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Prevalence of Ototoxic Medication Use among Older Adults in Beaver Dam, Wisconsin

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Abstract

Background and Purpose—Drug-related ototoxicity may exacerbate presbycusis (age-related hearing loss), yet few data are available on the prevalence of ototoxic medication use by older adults. The purposes of this study were to assess the impact of aging and ototoxicity on hearing loss, the prevalence of ototoxic medication use and, select characteristics associated with ototoxic medication use among older adults.

Methods—Cross-sectional analyses were conducted using select variables extracted from the baseline and 10-year follow-up assessments of the two population-based epidemiological studies to compare two points in time.

Results—Ninety-one percent of the sample was taking a medication reported to be ototoxic. Non-steroidal anti-inflammatory drugs were the most commonly used (75.2%), followed by acetaminophen (39.9%) and diuretics (35.6%). Hypertension, diabetes, cardiovascular disease, and history of smoking were associated with ototoxic medication use. Participants with hearing loss were taking a significantly greater number of ototoxic medications than those without hearing loss.

Conclusion—Known ototoxic medications are widely used. Any subsequent ototoxicity may interact with age changes and a more severe hearing loss than that associated with age alone.

Implications for Practice—Nurse practitioners should inform older adults about the possibility of drug-related ototoxicity and monitor hearing acuity of all older adults taking known ototoxic medications.

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Author contributions: Dr. Joo was responsible for the concept, design and conduct of the study, analysis and interpretation of the data. She prepared the draft manuscript and incorporated comments and suggestions from the co-authors. Dr. Wallhagen provided substantial contributions to the conception and design of the study and revised it critically for important intellectual content. Dr. Cruickshanks, Dr. BEK Klein and Dr. R. Klein were involved in the acquisition of subjects and data and provided comments on interpretation of results. The Drs. Klein obtained funding for and directed the conduct of the Beaver Dam Study, which medication use data were obtained. Dr. Cruickshanks obtained funding for and directed the Epidemiology of Hearing Loss Study which measured hearing and collected other risk factor data. Dr. Hong provided advice on the analyses and interpretation of results and contributed to the writing of the article. All authors approved the final version of the manuscript for submission to the *JAANP.*

Keywords

ototoxicity; medication use; older adults; age-related hearing loss; presbycusis; cross-sectional study

Additional keywords

Hearing loss

Introduction

Age-related hearing loss or presbycusis is one of the four leading chronic conditions reported by older adults; 30% of adults aged 65–74 years old and approximately half of adults older than 75 years report having hearing loss (National Institute on Deafness and Other Communication Disorders, 2017). Age-related hearing loss has multiple negative effects on an individual's physical, psychosocial, and social status (Karpa et al., 2010). For example, hearing loss is associated with diminished functional status as measured by activities of daily living (Dalton et al., 2003) as well as quality of life scores in both the physical and mental domains (Chia et al., 2007). Data support that many older adults with hearing loss suffer from depression, low self-esteem, and loneliness due to communication difficulties and social isolation (Gopinath et al., 2009; Wallhagen, Strawbridge, Shema, Kurata, & Kaplan, 2001). Hearing loss affects not only the individual, but also family members who may become frustrated as a result of communication difficulties (Lopez-Torres Hidalgo et al., 2009).

Age is the most common factor associated with developing hearing loss in the adult population (Bielefeld, Tanaka, Chen, & Henderson, 2010). However, age and exposure to life experiences that damage the inner ear contribute together to the development of hearing loss (Peterson, 1994). Older adults are often on multiple medications for concurrent chronic illnesses (Kaufman, Kelly, Rosenberg, Anderson, & Mitchell, 2002), many of which have been identified as ototoxic. Patients taking these ototoxic medications may experience accelerated hearing loss. Ototoxic drug-related hearing loss has been characterized as a bilateral sensorineural loss affecting the higher frequencies, similar to presbycusis (Rybak & Ramkumar, 2007). Similar to people with presbycusis, people with ototoxic drug-related hearing loss may take their hearing problem for granted or be unaware when it comes on slowly.

