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Association of plasma lead, cadmium and selenium levels with hearing loss in adults: National Health and Nutrition Examination Survey (NHANES) 2011–2012

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Abstract

To determine the association between hearing loss and environmental Pb, Cd and Se exposure, a total of 1503 American adults from National Health and Nutrition Examination Survey (NHANES) (2011–2012) were assessed. The average of four audiometric frequencies (0·5, 1, 2 and 4 kHz) was used to identify speech-frequency hearing loss (SFHL), while the average of 3 audiometric frequencies (3, 4 and 6 kHz) was used to identify high-frequency hearing loss (HFHL). HFHL adjusted OR determined by comparing the highest and lowest blood Pb and Cd quartiles were 1·98 (95 % CI: 1·27, 3·10) and 1·81 (95 % CI: 1·13, 2·90), respectively. SFHL was significantly associated with blood Cd with the OR = 2·42 for the highest quartile. When further stratified by age, this association appeared to be limited to adults aged 35–52 years. After stratified by gender, except for Pb and Cd, we observed that blood Se showed a dose-dependent association with SFHL in men. In women, only Cd showed a dose-dependent association with speech and high-frequency hearing loss. Hearing loss was positively associated with blood levels of Pb and Cd. Additionally, our study provided novel evidence suggesting that excessive Se supplement would increase SFHL risk in men.

Key words: Hearing loss: Lead: Cadmium: Selenium: Exposure

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Hearing loss is an extremely common chronic disorder, disrupting quality of life in those affected owing to resultant difficulties with language processing and communication, causing affected individuals to suffer from depression and social isolation[1,2]. Multiple aetiological factors, including genetics and noise exposure, have been well established as important risk factors[3,4]. Accumulating evidences suggest that chronic exposure to heavy metals or excessive intake of trace elements from both environment and pollution is risk factor for hearing impairment[5].

Pb and Cd are present in many consumer products, such as batteries, solar panels, pigments and plastic stabilisers[5]. Pb can cause the barrier between the cochlea and the blood becoming more permeable, enabling toxic compounds to enter the inner ear where they can damage hearing functionality[6]. Cd may cause ROS generation and cell death, further disrupting cochlear function. To date, certain epidemiological studies have identified a link between hearing loss and exposure to Pb and Cd. No significant associations of blood Pb with speech – frequency hearing loss was found in Korean adults[7], while another research reported that low levels of Pb exposure might be a significant risk factor for hearing loss in USA adults[8]. Choi *et al.*, for example, found that low level of Cd exposure was a significant risk factor for hearing loss[8], whereas Liu *et al.* found no such significant association between hearing loss and Cd[9]. Se is an essential micronutrient, leading many individuals to consume Se-containing supplements, especially in the USA where more than half of the population take dietary supplements[10]. It is known that the relationship between Se and health is U-shape[11]. The recommended Se intake is 53 μg per day for women and 60 μg per day for men[12]. Excess Se is suggested to be toxic, and thus the benefits of such supplementation remain debatable. To date, however, only one epidemiological study has assessed the relationship between hearing loss and Se exposure[13]. Therefore, it is important to investigate the relationship between Se and deafness.

Given the inconsistent conclusions and limited evidence produced by previous research efforts, in order to achieve a more complete understanding of the risks associated with exposure to these metals, we chose to assess the link between

Abbreviations: HFHL, high-frequency hearing loss; SFHL, speech-frequency hearing loss.

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environmental Pb, Cd and Se exposure and hearing loss using data from the most recently available NHANES 2011–2012 dataset.

Materials and methods

Study population

The 2011–2012 NHANES (https://www.cdc.gov/nchs/nhanes/) was the source of data used for this study. This study was considered to be national representative of USA civilians. All participants underwent in-home interviews and physical exams at mobile examination facilities. We focused on data from participants ≥ 20 years old who had complete audiometric results and blood heavy metal measurements. We excluded any participants missing variables of interest to the present study, yielding 1503 final participants, all of whom had given written informed consent. The survey study protocol had been approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board (ERB), and no further approval was required for this study as these data are public.

