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Prospective Study of Alcohol Use and Hearing Loss in Men

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Abstract

Objective—Hearing loss is a common and disabling sensory disorder, yet prospective data on potentially modifiable risk factors are limited. Previous studies suggest that alcohol consumption may influence the development of hearing loss, yet results have been inconsistent. The purpose of this study was to prospectively examine the relation between alcohol use and hearing loss in men.

Design—We examined prospectively the independent association between alcohol intake and self-reported professionally diagnosed hearing loss in 26,809 men aged 40–74 years at baseline in 1986. Study participants completed detailed questionnaires at baseline and every two years thereafter. Incident cases of hearing loss were defined as those professionally diagnosed after 1986. Cox proportional hazards multivariate regression was used to adjust for potential confounding factors.

Results—During 386,081 person-years of follow-up, 3447 incident cases of hearing loss were reported. Overall, there was no association between level of alcohol intake and risk of hearing loss. Compared to those who did not consume alcohol, the multivariate-adjusted hazard ratios (95% CI) were 1.00 (0.89–1.12) for those who consumed 5.0–9.9 grams/day, 1.08 (0.96–1.21) for 10.0–14.9 grams/day, and 0.98 (0.85–1.13) for 30.0–49.9 grams/day. The results did not differ by age group or folate intake. Among those with lower intake of vitamin B12, however, higher consumption of alcohol, specifically liquor, was associated with an increased risk of hearing loss.

Conclusions—Our data suggest that low or moderate alcohol consumption does not influence the risk of hearing loss in older men. A possible relation between vitamin B12 intake, alcohol consumption and hearing loss merits further investigation.

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Keywords

hearing loss; prospective study; alcohol

Introduction

Hearing loss is a common and disabling sensory disorder that afflicts over 36 million people in the US. (Pleis and Lethbridge-Cejku 2007) In adults aged 48 years and older, the 5-year incidence of developing hearing loss is 21%. (Cruickshanks et al. 2003) Hearing loss can compromise communication(Gordon-Salant 2005) and safety, (Girard et al. 2009) and can lead to social isolation, depression, and poorer quality of life. (Dalton et al. 2003; Gates and Mills 2005; Gates et al. 1996; Uhlmann et al. 1989)

Alcohol consumption may influence the development of hearing loss, however results from previous studies have been inconsistent. (Brant et al. 1996; Fransen et al. 2008; Helzner et al. 2005; Itoh et al. 2001; Popelka et al. 2000) It has been proposed that the cardioprotective effects of moderate alcohol intake, such as those mediated by higher levels of high density lipoprotein cholesterol (HDL) and anti-thrombotic activity, (Mukamal and Rimm 2008) extend to a decreased risk of hearing loss, potentially by protecting against disturbances in cochlear blood flow. (Seidman et al. 1999) Although chronic alcohol abuse has been reported to increase the risk of hearing loss, (Rosenhall et al. 1993) the relation between consumption of low or moderate levels of alcohol and hearing loss remains unclear. A protective association of low to moderate levels of alcohol intake was observed in some studies, (Fransen et al. 2008; Itoh et al. 2001; Popelka et al. 2000) but not in others, (Brant et al. 1996) or observed only in certain subgroups. (Helzner et al. 2005) Many of the previous studies were cross-sectional in design and have only evaluated alcohol consumption during the preceding year.

To further clarify this relation, we conducted a prospective study in 26,809 male participants in the Health Professionals Follow-Up Study (HPFS), to examine the association between updated alcohol use and the development of professionally diagnosed hearing loss. In addition, as higher levels of folate intake have been demonstrated to protect against hearing loss in a randomized controlled trial(Durga et al. 2007) and the modification of the impact of alcohol consumption by level of folate intake has been demonstrated to occur in other disease processes, (Baglietto et al. 2005; Rohan et al. 2000; Sellers et al. 2001; Zhang et al. 1999) we evaluated whether the relation between alcohol intake and hearing loss is modified by level of folate intake. As a previous study in this cohort suggested an association between vitamin B12 and hearing loss that was modified level of alcohol consumption, (Shargorodsky et al. 2010) we evaluated whether the association between alcohol intake and hearing loss was modified by level of vitamin B12 intake.