Although some studies have evaluated select medications in specific populations, such as infants or patients in hospitals, there are few data on the prevalence of known ototoxic medication use among older adults in the community. Thus, the purposes of this study were to review the impact of aging and ototoxicity on hearing loss, to investigate the prevalence of ototoxic medication use, and to explore characteristics associated with ototoxic medication use among older adults.

Effects of Aging and Ototoxicity on Hearing

From the cochlea to the brain, several structural and chemical changes accompany advancing age. Older adults can have both conductive and sensorineural hearing loss in addition to cognitive difficulties that affect sound interpretation (Walling & Dickson, 2012). However, the vast majority of older adults with hearing loss have age-related sensorineural loss caused mainly by changes within the cochlea. Age-related sensorineural hearing loss is associated with problems in transducing hydro-mechanical vibrations to electrical potential in the cochlea and/or in auditory nerve transmission to the brain. This hearing loss usually results from permanent damage in the organ of Corti (Walling & Dickson, 2012). Vulnerable sites in the cochlea that are affected by aging include the hair cells and the stria vascularis (Pickles, 2008). Loss of hair cells is initially more common in the basal region of the cochlea among older adults, which leads to high frequency hearing loss (Weinstein, 2000). Hair cells cannot be replaced and are susceptible to accumulated damage over time from a combination of aging and toxicity from ototoxic medications and other environmental exposures (Lin et al., 2012). The stria vascularis provides the blood supply to the organ of Corti and maintains the endocochlear resting potential (Lin et al., 2012). Damage from age-related changes in the stria vascularis result in loss of the endocochlear resting potential, leading to a less effective cochlear amplifier and elevated hearing thresholds (Lin et al., 2012). These age-related changes cause a gradual, symmetric hearing loss, predominantly of high frequencies (Yueh, Shapiro, MacLean, & Shekelle, 2003).

Free radicals (reactive oxygen species) are considered to be important causative factors in age-related hearing loss (Liu & Yan, 2007). The ability to correct the negative effects of oxidative processes becomes less efficient with age, leading to the damage of key cell components, such as mitochondria DNA. Over time, oxidative damage accumulates in the cochlea and causes tissue dysfunction (Yamasoba et al., 2013). In addition to the aging process itself, other factors, such as exposure to noise, chemicals, and drugs, can damage the cochlea and contribute to the decline in hearing experienced by older adults (Huang & Tang, 2010).

Ototoxicity is cellular degeneration in the inner ear caused by a drug’s side effects (Rybak & Ramkumar, 2007). The most common reported ototoxic drugs in clinical use are aminoglycoside antibiotics, macrolide antibiotics, salicylates, chemotherapeutic agents such as cisplatin, loop diuretics, antimalarials, non-steroidal anti-inflammatory drugs (NSAIDs), quinine, and acetaminophen (Rybak & Ramkumar, 2007; Tabuchi et al., 2011; Walling & Dickson, 2012). Aminoglycosides can activate the formation of free radicals, which can damage mitochondria in the cochlea and lead to hair cell death (Kovacic & Somanathan, 2008; Pickles, 2008). Cisplatin affects the outer hair cells, the spiral ganglion cells, and the stria vascularis. Loop diuretics mainly target the stria vascularis (Pickles, 2008; Rybak & Ramkumar, 2007). High dose of salicylates and NSAIDs may reduce cochlear blood flow and damage outer hair cells (Cazals, 2000; Jung, Rhee, Lee, Park, & Choi, 1993). Quinine induces vasoconstriction and decreases cochlear blood flow (Jung et al., 1993). Acetaminophen can cause oxidative stress which causes degeneration and impairment of hair cells (Yorgason, Kalinec, Luxford, Warren, & Kalinec, 2010). However, while these

various processes have been identified, the exact mechanisms by which medications cause ototoxicity is still not clear.

Ototoxic drug-related damage could be a more significant contributor to hearing loss in older adults than in younger groups for two major reasons. First, the high prevalence of ototoxic drug use for comorbid chronic diseases, and second, an increased vulnerability to ototoxic drug effects because of impaired renal function (Howarth & Shone, 2006). Given this, it is important to explore the prevalence of ototoxic medication use by older adults and its relationship to hearing loss.