Audiometric measurements and definition of hearing loss

All audiometric examinations were performed by a trained examiner in a sound-isolating room. The MEC Health Technicians who performed the Audiometry Examination Component of NHANES were professionally trained by a certified audiologist from the National Institute for Occupational Safety & Health. For each ear, 0·5, 1, 2, 3, 4 and 6 kHz frequencies were used for assessing pure-tone air conduction hearing thresholds over a −10 to 110 dB intensity ranges. The average of four audiometric frequencies (0·5, 1, 2 and 4 kHz) was used to identify speech-frequency hearing loss (SFHL), while the average of three audiometric frequencies (3, 4 and 6 kHz) was used to identify high-frequency hearing loss (HFHL). SFHL or HFHL ≥ 25 dB in either ear was sued to define hearing loss, based on the WHO definition for this condition[14].

Measurements of blood lead, cadmium and selenium

All the measurements were detected in the laboratory of the CDC. The subjects' whole blood samples were stored at −30° C until assessment. Amounts of blood Se, Cd and Pb therein were assessed by inductively coupled plasma mass spectrometry, with lower detection limits of 0·25 μg/dl for Pb, 0·16 μg/l for Cd and 30μg/l for Se, and this method have been reported by Wu et al.[15].

Covariates

For analyses in this study, the following covariates were considered: age, sex, marital status, education level, current smoking status, alcohol consumption, BMI, noise exposure, hypertension[16] and diabetes[17]. We obtained information of age, sex, marital status and education from household interview. Possible education levels were as follows: elementary, middle or high school or college and over. Marital status was: married or other. BMI was determined based on weight divided by height squared (kg/m^2). History of cigarette smoking was categorised as self-reported current smoker, former smoker or never smoker[18]. Noise exposure includes occupational, firearm and recreational noise exposure. The definition of hypertension was BP ≥ 140/90 mmHg or using anti-hypertensive medications. The definition of diabetes was fasting glucose ≥ 126 mg/dl, HbAc1 ≥ 6·5 % or using anti-diabetic medication.

Statistical analyses

Continuous variables were described based upon interquartile ranges when non-normally distributed, and categorical variables were showed in percentages. Both *t* tests and Mann–Whitney U tests were utilised for comparing continuous baseline variables, while χ^2 tests were employed to compare categorical baseline variables. In order to account for the complex sampling design and non-response in NHANES, the mobile examination centre sample weights was used to analyse. OR of hearing loss linked to levels of Se, Pb and Cd in the blood were estimated via multivariate logistic regression model controlling for age, sex, education, marital status, BMI, smoking, noise exposure, hypertension and diabetes. We conducted tests for linear trend by entering the median value of each category of heavy metal concentrations as a continuous variable in the models. The risk analyses were further stratified by sex and age. Age groups were stratified as follows: <35, 35–52 and >52 years. We used SAS survey procedures (version 9.2; SAS Institute Inc.) to analyse the complex sample design and weights in NHANES 2011–2012. In our study, we used 2-years mobile examination centre sample weights for individual probabilities extracted from the blood metals data set and the auditory test data set according to the NHANES analysis tutorial. All of the tests were double sided, with P values < 0·05 as significance threshold.

Results

Basic study subject characteristics

Participant characteristics were shown in Table 1. A total of 1503 adult participants ages 20–69 years had available data for the analysis, 14·17 and 32·27 % had SFHL and HFHL, respectively. In comparison with the controls, patients with hearing impairment were more likely to have diabetes and hypertension. They had significantly higher expose to recreational, occupational and firearm noise. In addition, they were less likely to have a college or above education. Compared with nonsmokers, each level of blood Pb, Cd and Se was seemed to be higher in smokers. No significant differences were found for drinking. Concentrations of Pb and Cd were nearly 1·5–2 folds higher than that of the controls (P < 0·000). Se concentrations were only significantly higher in persons with high-frequency hearing loss (Table 1).