Methods

Study Population

The Health Professionals Follow-up Study originally enrolled 51,529 male dentists, optometrists, osteopaths, pharmacists, podiatrists, and veterinarians who were 40–75 years of age at baseline in 1986. Study participants filled out detailed questionnaires about diet, medical history, and medication use. Questionnaires have been administered every other year, and the 20-year follow-up exceeds 90%. The 2004 long form questionnaire included a question regarding whether the participant had been professionally diagnosed with hearing loss, and if so, the date of diagnosis. Of the 31,496 men who returned the long form questionnaire, 8291 (26.3%) reported a diagnosis of hearing loss. We excluded men who

reported hearing loss diagnosed before 1986 (n=2950) or cancer other than non-melanoma skin cancer (due to possible exposure to ototoxic chemotherapeutic agents) from the analysis. In addition, because age is such a strong risk factor and the prevalence of hearing loss is so high among the elderly, (Agrawal et al. 2008) we also excluded men as they reached age 75 during follow-up. The number of men included in the analysis was 26,809.

Ascertainment of Alcohol Intake

At baseline, men reported their alcohol consumption on a 131-item semiquantitative food frequency questionnaire (FFQ) that included separate items for beer, white wine, red wine, and liquor. Participants were asked how often, on average over the past year, they consumed each beverage. We calculated total alcohol intake by multiplying the average consumption of each beverage by the alcohol content of the specified portion size (12.8 g for beer, 11.0 g for wine, and 14.0 g for liquor) and summing across beverages. The FFQ subsequently was administered every 4 years, with an item for light beer added in 1994.

The validity of alcohol consumption estimated from the food frequency questionnaire (FFQ) has been demonstrated. (Giovannucci et al. 1991) The Spearman correlation coefficient between alcohol intake estimated from the FFQ and corresponding intake from diet records was 0.86. (Feskanich et al. 1993) Alcohol use assessed in this manner has been shown to be associated with a number of important outcomes in this cohort, such as myocardial infarction, (Mukamal et al. 2006) colon cancer, (Giovannucci et al. 1995) and gout. (Choi et al. 2004)

Ascertainment of Outcome

Information on the primary outcome, self-reported professionally diagnosed hearing loss, was obtained on the 2004 long form questionnaire along with the year of first diagnosis.

We defined incident cases as those diagnosed after 1986. Although standard pure-tone audiometry is generally considered the gold standard for hearing loss evaluation, several survey instruments have been developed to evaluate large populations due to the cost and logistic limitations of audiometric screening. Studies that have compared the reliability of self-report to the gold standard of audiometry(Gates et al. 1990; Nondahl et al. 1998; Sindhusake et al. 2001; Valete-Rosalino and Rozenfeld 2005) demonstrated that self-reported hearing loss is a reasonably reliable measure of hearing loss. For example, based on NHANES data using the definition of hearing loss to be a pure-tone average (at 500, 1000, 2000 and 4000 Hz) ≥25dB in both ears, the sensitivity was 65% and the specificity was 83% for self-report compared to audiometry. (Agrawal et al. 2008) Notably, in contrast to previous studies that used a general question such as, “Do you feel you have a hearing loss,” our questionnaires queried participants specifically about professionally diagnosed hearing loss.

