poor to fair general health condition, and with history of diabetes, cardiovascular diseases, hypertension, and cancer, and these characteristics are also risk factors for increased risk of death. Furthermore, individuals with progressive levels of hearing impairment showed a dose-response decreased pattern for physical functioning, mental health, and social functioning (Strawbridge et al. 2000). As reported previously, hearing loss has been associated with cognitive decline/dementia (Lin et al. 2011), depression (Scinicariello et al. 2019), walking speed (Li et al. 2013), falls (Viljanen et al. 2009), metabolic syndrome (Han et al. 2018), and cardiovascular diseases (Fang et al. 2018), all of which have been associated with increased risk of death (Houle 2013, Käräjämäki et al. 2020, Mirelman et al. 2016, Studenski et al. 2011, Torisson et al. 2012). The Blue Mountains Hearing Study previously demonstrated that disability in walking, cognitive impairment, and self-rated health mediated the association between hearing loss and total mortality by structural equation modeling (Karpa et al. 2010). Herein, our results also showed that the association of hearing loss and mortality was attenuated after adjustment for general health condition and cardiovascular diseases. Meanwhile, the association became stronger among individuals with poor to fair general health condition.

Notably, the effect of SFHL on total mortality was more obvious than HFHL. It has been reported that approximately 104 million people are at risk of noise-induced hearing loss in the US (Hammer et al. 2014). The effect of noise on hearing often begins at the higher frequencies of 3000, 4000, or 6000 Hz, which are more susceptible to noise (Anonymous 2003). And the influence from PTA of speech frequency is lower than that of high frequency in early noise-induced hearing loss (Anonymous 2003). Thus, SFHL may reflect more severe hearing impairment, which is more likely to cause or be associated with a series of negative health outcomes (Fang et al. 2018, Jayakody et al. 2018, Scinicariello et al. 2019). That significant associations between hearing thresholds at low frequencies (500, 1000 and 2000 Hz) and total mortality in this study further proved it. Initial HFHL may partly predict the risk of total mortality at an earlier stage before SFHL as previously mentioned (Feeny et al. 2012), and to prevent the further development of hearing loss may somewhat

decrease the risk of death. In addition, inconsistent with the results from Karpa *et al.* (2010) and Gopinath *et al.* (2013) they failed to discover a significant association between hearing loss and cardiovascular disease mortality in fully adjusted models. We found SFHL rather than HFHL was significantly connected with heart disease mortality in this study. SFHL has been reported to be associated with microvascular damage (Fang et al. 2019), and often accompanied by cardiovascular disease risk factors such as smoking, inactive physical activity, with a history of hyperglycemia, and hypertension (Han et al. 2018), which would promote the development of heart disease to further increase the risk of heart disease mortality (Fang et al. 2018, Gan et al. 2016, Karpa et al. 2010).

There are some strengths in our study. We first conducted a prospective cohort study to investigate the associations of HFHL and SFHL with total and cause-specific mortality in a large nationally representative US sample. Furthermore, we also evaluated the associations between hearing thresholds at different frequencies and total and cause-specific mortality. Several limitations in our study should also be identified. The hearing thresholds were measured only once at baseline, and covariates adjusted in our study were also available at baseline. It is unclear whether hearing thresholds and covariates changed during follow-up. In addition, participants in our study were US adults aged 18-85 years, thus the results might not be adapted to children or other ethnicities.

Conclusion

Hearing loss and hearing thresholds, especially at low frequencies, are associated with increased risk of total and heart disease mortality. Prevention for the occurrence and development of hearing loss may markedly reduce the risk of total and heart disease mortality. More research should be conducted to further elucidate the underlying mechanisms responsible for these associations.

Declarations

Ethics approval and consent to participate

The National Health and Nutrition Examination Survey protocol was approved by the National Center for Health Statistics Ethics Review Board and written informed consent was obtained from all participants.

Consent for publication: Not applicable.

Availability of data and materials: No additional data available.

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Conflict of interest: The authors declare no conflict of interest.