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Table 1. Selected characteristics of study population
(Number and percentages)

Characteristic	Total	Speech-frequency ≤ 25dB 1291 (85·8)		Speech-frequency > 25dB 212 (14·2)		*P*-value	High-frequency ≤ 25dB 1018 (67·7)		High-frequency > 25dB 485 (32·3)		*P*-value*
		n	%	*n*	%		*n*	%	*n*	%	
Age						<0·001					<0·001
<35	489	476	36·9	13	6·1		446	43·8	43	8·9	
35–52	535	482	37·3	53	25·0		397	39·0	138	28. 5	
>52	479	333	25·8	146	68·9		175	17·2	304	62·7	
Sex						<0·001					<0·001
Male	802	664	51·4	138	65·1		473	46·5	329	67·8	
Female	701	627	48·6	74	34·9		545	53·5	156	32·2	
Marital status						0·004					<0·001
Living with spouse	695	577	44·7	118	55·7		422	41·5	273	56·3	
others	808	714	55·3	94	44·3		596	58·5	212	43·7	
Education						<0·001					<0·001
No or elementary school	77	54	4·2	23	10·9		36	3·5	41	8·4	
Middle school	206	163	12·6	43	20·3		119	11·7	87	17·9	
High school	310	262	20·3	48	22·6		188	18·5	122	25·2	
College or over	910	812	62·9	98	46·2		675	66·3	235	48·5	
Smoking						<0·001					<0·001
Never smoker	843	752	58·2	91	42·9		618	60·7	225	46·4	
Former smoker	286	229	17·7	57	26·9		168	16·5	118	24·3	
Current smoker	374	310	24·1	64	30·2		232	22·8	142	29·3	
Drinking						0·700					0·310
No	331	287	22·2	44	20·8		216	21·2	115	23·7	
Yes	1172	1004	77·8	168	79·3		802	78·8	370	76·3	
BMI (kg/m^2)											
Median		27·8		28·90		0·159	27·35		29·30		<0·001
IQR		24·0–32·5		24·7–32·7			23·6–31·9		25·2–33·2		
Diabetes						<0·001					<0·001
No	1295	1133	87·8	162	76·4		922	90·6	373	76·9	
Yes	208	158	12·2	50	23·6		96	9·4	112	23·1	
Hypertension						<0·001					<0·001
No	1072	958	74·2	114	53·8		798	78·4	274	56·5	
Yes	431	333	25·8	98	46·2		220	21·6	211	43·5	
Occupational noise						0·007					<0·001
No	951	835	64·7	116	54·7		696	68·4	255	52·6	
Yes	552	456	35·3	96	45·3		322	31·6	230	47·4	
Recreational noise						0·170					0·028
No	1316	1137	88·1	179	84·4		905	88·9	411	84·7	
Yes	187	154	11·9	33	15·6		113	11·1	74	15·3	
Firearm noise						0·002					<0·001
No	933	822	63·7	111	52·4		666	65·4	267	55·0	
Yes	570	469	36·3	101	47·6		353	34·6	218	45·0	

	Median	IQR	Median	IQR		Median	IQR	Median	IQR	
Lead(μg/l)	1·00	0·65–1·53	1·51	1·02–2·21	<0·001	0·92	0·61–1·40	1·40	0·95–2·16	<0·001
Cadmium(μg/l)	0·29	0·18–0·54	0·41	0·27–0·79	<0·001	0·29	0·18–0·51	0·34	0·23–0·70	<0·001
Selenium(μg/l)	192·1	178·1–209·1	195·31	177·7–212·4	0·267	192·1	177·7–209·0	194·08	179·4–211·9	0·042

The interquartile ranges (IQR) were used to describe continuous variables for their skewed distribution, whereas categorical variables were showed in percentages. BMI: BMI.
* *P*-values were derived from *t* tests or Mann–Whitney *U* tests for continuous variables and χ^2 tests for categorical variables.