Methods

Study Design and Participants

This secondary analysis of cross-sectional data was conducted using selected variables extracted from the existing datasets from two population-based epidemiological studies: Beaver Dam Eye Study (BDES) and Epidemiology of Hearing Loss Study (EHLS). The cohort was examined in 1993–1995, 1998–2000, and 2003–2005 in Beaver Dam, Wisconsin, when the ages of the participants ranged from 48–92 (Cruickshanks et al., 2010). This study included data from the baseline EHLS examination (1993–1995) and the 10-year follow-up (2003–2005) to assess any changes in use of ototoxic medications. Participants who completed the survey for medication use were included in his study.

A signed informed consent was obtained from all study participants at the baseline and follow-up examinations. The Health Sciences Institutional Review Board of the University of Wisconsin approved this study with a waiver of review from the Human Research Protection Program Committee on Human Research of the University of California, San Francisco because only de-identified data were used.

Study Variables and Measures

Medication use among the EHLS participants was obtained from the concurrent BDES on the same cohort. Medication use was obtained from the standardized questionnaire (Klein & Klein, 1999) that was administered by the data collector (Klein, Klein, Lee, Cruickshanks, & Gangnon, 2006). Participants were asked to bring all prescription and over-the-counter medications that they were regularly taking at least once per week. The examiner recorded the medication from the label of the bottle and checked whether the medication bottle was the correct one for the medicine the participant reported taking. The examiner also asked whether there were other medications being taken that were not brought to the interview. If so, the data collector then phoned the participant at home to have the participant read the name of the medication over the phone. When necessary to verify medication and reason for use, the data collector phoned the participants, their physicians, and/or their pharmacies. In addition, participants were asked whether they had a history of hospitalization with fever requiring intravenous antibiotics and if they had a history of receiving chemotherapy. If yes to the latter, they were asked about the type of chemotherapy received, duration of chemotherapy, and age at first chemotherapy. Medications selected for the current study and defined here as “ototoxic medications” were those that have been identified as ototoxic in

the literature reviewed above. These included diuretics, NSAIDs, antibiotics, chemotherapeutic agents, quinine, and acetaminophen. Concomitant ototoxic medications use was defined by the use of more than one of these medications.

Hearing loss was defined as a pure tone average (PTA) at 500, 1000, 2000, and 4000 Hz greater than 25 dB HL (decibels Hearing Level) in either ear. Trained data collectors administrated the questionnaire at the baseline and 10-year follow-up examination for medical history, noise exposure, and socioeconomic status (Cruickshanks et al., 2010). Medical history included self-reported clinician diagnosis of diabetes, and cardiovascular disease (CVD) (stroke, heart attack, or angina). Diabetes was defined as a hemoglobin A1c level greater than or equal to 6.5% at the time of the examination, or self-reported clinician diagnosis. Hypertension was defined as systolic blood pressure greater than or equal to 140 mm Hg, diastolic blood pressure greater than or equal to 90 mm Hg, or a self-reported clinician diagnosis of hypertension and current use of antihypertensive medication. Noise exposure was assessed by current (within past year) noisy job. Smoking status was categorized as non-smoker, past smoker, or current smoker.

Statistical Analysis

Descriptive analyses are presented as means with standard deviations for continuous variables and as frequencies and percentages for categorical variables. Comparison analyses used the Chi-square test of association for categorical variables, and *t*-tests of differences in means for continuous variables. Logistic regression was used to evaluate the factors associated with the use of ototoxic medication. Ototoxic medication use was dichotomous (No/Yes) variable and number of ototoxic medication use was continuous variable. Multicollinearity was checked among independent variables. Statistical significance was defined as $p < .05$. All statistical analyses were conducted using SPSS software, version 24 (SPSS, Inc., Chicago, IL).

Results

The descriptive characteristics of the participants are shown in Table 1. The mean age of the 3574 participants at baseline was 65.1 (SD=10.4), more than 50% were women, 46% had hearing loss, and 50% had hypertension. At 10-year follow-up, the mean age of the 2280 participants was 71.7 (SD=8.7), more than 50% were women, 58% had hearing loss, 48% had progression of hearing thresholds greater than 10dB HL over 10 years, and 76% had hypertension. The prevalence of hearing loss and chronic diseases, such as hypertension, diabetes and CVD, increased greatly over 10 years.