Authors' Contributions: XF, WC and DW designed research. XF and DW conducted research, analyzed data, and wrote the paper. WL, MC, WQ, RL, ML and WC contributed to the acquisition, analysis, or interpretation of the data, and revised the manuscript for important intellectual content. DW and WC have primary responsibility for final content and is the study guarantor. All authors read and approved the final manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Tables

Table 1. Baseline characteristics of study participants in NHANES 1999-2012 according to hearing loss levels (N=11,732)

	HFHL				P value	SFHL				P value
	Normal	Mild	Moderate	Severe		Normal	Mild	Moderate	Severe	
Participants	7,277	1,721	1,447	1,287		9,030	1,573	827	302	
Male	3,026 (40.43)	912 (56.90)	868 (64.54)	962 (77.92)	<0.0001	4,148 (45.92)	924 (61.70)	509 (60.54)	187 (55.37)	<0.0001
Age, years, mean (95%CI)	37.46 (36.93- 38.00)	50.38 (49.49- 51.26)	57.20 (56.11- 58.29)	62.31 (60.89- 63.73)	<0.0001	40.07 (39.55- 40.60)	57.26 (56.08- 58.45)	63.35 (61.58- 65.12)	63.13 (60.48- 65.78)	<0.0001
BMI, kg/m ²					<0.0001					<0.0001
<25	2,710 (38.40)	465 (26.21)	390 (25.42)	382 (28.78)		3,183 (35.98)	426 (26.00)	242 (28.15)	96 (31.65)	
25-30	2,261 (31.34)	625 (38.17)	516 (35.62)	512 (39.52)		2,915 (32.85)	573 (37.50)	317 (34.99)	109 (33.21)	
>=30	2,306 (30.26)	631 (35.62)	541 (38.96)	393 (31.70)		2,932 (31.17)	574 (36.51)	268 (36.86)	97 (35.15)	
Race/ethnicity					<0.0001					<0.0001
Mexican American	1,360 (8.78)	304 (6.98)	235 (5.96)	167 (3.81)		1,675 (8.43)	238 (4.93)	108 (4.78)	45 (5.34)	
Non-Hispanic White	2,799 (65.19)	755 (73.39)	807 (78.43)	900 (85.46)		3,636 (67.47)	887 (78.32)	544 (79.80)	194 (79.29)	
Non-Hispanic Black	1,908 (13.46)	405 (9.77)	233 (5.85)	120 (3.82)		2,269 (12.39)	264 (6.80)	94 (4.87)	39 (7.00)	
Others	1,210 (12.58)	257 (9.86)	172 (9.75)	100 (6.91)		1,450 (11.71)	184 (9.95)	81 (10.55)	24 (8.37)	
Educational level					<0.0001					<0.0001
Less than high school	1,486 (14.67)	512 (19.69)	520 (25.78)	480 (26.30)		1,986 (15.48)	556 (24.68)	335 (32.37)	121 (28.01)	
High school or equivalent	1,684 (22.35)	431 (25.51)	383 (29.83)	299 (27.12)		2,137 (23.41)	400 (27.68)	185 (24.23)	75 (28.61)	
College or above	4,107 (62.99)	778 (54.80)	544 (44.39)	508 (46.58)		4,907 (61.10)	617 (47.64)	307 (43.40)	106 (43.38)	
Family income-poverty ratio level					0.0002					<0.0001
0-1.0	1,671 (15.71)	356 (13.87)	255 (11.72)	189 (9.97)		2,006 (15.04)	271 (11.24)	139 (13.22)	55 (16.46)	
1.1-3.0	2,949 (37.01)	724 (34.30)	670 (39.61)	660 (41.81)		3,657 (36.10)	737 (39.35)	447 (49.34)	162 (45.19)	
>3.0	2,657 (47.29)	641 (51.82)	522 (48.67)	438 (48.22)		3,367 (48.86)	565 (49.40)	241 (37.45)	85 (38.35)	
Married status					<0.0001					<0.0001
Married	3085 (50.55)	967 (61.45)	835 (65.25)	755 (63.93)		4148 (53.69)	912 (62.84)	440 (57.55)	142 (50.47)	
Separated	1487 (17.63)	463 (23.26)	463 (23.71)	435 (26.57)		1919 (18.25)	487 (23.60)	320 (32.64)	122 (36.44)	
Never married	2705 (31.82)	291 (15.29)	149 (11.05)	97 (9.50)		2963 (28.06)	174 (13.56)	67 (9.80)	38 (13.09)	