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Correlation between lead, cadmium and selenium levels and hearing loss risk

Table 2 showed logistic regression results for hearing impairment risk (speech and high frequency) with blood Pb, Cd and Se. We detected a significant positive association between the risk of hearing impairment and elevated Pb and Cd in the covariate-adjusted models. HFHL adjusted OR determined by comparing the highest and lowest blood Pb and Cd quartiles were 1·98 (95 % CI: 1·27, 3·10) and 1·81 (95 % CI: 1·13, 2·90), respectively. SFHL was significant associated with blood Cd with the OR = 2·42 (95 % CI: 1·35, 4·37) for the highest quartiles. There was no significant association between blood Se and hearing loss.

Given the evidence that age and sex might be risk factors for hearing loss, we explored the effect modification by age and sex on the relationship between hearing loss and heavy metal concentrations in blood. We detected a significant dose–response relationship between blood lead levels and risk of HFHL in men (HFHL: OR (95 % CI) = 2·53 (1·22, 4·46)), while in females this relationship was not significant (HFHL: OR (95 % CI) = 1·50 (0·55, 4·09)). There was a significant association between blood Cd levels and speech and high frequency hearing loss in women with the OR = 5·30 (95 % CI: 1·42, 19·18) and 4·97 (95 % CI: 1·69, 12·32) for the highest quartiles, respectively ($P_{trend} < 0·05$). Speech and high-frequency hearing loss were significantly associated with blood Se in men with the OR = 2·94 (95 % CI: 1·27, 6·83) and OR = 2·42 (95 % CI: 1·10, 5·34) for the highest quartile, respectively (Table 3). No significant relationships of blood Se with hearing impairment were detected in women. Table 4 showed the relationships between hearing loss and levels of heavy metals stratified by age. Among middle-aged adults (35 ≤ and ≤ 52), there was a significant relationship between hearing loss risk and blood lead (SFHL: OR (95 % CI) = 4·03 (1·24, 13·07); HFHL: OR (95 % CI) = 2·90 (1·26, 6·68)) and cadmium levels (SFHL: OR (95 % CI) = 7·06 (1·51, 33·01); HFHL: OR (95 % CI) = 4·08 (1·60, 10·38)) concentration. HFHL was marginal and significantly associated with blood Se in young and older adults with the OR = 2·92 (95 % CI: 1·14, 7·52; $P_{trend} = 0·061$) and OR = 2·00 (95 % CI: 1·00, 4·00; $P_{trend} = 0·302$) for the highest quartile, respectively.

Discussion

In the general population, Cd exposure is mainly attributed to dietary intake (such as offal, shellfish and vegetables), cigarette smoke and ambient air (especially in urban and industrial areas)[19]. Although many countries have been greatly reduced the sources of Pb exposure such as gasoline, paint and solder, Pb is still widely used, and its accumulation in the human body can affect the development of chronic diseases[20]. There is increasing evidence that Pb and Cd levels in the current environment have adverse effects on various health outcomes, including macular degeneration, renal function and diabetes[18,21,22]. In a study of 5187 adults in Korea, Choi et al found blood Pb and Cd levels to be linked with hearing loss. Subjects in the highest blood Cd interquartile (1·471–6·422 μg/l) relative to those in the lowest interquartile (0·068–0·689 μg/l) exhibited an OR of 1·47 (95 % CI: 1·05, 2·05) for HFHL with a significant linear trend. Blood Pb levels >2·823 μg/l had a 1·70-fold elevation in their risk of HFHL compared with adults with Pb levels <1·593μg/l[7]. Shargorodsky *et al.* found a similar result[19] by investigating 3389 subjects selected from the NHANES 2005–2008 data sets. A blood Pb concentration above or equal to 2 μg/dl significantly increased the risk of high-frequency hearing loss (OR, 2·22; 95 % CI, 1·39, 3·56) compared with a blood Pb concentration below 1 μg/dl. Individuals with the highest quartile of urinary Cd had a significantly higher risk of low-frequency hearing loss than those with the lowest quartile (OR, 3·08; 95 % CI, 1·02, 9·25). However, our present study found no significant relationship between blood Pb levels and hearing loss in women. Additionally, in our research, each level of blood Pb, Cd and Se was seemed to be higher in smokers compared with nonsmokers. The carbon monoxide released from cigarette smoke is considered a potential ototoxin that can shift the hearing threshold. Additionally, cigarette smoke is a resource of Cd pollution, and its ototoxic effect is probably attributed to Cd to some extent, which can be supported by our results.