Participants taking ototoxic medications were more likely to be older and female, and to have hypertension, diabetes, CVD, and cancer at baseline. At 10-year follow-up, participants taking ototoxic medications were more likely to have hypertension.

Prevalence of Ototoxic Medication Use

Overall, 84 % of participants were using any ototoxic medications at baseline, and the prevalence of ototoxic medication use increased to 91.1% over 10 years (Table 1). The most common ototoxic medication taken by older adults was NSAIDs (75.2%), followed by

acetaminophen (39.9%) and diuretics (35.6%) at 10-year follow-up (Table 2). The number of participants taking NSAIDs and diuretics had substantially increased over 10 years (58.3% vs. 75.2% and 23% vs. 35.6% respectively).

Among ototoxic medication users, half of participants were taking more than one type of ototoxic medication at baseline, and 60% were concomitant users at 10-year follow-up. The mean number of ototoxic medications used was 1.88 (±0.89) and more than 21% of participants were combined users of three or more ototoxic medications at 10-year follow-up (Figure 1).

The association between any ototoxic medication use and hearing loss was not statistically significant. However, participants taking a greater number of ototoxic medications demonstrated more hearing loss than those taking less at both baseline and 10-year follow-up (Table 3).

Characteristics Associated with Ototoxic Medication Use/Change

Females had significantly greater odds of taking ototoxic medication at baseline (odds ratio [OR]=2.44, 95% confidence interval [CI] 1.98, 3.0) than males, but this sex difference was not significant at the 10-year follow-up. CVD (OR=3.52, 95% CI 2.28, 5.43), hypertension (OR=1.82, 95% CI 1.48, 2.24), diabetes (OR=1.88, 95% CI 1.23, 2.89) and history of smoking (OR=1.29, 95% CI 1.05, 1.58) were significantly associated to ototoxic medication use at baseline, while CVD (OR=2.86, 95% CI 1.37, 6.0) and hypertension (OR=2.45, 95% CI 1.70, 3.51) were significantly associated at 10-year follow-up (Table 4).

Further analysis was conducted with a subgroup of participants who reported no use of an ototoxic medication at baseline. Among participants who were not taking any ototoxic medication (n=560) at baseline, 385 participants completed remained at 10-year follow-up. Of these 385 participants, 312 participants were taking ototoxic medication at 10-year follow-up. Age (OR for 10yr=1.68, 95%, CI 1.11–2.54) and hypertension (OR=2.95, 95% CI 1.58–5.52) were associated with the change of ototoxic medication use over 10 years (Table 5).

Discussion

The prevalence of any potentially ototoxic medication use increased from 84% at the baseline to 91% at the 10-year follow-up among older adults in this population-based study. NSAIDs were the most commonly used medication (75.2%), followed by acetaminophen (39.9%) and diuretics (35.6%) at 10-year follow-up. This high prevalence may be related to the increased prevalence of chronic diseases with age (Forman, Rimm, & Curhan, 2007). Chronic diseases such as hypertension, CVD, or diabetes were significantly associated with ototoxic medication use in this study.

A study using data from the National Health and Nutrition Examination Survey (NHANES) found 25% of adults aged 20 to 69 years used ototoxic medications including NSAIDs (7.3%), antineoplastic drugs (5%), loop diuretics (1.5%), and aminoglycoside antibiotics (0.03%) (Bainbridge, Hoffman, & Cowie, 2008). This NHANES study also found that the

prevalence of ototoxic medication use was greater in the hearing loss group than in the normal hearing group (p=0.001).