Ascertainment of Covariates

We selected covariates purported to be risk factors for hearing loss. Covariates considered in the multivariate analyses included: age, (Agrawal et al. 2008) race, (Agrawal et al. 2008) body mass index (BMI), (Seidman 2000) folate intake, (Durga et al. 2007) Vitamin B12, (Holt 2007; Houston et al. 1999) Vitamin C intake, (Takumida and Anniko 2005) beta carotene, (Seidman 2000) physical activity, (Li et al. 2006) smoking, (Itoh et al. 2001) hypertension, diabetes, (Bainbridge et al. 2008) cardiovascular disease, (Gates et al. 1993) elevated cholesterol, (Gates et al. 1993) use of furosemide, (Rybak et al. 1991) and regular use of aspirin, acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs). (Curhan et al. 2010)

Age and race were obtained from biennial questionnaires. Height and weight were obtained from the baseline questionnaire with self-reported weight updated every two years. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Information on smoking status and physical activity was updated every two years. Intake of folate and B12 was calculated from semiquantitative food frequency questionnaires and updated every four years. Information on other covariates was available from the biennial questionnaires.

Questionnaire derived information on daily intake of nutrients and for many of the covariates has been validated by comparison with directly measured values or detailed diaries, with correlations of 0.71 for folate, (Rimm et al. 1992) 0.50 for vitamin B12, (Rimm et al. 1992) 0.97 for weight, (Rimm et al. 1990) and 0.79 for physical activity. (Chasan-Taber et al. 1996)

Statistical Analysis

All analyses were prospective, using information on alcohol consumption that was collected prior to the diagnosis of hearing loss. Alcohol use was categorized according to level of average daily ethanol intake in grams: none, 0.1 to 4.9, 5.0 to 9.9, 10.0 to 14.9, 15.0 to 29.9, 30.0 to 49.9, and 50.0 g or more. (Choi et al. 2004) We also categorized frequency of intake of individual alcoholic beverages (beer, red wine, white wine, liquor) into five frequency categories (servings/time): <1/mo, 1/mo–1/wk, 2–4/wk, 5/wk-1/day, and >1/day. (Choi et al. 2004) For each participant, person-time was allocated based on the response to the alcohol consumption questions at the beginning of each follow-up period. Alcohol intake as well as dietary and other exposure information was updated every four years. Participants were censored at the date of diagnosis of hearing loss, report of cancer other than non-melanoma skin cancer, age 75, the date of death, or the end of follow-up, whichever came first. Age- and multivariable-adjusted hazard ratios (HRs) were calculated using Cox proportional hazards regression models. Multivariable models were adjusted for potential confounders listed above.

As advancing age is a strong risk factor for hearing loss, the relative contribution of additional risk factors may be more pronounced in younger individuals. For example, the relation between diabetes mellitus and hearing loss is modified by age, (Bainbridge et al. 2008) as is the relation between regular analgesic use and hearing loss in men that was demonstrated in this cohort previously. (Curhan et al. 2010) To examine whether the relation between intake of alcohol and hearing loss varied by age, we performed analyses stratified by age <50 years, 50–59 years, and 60 years and older. In addition, to examine whether the relation between intake of alcohol and hearing loss varied by folate intake, (Baglietto et al. 2005; Sellers et al. 2001) we performed analyses stratified by the median of folate intake. To examine whether the relation between intake of alcohol and hearing loss varied by vitamin B12 intake, we performed analyses stratified by the median of vitamin B12 intake.

For all HRs, we calculated 95% confidence intervals (CIs). All P values are two-tailed. Statistical tests were performed using SAS statistical software, version 9 (SAS Institute Inc., Cary, NC).

Results

Characteristics of participants according to level of alcohol use at baseline are shown in Table 1. Those who consumed 30 grams or more per day of alcohol were more likely to report hypertension, gout, current smoking, regular use of aspirin and regular use of NSAIDs, as compared to those who consumed no or lower amounts of alcohol.