Food is the main source of Se in the human body; however, the intake of Se in the diet varies widely, depending on the soil on which fodder and crops are grown[23]. The addition of Se to various dietary supplements is a popular supplement because lack of Se can be harmful to health. The recommended Se intake is 53 μg per day for women and 60 μg per day for men[11]. Studies have shown that both Se excess and deficiency could lead to neurotoxicity. The lack of Se may link to some adverse mood states, such as confusion, anxiety and hostility[24]. In addition, many studies have evaluated the health effects of acute or chronic Se exposure. For instance, a randomised trial of 501 elderly people with low levels of Se found that a low dose of Se supplementation significantly reduced total and non-high-density lipoprotein cholesterol concentrations, whereas the effect was not found to be significant in a high-dose Se supplementation group (300 μg/d)[25]. Similarly, a large NHANES in USA found that high serum Se concentration contribute to the development of diabetes[26,27]. Taken together, the relationship between the level of Se and health is U-shaped. In a study, Chuang et al. identified an inverse relationship between Se levels and hearing thresholds, suggesting that Se may actually protect hearing[13]. However, our present study found that blood Se showed a dose-dependent association with speech and high frequency hearing loss in men. These discrepant results may be due to differences in the populations assessed, the study designs, differences in exposure assessments or other possible differences. Further studies with larger sample sizes are therefore needed to confirm our findings.

We found that men, relative to women, were more likely to suffer hearing loss if exposed to high heavy metal levels. One reason for this may be that those middle-aged men are more likely to be exposed to heavy metals because of occupation or smoking[28,29]. However, due to factors such as fertility and physiology (menstruation), women are more likely to be deficient in Fe, subsequently Cd absorption is significantly increased under low iron reserves[30]. This explains why we only found Cd in women to have a significant impact on hearing.

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Table 2. Odds ratio of hearing loss associated with lead, cadmium and selenium levels
(Odd ratios and 95 % confidence intervals)

	SFHL†			HFHL‡		
Heavy metal concentrations(μg/l)	Hearing loss*/Total	OR	95 % CI§	Hearing loss*/Total	OR	95 % CI§
All (*n* 1503)						
Lead Q1 (<0·69)	21/372	1·00		51/372	1·00	
Q2 (0·69–1·07)	36/373	0·92	0·50, 1·68	92/373	1·01	0·66, 1·54
Q3 (1·07–1·62)	62/378	1·16	0·65, 2·08	144/378	1·49	0·93, 2·38
Q4 (>1·62)	93/380	1·46	0·81, 2·64	198/380	1·98	1·27, 3·10
$P_{\text{for trend}}$‖		0·047			0·000	
Cd Q1 (<0·18)	28/351	1·00		84/351	1·00	
Q2 (0·18–0·30)	45/389	1·20	0·70, 2·04	121/389	1·18	0·80, 1·75
Q3 (0·30–0·58)	59/389	1·70	1·00, 2·88	126/389	1·39	0·92, 2·09
Q4 (>0·58)	80/374	2·42	1·35, 4·37	154/374	1·81	1·13, 2·90
$P_{\text{for trend}}$‖		0·002			0·039	
Se Q1 (<175·53)	55/375	1·00		112/375	1·00	
Q2 (175·53–191·01)	45/377	1·10	0·71, 1·72	123/377	1·29	0·86, 1·93
Q3 (191·01–207·01)	47/376	0·97	0·53, 1·75	116/376	1·05	0·65, 1·71
Q4 (>207·01)	65/375	1·58	0·85, 2·93	134/375	1·51	0·92, 2·47
$P_{\text{for trend}}$‖		0·120			0·967	