Additional large population-based studies have focused on the association between hearing loss and analgesic uses such as aspirin, NSAIDs, and acetaminophen (Curhan, Eavey, Shargorodsky, & Curhan, 2010; Curhan, Shargorodsky, Eavey, & Curhan, 2012). In the Nurses' Health Study II, women aged 31 to 48 years commonly used NSAIDs (69%), acetaminophen (62%), and aspirin (30%) at least once a week (Curhan et al., 2012). The Health Professionals Follow-up Study found that in men aged 40 to 75 years the prevalence of NSAIDs, aspirin, and acetaminophen was 4.9%, 26.8%, and 5.6% respectively (Curhan et al., 2010). In these two studies, NSAIDs and acetaminophen were significantly associated with the risk of self-reported hearing loss, but findings for aspirin were conflicting. Conflicting results for aspirin were also found in other studies (Chen et al., 2007; Jung et al., 1993; Sha, Qiu, & Schacht, 2006). Aspirin was included within the NSAIDs category in the current study and not isolated for analysis. In addition, the Health, Aging and Body Composition study reported that participants were aged from 73 to 84 years and were taking salicylates (44%), loop diuretics (9.7%), and quinine (1.2%) (Helzner et al., 2005). Also, the Framingham Heart Study reported that only a very small percentage (0.4%) of the 2293 participants aged 57 to 89 years were taking ototoxic medications (Moscicki, Elkins, Baum, & McNamara, 1985). However, they did not describe in the article which classes of medications were included in their analyses.

We found a much higher prevalence of any ototoxic medication use than in other previous studies. This might be related to the inclusion of a greater number of known ototoxic medications than those included in other studies. Additionally, in the current study the prevalence of use of each individual category of ototoxic medication, whether NSAIDs, diuretics, or antibiotics was also higher than in other prevalence studies. This might be partially explained by the fact that our study included participants who were older than those studied in NHANES and many of the other studies, and continued to follow participants who had entered nursing homes and assisted living, unlike most other studies. These individuals tend to take more medications. Additionally, the assessment of ototoxic medication use in the current study involved actually identifying and confirming the medications used and was not just based on self-report. More than half of participants used multiple ototoxic medications, and the association between number of ototoxic medication used and hearing loss was significant. A previous study documented that the impact of concomitant use of more than one class of aspirin, acetaminophen, or NSAIDs on self-reported hearing loss was additive (Curhan et al., 2010). This may be partly explained by the fact that different classes of ototoxic medications affect auditory function through different mechanisms (Curhan et al., 2010).

Hypertension, diabetes, and CVD are frequently found concurrently as comorbid diseases with cardiovascular complications (Sowers, Epstein, & Frohlich, 2001), although their correlations were low (r <.20) in this study (data not shown). Therefore, it is difficult to tease out the unique variance explained by each factor on ototoxic medication use. However, certain chronic conditions may add significant risk for hearing loss among ototoxic medication users because these diseases themselves are also risk factors for age-related

hearing loss (Frisina, Mapes, Kim, Frisina, & Frisina, 2006; Gates, Cobb, D'Agostino, & Wolf, 1993).

The strengths of the present study include having good quality data, including audiometric data documenting hearing loss, from a large population-based cohort of community-dwelling older adults. The data collected could address the question of prevalence of ototoxic medication use, a topic on which minimal research exists. Data were collected using standardized protocols and methodologies for measuring medication use. However, our study has limitations. The population is mostly non-Hispanic White from Beaver Dam, thus the results may not be generalizable to other ethnic groups. There was an association between number of ototoxic medication use and hearing loss, but the association between any ototoxic medication use and hearing loss was not statistically significant in this study. Because this study was cross sectional, it is difficult to know whether ototoxic medications preceded the hearing loss or vice versa. A longitudinal analysis could help to clarify the association between the incidence of hearing loss and ototoxicity from medications used by older adults. The short-term ototoxic effect of medications is relatively well documented (Lanvers-Kaminsky, Zehnhoff-Dinnesen, Parfitt, & Ciarimboli, 2017) and is generally known to clinicians. However, the effects on hair cells over the short term in vitro may not be the same as ototoxicity produced in vivo where the damage develops over longer periods and where much lower concentrations can be ototoxic (Pickles, 2008). Long-term consequences of ototoxic drug use, especially at lower doses than commonly thought to cause ototoxicity, have not been adequately studied, and more research still needs to be done in this field. Future studies with large diverse elderly populations are needed to replicate the findings of this study, thus expanding the generalizability of the findings.