Smoking status	<0.0001				<0.0001					
Never smoker	4,084 (55.04)	844 (45.62)	642 (41.38)	502 (37.00)		4,888 (52.51)	694 (42.10)	354 (42.14)	136 (44.35)	
Former smoker	1,759 (21.52)	477 (27.11)	524 (34.48)	585 (42.90)		2,303 (23.49)	563 (32.17)	357 (41.25)	122 (33.88)	
Current smoker	1,434 (23.44)	400 (27.27)	281 (24.14)	200 (20.11)		1,839 (24.01)	316 (25.73)	116 (16.61)	44 (21.77)	
Drinking status	0.0025				<0.0001					
Never drinker	1,420 (17.72)	467 (18.51)	395 (20.39)	367 (21.40)		1,819 (17.16)	454 (21.49)	260 (26.50)	116 (36.01)	
Low to moderate drinker	2,165 (29.10)	520 (30.15)	496 (32.78)	490 (33.74)		2,700 (29.23)	530 (31.67)	321 (38.26)	120 (34.54)	
Heavy drinker	3,692 (53.18)	734 (51.34)	556 (46.83)	430 (44.86)		4,511 (53.61)	589 (46.84)	246 (35.24)	66 (29.45)	
Physical activity, times/week	<0.0001				0.0003					
0	2,303 (25.49)	745 (36.03)	701 (39.60)	665 (41.84)		3,040 (27.27)	766 (40.78)	441 (44.02)	167 (44.62)	
1-2	3,257 (53.60)	668 (49.75)	516 (45.11)	422 (40.97)		3,935 (52.58)	555 (45.56)	281 (43.04)	92 (37.64)	
≥3	1,717 (20.92)	308 (14.21)	230 (15.29)	200 (17.19)		2,055 (20.15)	252 (13.66)	105 (12.94)	43 (17.74)	
General health condition	<0.0001				<0.0001					
Very good to excellent	3,133 (49.52)	566 (40.50)	479 (39.51)	429 (39.90)		3,755 (48.23)	518 (39.55)	244 (32.40)	90 (38.40)	
Good	3,087 (39.85)	725 (41.60)	585 (40.62)	524 (40.67)		3,828 (40.28)	624 (38.94)	350 (44.35)	119 (36.91)	
Poor to fair	1,057 (10.63)	430 (17.90)	383 (19.87)	334 (19.43)		1,447 (11.48)	431 (21.51)	233 (23.25)	93 (24.69)	
Healthy eating index	<0.0001				0.0004					
Q1	2,059 (29.46)	342 (21.52)	269 (23.84)	263 (23.06)		2,397 (27.95)	307 (23.76)	169 (22.74)	60 (23.15)	
Q2	1,902 (25.66)	400 (25.74)	351 (24.18)	280 (23.09)		2,316 (25.74)	364 (23.76)	190 (24.04)	63 (18.15)	
Q3	1,725 (23.29)	470 (25.96)	397 (28.25)	341 (24.27)		2,193 (23.75)	442 (27.68)	223 (25.56)	75 (24.03)	
Q4	1,591 (21.59)	509 (26.78)	430 (23.73)	403 (29.58)		2,124 (22.56)	460 (24.80)	245 (27.65)	104 (34.67)	
Occupational noise exposure	1,724 (23.06)	563 (34.37)	532 (39.80)	613 (47.99)	<0.0001	2,390 (26.41)	566 (37.07)	348 (42.85)	128 (37.97)	<0.0001
History of diseases										
Diabetes	364 (3.69)	287 (10.70)	254 (15.37)	225 (15.18)	<0.0001	632 (4.98)	293 (14.84)	152 (18.49)	53 (15.09)	<0.0001
Cardiovascular disease	250 (3.20)	192 (8.90)	292 (16.71)	355 (21.91)	<0.0001	452 (4.41)	316 (15.81)	239 (25.85)	82 (21.27)	<0.0001