* Hearing loss was define as pure tone average >25dB.
† SFHL: Speech-frequency hearing loss (0·5, 1, 2 and 4 kHz).
‡ HFHL: High-frequency hearing loss (3, 4 and 6 kHz).
§ Models were adjusted for age, sex, marital status, education, smoking, drinking, BMI, noise exposure, hypertension and diabetes.
‖ $P_{\text{for trend}}$ were derived using a continuous variable with the median value of each quartile.

Table 3. Odds ratio of hearing loss associated with lead, cadmium and selenium levels stratified by gender
(Odd ratios and 95 % confidence intervals)

	SFHL†			HFHL‡		
Heavy metal concentrations(μg/l)	Hearing loss*/Total	OR	95 % CI§	Hearing loss*/Total	OR	95 % CI§
Male (*n* 802)						
Lead Q1 (<0·69)	6/124	1·00		22/124	1·00	
Q2 (0·69–1·07)	20/186	1·43	0·50, 3·67	53/186	1·34	0·66, 2·74
Q3 (1·07–1·62)	40/230	1·52	0·58, 4·00	102/230	1·83	0·94, 3·57
Q4 (>1·62)	72/262	2·13	0·81, 5·61	152/262	2·53	1·22, 4·46
P for trend‖		0·045			0·001	
Cd Q1 (<0·18)	25/232	1·00		76/232	1·00	
Q2 (0·18–0·30)	30/214	0·96	0·51, 1·78	90/214	1·38	0·76, 2·53
Q3 (0·30–0·58)	33/161	1·38	0·73, 2·63	66/161	1·16	0·53, 2·53
Q4 (>0·58)	50/195	2·06	0·99, 4·30	97/195	2·10	0·79, 5·57
P for trend‖		0·029			0·172	
Selenium Q1 (<175·53)	28/169	1·00		67/169	1·00	
Q2 (175·53–191·01)	28/197	1·46	0·75, 2·83	86/197	1·90	1·04, 3·48
Q3 (191·01–207·01)	31/212	1·14	0·57, 2·27	77/212	1·28	0·55, 3·00
Q4 (>207·01)	51/224	2·94	1·27, 6·83	99/224	2·42	1·10, 5·34
P for trend‖		0·011			0·839	
Female (*n* 701)						
Lead Q1 (<0·69)	15/248	1·00		29/248	1·00	
Q2 (0·69–1·07)	16/187	0·48	0·21, 1·08	39/187	0·84	0·51, 1·38
Q3 (1·07–1·62)	22/148	1·37	0·40, 4·62	42/148	1·36	0·53, 3·52
Q4 (>1·62)	21/118	1·75	0·58, 5·30	46/118	1·50	0·55, 4·09
P for trend‖		0·086			0·317	
Cd Q1 (<0·18)	3/119	1·00		8/119	1·00	
Q2 (0·18–0·30)	15/175	2·96	0·80, 10·90	31/175	2·47	1·02, 6·00
Q3 (0·30–0·58)	26/228	3·90	1·12, 13·67	60/228	4·31	1·85,10·05
Q4 (>0·58)	30/179	5·30	1·42, 19·18	57/179	4·97	1·69, 12·32
P for trend‖		0·028			0·004	
Selenium Q1 (<175·53)	27/206	1·00		45/206	1·00	
Q2 (175·53–191·01)	17/180	0·70	0·29, 1·73	37/180	1·02	0·52, 1·99
Q3 (191·01–207·01)	16/164	0·87	0·33, 2·27	39/164	1·02	0·55, 1·91
Q4 (>207·01)	14/151	0·51	0·29, 1·73	35/151	1·03	0·43, 2·44
P for trend‖		0·757			0·697	