Implications

Our findings support that known ototoxic medications are widely used for treating various conditions and ototoxicity may interact with aging leading to a more severe hearing loss than that associated with age alone. Given the high prevalence of hearing loss and its impact on health and activities of daily living, the high prevalence of ototoxic medication use by older adults may be a critical public health problem. Their use highlights the potential for increased hearing loss as a result of the increased use of ototoxic medications to treat chronic illnesses loss across time. Nurse practitioners (NPs) may not consider ototoxic side effects or consider them less important than the main effect of the drug when they choose medications for certain diseases (Albert et al., 2011). Also, NPs need to weigh the potential ototoxic side effects of medications commonly used for people who have diabetes, hypertension, or CVD, which may increase risk of age-related hearing loss. This study emphasizes the importance of understanding the potential for a drug's side effects, the need for proper monitoring, and the consideration of appropriate substitutions or drugs with less ototoxicity when taking care of older adults. Also, it is important for NPs to discuss with older people who are taking multiple ototoxic medications whether to stop or change the medications before hearing is adversely affected. When medications cannot be stopped or changed, NPs need to be cautious and closely monitor hearing of their patients. Screening hearing evaluations should be a part of any routine health checklist, but especially for people who have CVD and diabetes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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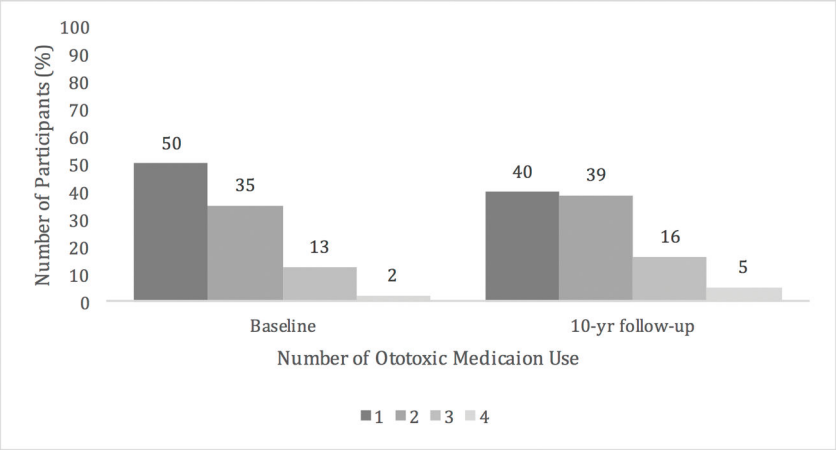

Figure 1.

Table 1

Characteristics of Participants at Baseline and 10-year Follow-up

	Ototoxic medication				Ototoxic medication			
	Baseline	**Yes**	**No**		**10-yr follow-up**	**Yes**	**No**	
Characteristic, n (%)	**n=3574**	**n=3002**	**n=572**	**p-Value**	**n=2280**	**n=2078**	**N=202**	**p-Value**
Age *	65.1 (10.4)	65.4 (10.5)	63.4 (10.0)	< .001	71.7 (8.7)	71.8 (8.6)	71.1 (8.9)	<.001
Sex								
female	2018 (56.7)	1771 (59.1)	247 (44.1)	< .001	1313 (58.4)	1206 (58.8)	107 (54.0)	.192
male	1538 (43.3)	1225 (40.9)	313 (55.9)		985 (41.6)	844 (41.2)	91(46.0)	
Education (years)								
< 12	847 (23.8)	728 (24.3)	119 (21.3)		364 (16.2)	336 (16.4)	28 (14.2)	
12	1632 (45.9)	1366 (45.6)	266 (47.6)	.348	1092 (48.6)	996 (48.6)	96 (48.7)	.829
13–15	549 (15.4)	466 (15.6)	83 (14.8)		385 (17.1)	351 (17.1)	34 (17.3)	
≥ 16	527 (14.8)	436 (14.6)	91 (16.3)		406 (18.1)	367 (17.9)	39 (19.8)	
Hearing loss (> 25dB)	1631 (45.8)	1381 (46.0)	250 (44.2)	.431	1283 (57.6)	1180 (57.6)	103 (57.9)	.943
Progression of hearing thresholds (>=10dB)					1031 (48.0)	945 (47.6)	86 (52.4)	.236
Current noise job	296 (8.3)	248 (8.3)	48 (8.6)	.819	69 (3.2)	65 (3.2)	4 (2.4)	.545
Smoking history								
Non-smoker	1600 (45.9)	1368 (45.9)	232 (45.9)		1032 (48.3)	957 (47.9)	75 (54.0)	