Hypertension	1,452 (18.59)	753 (36.51)	705 (40.17)	700 (47.67)	<0.0001	2,196 (21.81)	803 (42.35)	446 (49.06)	165 (51.27)	<0.0001
Cancer	285 (5.08)	181 (10.64)	220 (13.91)	284 (16.92)	<0.0001	480 (6.13)	246 (13.75)	178 (19.56)	66 (17.04)	<0.0001
Follow up time, years, median (95%CI)	12.42 (12.10- 12.74)	12.15 (11.70- 12.61)	11.14 (10.46- 11.81)	9.71 (8.13- 11.29)	<0.0001	12.35 (12.06- 12.65)	11.28 (10.74- 11.83)	8.94 (7.35- 10.54)	6.74 (4.84- 8.64)	<0.0001

The Rao-Scott χ^2 test was used to compare for categorical variables and analysis of variance adjusted for sampling weights was used to compare for continuous variables. Categorical variables were expressed as number (percentage) and continuous

variables were shown as mean/median (95%CI). Abbreviation: HFHL: high-frequency hearing loss; SFHL: speech-frequency hearing loss; CI: confidence interval.

Table 2. Associations of hearing loss levels with total and cause-specific mortality (N=11,732)

	HRs (95% CIs) by different hearing status				<i>P</i> for trend
	Normal	Mild	Moderate	Severe	
HFHL					
Total mortality					
Age adjusted mortality rate#	6.00 (4.98-7.01)	9.27 (7.16-11.39)	12.75 (10.58-14.93)	18.06 (9.97-26.16)	
Number of deaths/person years	311/66,870	207/15,151	302/11,686	433/9,566	
Model 1	1 (ref.)	1.42 (1.04, 1.94)	1.83 (1.47, 2.27)	2.23 (1.82, 2.72)	<0.0001
Model 2	1 (ref.)	1.25 (0.90, 1.73)	1.38 (1.05, 1.82)	1.56 (1.17, 2.09)	0.0019
Model 3	1 (ref.)	1.20 (0.86, 1.68)	1.27 (0.94, 1.72)	1.42 (1.05, 1.92)	0.0207
Heart diseases mortality					
Number of deaths/person years	40/66,870	28/15,151	55/11,686	95/9,566	
Model 1	1 (ref.)	1.30 (0.61, 2.77)	2.53 (1.20, 5.34)	3.51 (1.74, 7.10)	<0.0001
Model 2	1 (ref.)	1.00 (0.44, 2.25)	1.60 (0.76, 3.34)	1.91 (0.81, 4.51)	0.0623
Model 3	1 (ref.)	0.84 (0.36, 1.98)	1.28 (0.60, 2.73)	1.50 (0.62, 3.60)	0.2042
Cancer mortality					
Number of deaths/person years	87/66,870	55/15,151	61/11,686	83/9,566	
Model 1	1 (ref.)	1.43 (0.81, 2.51)	1.61 (1.05, 2.49)	1.93 (1.14, 3.28)	0.009
Model 2	1 (ref.)	1.20 (0.69, 2.09)	1.19 (0.73, 1.93)	1.37 (0.77, 2.44)	0.3038
Model 3	1 (ref.)	1.28 (0.73, 2.22)	1.21 (0.71, 2.04)	1.37 (0.74, 2.52)	0.3619
Other causes mortality					
Number of deaths/person years	184/66,870	124/15,151	186/11,686	255/9,566	
Model 1	1 (ref.)	1.45 (0.96, 2.19)	1.77 (1.24, 2.52)	2.07 (1.50, 2.85)	<0.0001
Model 2	1 (ref.)	1.35 (0.88, 2.06)	1.43 (0.97, 2.12)	1.55 (1.00, 2.40)	0.045
Model 3	1 (ref.)	1.27 (0.83, 1.96)	1.31 (0.87, 1.96)	1.41 (0.89, 2.21)	0.1376
SFHL					
Total mortality					
Age adjusted mortality rate#	6.75 (5.96-7.54)	12.37 (9.83-14.92)	23.61 (16.50-30.73)	16.89 (10.66-23.11)	
Number of deaths/person years	515/82,247	336/12,970	283/6,015	119/2,040	
Model 1	1 (ref.)	1.59 (1.29, 1.95)	2.31 (1.80, 2.97)	2.79 (2.03, 3.82)	<0.0001
Model 2	1 (ref.)	1.23 (0.97, 1.57)	1.66 (1.28, 2.16)	1.92 (1.38, 2.66)	<0.0001
Model 3	1 (ref.)	1.16 (0.91, 1.47)	1.54 (1.19, 2.00)	1.85 (1.36, 2.50)	0.0003
Heart diseases mortality					
Number of deaths/person years	75/82,247	55/12,970	55/6,015	33/2,040	