* Hearing loss was define as pure tone average >25dB.
† SFHL: Speech-frequency hearing loss (0·5, 1, 2 and 4 kHz).
‡ HFHL: High-frequency hearing loss (3, 4 and 6 kHz).
§ Models were adjusted for age, sex, marital status, education, smoking, drinking, BMI, noise exposure, hypertension and diabetes.
‖ *P* for trend were derived using a continuous variable with the median value of each quartile.

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Table 4. Risk of hearing loss associated with lead, cadmium and selenium levels stratified by age
(Odd ratios and 95 % confidence intervals)

	SFHL†			HFHL‡		
Heavy metal concentrations (μg/l)	Hearing loss*/Total	OR	95 % CI§	Hearing loss*/Total	OR	95 % CI§
Age <35 (*n* 489)						
Lead Q1 (<0·69)	2/215	1·00		11/215	1·00	
Q2 (0·69–1·07)	5/133	4·79	0·67, 35·0	12/133	1·87	0·59, 5·96
Q3 (1·07–1·62)	3/84	2·72	0·72, 10·3	13/84	2·19	0·73, 6·59
Q4 (>1·62)	3/57	3·53	0·56, 22·2	7/57	2·34	0·70, 7·78
$P_{for\ trend}$‖		0·681			0·285	
Cd Q1 (<0·18)	5/163	1·00		20/163	1·00	
Q2 (0·18–0·30)	2/136	0·35	0·03, 4·02	10/136	0·87	0·31, 2·44
Q3 (0·30–0·58)	1/109	0·09	0·01, 0·99	5/109	0·36	0·10, 1·23
Q4 (>0·58)	5/81	2·65	0·62, 11·3	8/81	1·08	0·27, 4·36
$P_{for\ trend}$‖		0·01			0·844	
Se Q1 (<175·53)	3/127	1·00		9/127	1·00	
Q2 (175·53–191·01)	4/122	1·17	0·15, 8·90	10/122	0·63	0·15, 2·59
Q3 (191·01–207·01)	3/132	2·89	0·37, 22·5	10/132	1·39	0·39, 4·99
Q4 (>207·01)	3/108	2·04	0·17, 24·1	14/108	2·92	1·14, 7·52
$P_{for\ trend}$‖		0·568			0·061	
35 ≤ Age ≤ 52 (*n* 535)						
Lead Q1 (<0·69)	9/124	1·00		20/124	1·00	
Q2 (0·69–1·07)	8/143	1·45	0·54, 3·91	27/143	1·16	0·60, 2·23
Q3 (1·07–1·62)	15/138	2·69	0·94, 7·68	38/138	1·83	0·97, 3·47
Q4 (>1·62)	21/130	4·03	1·24,13·07	53/130	2·90	1·26, 6·68
$P_{for\ trend}$‖		0·029			0·024	
Cd Q1 (<0·18)	6/124	1·00		23/124	1·00	
Q2 (0·18–0·30)	10/126	1·93	0·49, 7·63	34/126	2·85	1·17, 6·96
Q3 (0·30–0·58)	15/138	8·03	2·13, 30·2	33/138	4·59	2·28, 9·24
Q4 (>0·58)	22/147	7·06	1·51, 33·0	48/147	4·08	1·60, 10·4
$P_{for\ trend}$‖		0·0075			0·011	
Se Q1 (<175·53)	6/136	1·00		33	1·00	
Q2 (175·53–191·01)	12/130	1·29	0·42, 3·98	35	1·64	0·91, 2·96
Q3 (191·01–207·01)	11/123	0·42	0·11, 1·56	33	1·27	0·58, 2·78
Q4 (>207·01)	14/146	1·11	0·40, 3·06	37	1·54	0·79, 2·99
P for trend‖		0·022			0·168	
Age >52 (*n* 479)						
Lead Q1 (<0·69)	10/33	1·00		20/33	1·00	
Q2 (0·69–1·07)	23/97	0·56	0·22, 1·39	53/97	0·34	0·13, 0·88
Q3 (1·07–1·62)	44/156	0·67	0·28, 1·57	93/156	0·41	0·14, 1·21
Q4 (>1·62)	69/193	0·77	0·32, 1·86	138/193	0·58	0·15, 2·23
$P_{for\ trend}$‖		0·525			0·605	
Cd Q1 (<0·18)	17/64	1·00		41/64	1·00	
Q2 (0·18–0·30)	33/127	1·11	0·55, 2·25	77/127	0·55	0·14, 2·14
Q3 (0·30–0·58)	43/142	1·44	0·72, 2·89	88/142	1·23	0·41, 3·66
Q4 (>0·58)	53/146	1·84	0·86, 3·92	98/146	1·31	0·29, 5·92
$P_{for\ trend}$‖		0·088			0·320	
Se Q1 (<175·53)	36/112	1·00		70/112	1·00	
Q2 (175·53–191·01)	29/125	0·84	0·47, 1·51	78/125	1·02	0·52, 2·00
Q3 (191·01–207·01)	33/121	0·90	0·50, 1·62	73/121	1·21	0·51, 2·87
Q4 (>207·01)	48/121	1·13	0·63, 2·02	83/121	2·00	1·00, 4·00
$P_{for\ trend}$‖		0·595			0·302	