	Ototoxic medication				Ototoxic medication			
	Baseline	**Yes**	**No**		**10-yr follow-up**	**Yes**	**No**	
Characteristic, n (%)	**n=3753**	**n=2996**	**n=560**	**p-Value**	**n=2902**	**n=2078**	**N=202**	**p-Value**
Ex-smoker	1375 (39.4)	1185 (39.7)	189 (37.4)	.355	918 (42.9)	867 (43.3)	51 (36.7)	.301
Current smoker	513 (14.7)	429 (14.4)	84 (16.6)		188 (8.8)	175 (8.8)	13 (9.4)	
Hypertension	1760 (50.4)	1584 (53.3)	176 (33.8)	< .001	1486 (66.5)	1392 (67.6)	94 (52.8)	< .001
Diabetes	369 (10.4)	334 (11.5)	25 (4.6)	< .001	412 (19.1)	389 (19.3)	23(15.9)	.303
Cardiovascular disease	504 (14.3)	480 (16.1)	24 (4.4)	< .001	406 (18.8)	386 (19.2)	20 (13.2)	.064
History of cancer	584 (16.8)	520 (17.4)	64 (13.1)	.019	571 (25.5)	536 (26.0)	35 (20.2)	.095
History of kidney disease	83 (2.4)	74 (2.5)	9 (1.6)	.212	113 (5.2)	109 (5.5)	4 (2.4)	.084

* Mean (SD)

Table 2

Categories of Ototoxic Medication

	Baseline	10-year follow-up
Medication	**n (%)**	**n (%)**
NSAIDs	2025 (58.3)	1610 (75.2)
Acetaminophen	1275 (36.5)	892 (39.9)
Diuretics	793 (23.0)	795 (35.6)
Loop diuretic	210 (6.1)	234 (10.5)
Antibiotics (IV)	657 (19.3)	314 (14.8)
Antibiotics (oral)	173 (5.0)	173 (7.7)
Chemo	68 (1.9)	98 (4.5)
Quinine	38 (1.1)	15 (0.7)

Table 3

Number of Ototoxic Medications and Hearing Loss

	Number of ototoxic medications			
	Baseline		10-year follow-up	
Hearing loss	**Mean (SD)**	**p-Value^**	**Mean (SD)**	**p-Value^**
Yes	1.47(1.0)	0.001	1.78 (1.0)	0.001
No	1.36 (0.9)		1.67 (1.0)	

^T-test

Table 4

Characteristics Associated with Ototoxic Medication Use at Baseline and 10-year Follow-up[^]

	Baseline	10-year follow-up
	OR (95% CI)	**OR (95% CI)**
Sex (female)	2.44 (1.99–3.0) **	1.40 (0.98–2.02)
Age (year)	1.01 (.998–1.02)	1.02 (0.99–1.04)
CVD	3.52 (2.28–5.43) **	2.86 (1.37–6.0) *
Hypertension	1.82 (1.48–2.24) **	2.45 (1.70–3.51) **
Diabetes	1.88 (1.23–2.89) *	1.28 (0.74–2.21)
History of smoking	1.29 (1.05–1.58) *	1.33 (0.92–1.91)

[^] Logistic regression

* p-Value < .05

** p-Value < .001

Table 5

Characteristics Associated with Change of Ototoxic Medication Use from Baseline to 10-year Follow-up[^] (n=385)

	OR (95% CI)
Sex (female)	0.88 (0.47–1.66)
Age (10yr)	1.68 (1.11–2.54) *
CVD	2.12 (0.47–9.57)
Hypertension	2.95 (1.58–5.52) *
Diabetes	1.29 (0.47–3.56)
History of smoking	1.45 (0.76–2.74)

[^] Logistic regression

* p-Value < .05