Model 1	1 (ref.)	1.61 (0.90, 2.88)	3.50 (2.04, 6.01)	6.30 (2.52, 15.76)	<0.0001
Model 2	1 (ref.)	1.04 (0.59, 1.83)	2.15 (1.33, 3.46)	3.90 (1.48, 10.30)	0.005
Model 3	1 (ref.)	0.88 (0.50, 1.53)	1.90 (1.20, 3.00)	3.50 (1.38, 8.86)	0.0102
Cancer mortality					
Number of deaths/person years	146/82,247	74/12,970	50/6,015	16/2,040	
Model 1	1 (ref.)	1.19 (0.81, 1.76)	1.36 (0.80, 2.31)	1.23 (0.55, 2.75)	0.2586
Model 2	1 (ref.)	0.93 (0.61, 1.41)	1.09 (0.66, 1.82)	1.00 (0.44, 2.26)	0.9164
Model 3	1 (ref.)	0.94 (0.61, 1.46)	1.04 (0.62, 1.75)	0.93 (0.38, 2.28)	0.9528
Other causes mortality					
Number of deaths/person years	294/82,247	207/12,970	178/6,015	70/2,040	
Model 1	1 (ref.)	1.82 (1.40, 2.38)	2.58 (1.79, 3.72)	2.80 (1.97, 3.99)	<0.0001
Model 2	1 (ref.)	1.49 (1.10, 2.03)	1.84 (1.23, 2.76)	1.83 (1.15, 2.90)	0.0022
Model 3	1 (ref.)	1.40 (1.04, 1.90)	1.73 (1.15, 2.58)	1.77 (1.11, 2.84)	0.0053

Model 1: adjusted age; Model 2: model1+adjusted gender, race, educational levels, BMI, family income-poverty ratio level, married status, smoking status, drinking status, physical activity, general health condition, healthy eating index and occupational noise exposure; Model 3: Model 2+adjusted history of diabetes, cardiovascular disease, hypertension and cancer. #Mortality rates per 1000 person years, standardized to age distribution of entire study population and represented as estimated mortality rates (95%CI). Abbreviation: HFHL: high-frequency hearing loss; SFHL: speech-frequency hearing loss; HRs: hazard ratios; CIs: confidence intervals.

Figures

Figure 1

Associations of hearing loss levels with total and cause-specific mortality (N=11,732). Adjusted age, gender, race, educational levels, BMI, family income-poverty ratio level, married status, smoking status, drinking status, physical activity, general health condition, healthy eating index, occupational noise exposure, history of diabetes, cardiovascular disease, hypertension and cancer. Abbreviation: HFHL: high-frequency hearing loss; SFHL: speech-frequency hearing loss; HR: hazard ratio; CI: confidence interval.

Figure 2

Association of high-frequency and speech-frequency PTA of hearing thresholds with the survival probability during the follow-up time (N=11,732).

Figure 3

Associations of hearing thresholds at different frequencies with all cause and cause specific mortality (N=11,732). Adjusted age, gender, race, educational levels, BMI, family income-poverty ratio level, married status, smoking status, drinking status, physical activity, general health condition, healthy eating index, occupational noise exposure, history of diabetes, cardiovascular disease, hypertension and cancer. Abbreviation: HR: hazard ratios; CI: confidence interval.

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