* Hearing loss was define as pure tone average >25dB.
† SFHL: Speech-frequency hearing loss (0·5, 1, 2 and 4 kHz).
‡ HFHL: High-frequency hearing loss (3, 4 and 6 kHz).
§ Models were adjusted for age, sex, marital status, education, smoking, drinking, BMI, noise exposure, hypertension and diabetes.
‖ $P_{for\ trend}$ were derived using a continuous variable with the median value of each quartile.

One major study strength is our large sample size and strong statistical power. Our study examined the relationship between blood Pb, Cd and Se levels and hearing loss in the USA general population, rather than focusing on occupational workers or animals. Importantly, the survey that generated these data was nationally representative, reducing selection bias risks. Trained personnel collected all heavy metal and audiometric data, ensuring no risk of measurement bias. Nevertheless, several limitations in this study should also be considered. First, as this study is cross-sectional, it does not take into consideration time-based relationships between variables, limiting interpretations of causality and warranting further studies to confirm these findings. Second, levels of Pb in participant blood primarily indicate recent exposure and thus may not predict the effect of long-term expose to lead, whereas bone Pb is a superior biomarker of accumulative Pb exposure[31]. Third, while we adjusted for as many potential confounding variables as possible, there is still the risk that other factors not considered may have confounded these results. Such possible confounders could include the use of medicines known to be toxic to auditory functions such as aminoglycoside antibiotics, exposure to ototoxic chemicals, genetic variation and use of appropriate hearing protection at work[32–34].

In conclusion, our findings are important for public health as they show that decreasing exposure to Pb and Cd in the environment may decrease hearing loss rate. Additionally, our study provides novel evidence suggesting that excessive Se supplement will increase hearing loss risk in men, and further larger cohort studies are warranted to examine this adverse effect.

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Y. T. and H. X. designed the research; N. W. and H. W. performed the statistical analysis; Y. T. and G. F. wrote the paper; all authors contributed to writing and reviewing the manuscript and read and approved the final manuscript.

The authors declare that they have no competing interests.

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