During 386,081 person-years of follow-up, 3447 cases of incident hearing loss were reported. Overall, there was no association between level of alcohol intake and the risk for developing hearing loss (Table 2). In multivariable models, compared to those who did not consume alcohol, the hazard ratios for risk of hearing loss were: 1.00 (95% CI 0.89–1.12) for those who consumed 5.0–9.9 grams/day; 1.08 (95% CI 0.96–1.21) for 10.0–14.9 grams/day; 1.09 (95% CI 0.97–1.22) for 15.0–29.9 grams/day; 0.98 (95% CI 0.85–1.13) for 30.0–49.9 grams/day; and 1.04 (95% CI 0.84–1.30) for 50.0 grams per day or more. Additional analyses that evaluated the intake of specific alcoholic beverages (beer, red wine, white wine, or liquor) did not reveal any consistent significant associations between the intakes of specific beverages and the risk of hearing loss (Table 3).

The lack of association between level of alcohol intake and the risk of hearing loss did not vary by age (p for interaction = 0.58) or folate intake (p for interaction = 0.22). However, the relation between alcohol intake and hearing loss varied by vitamin B12 intake. Among those with vitamin B12 intake below the median (9.0 mcg/d at baseline), the risk of hearing loss increased with higher levels of alcohol intake (p-interaction =0.005) (Table 4). Specifically, among those with vitamin B12 intake below the median, the hazard ratios for risk of hearing loss were 1.19 (95% CI 1.00–1.41) for those who consumed 15–29.9 grams of alcohol per day and 1.26 (95% CI 1.03–1.54) for those who consumed 30–49.9 grams of alcohol per day, as compared to those who did not consume alcohol. There were only 46 cases in the category of men who consumed 50 grams or more of alcohol per day; thus, the results in this group are difficult to interpret due to the small number of cases. Further analyses of each specific type of alcoholic beverage (beer, red wine, white wine or liquor), showed that among those with vitamin B12 intake below the median, the risk of hearing loss increased only with higher levels of liquor intake (p-interaction=0.003) (Table 5). The hazard ratios for risk of hearing loss was 1.22 (95% CI 1.01–1.47) for those who consumed 5–7 servings per week of liquor and 1.36 (95% CI 1.09–1.70) for those who consumed more than one serving per day, as compared to those who consumed liquor less than once per month.

Discussion

In this prospective study of 26,809 male health professionals, we found no overall association between alcohol intake and the risk of hearing loss. However, among those with lower levels of vitamin B12 intake, consumption of higher levels of alcohol, specifically liquor (spirits), was associated with an increased risk of hearing loss.

Several lines of evidence suggest that alcohol may influence the preservation of hearing function. Disturbances in cochlear blood flow, particularly hypoperfusion and possible ischemia, have been associated with adult hearing loss. (Seidman et al. 1999) Moderate alcohol consumption may aid in the maintenance of optimal cochlear blood flow, possibly mediated by increased HDL cholesterol or reduced coagulation. In prospective cohort studies, moderate intake of alcohol has been associated with a lower risk for myocardial infarction as compared to abstention, (Maclure 1993) an association thought to be due to higher levels of HDL cholesterol in moderate drinkers (Linn et al. 1993) that have been demonstrated in short-term randomized trials of alcohol administration. (Rimm et al. 1999) Similarly, Gates et al (Gates et al. 1993) observed an inverse relation between HDL levels and hearing thresholds, suggesting a protective effect of HDL on hearing.

Although chronic alcohol abuse has been associated with hearing impairment, (Rosenhall et al. 1993) results from studies of the relation between low or moderate levels of alcohol intake and hearing loss have been inconsistent. Several cross-sectional studies have suggested that consumption of moderate amounts of alcohol may have a protective effect. (Fransen et al. 2008; Helzner et al. 2005; Popelka et al. 2000) For example, a cross-sectional

study based on audiometric evaluations in participants of the Epidemiology of Hearing Loss Study (n=3571), found an inverse association (OR=0.71) between moderate alcohol use (>140 g/wk) during the previous year and hearing loss [defined by pure tone average as measured by audiometry: PTA (0.5,1,2,4) > 25 dB HL]. This association was even stronger (OR=0.49) when hearing loss was defined according to more stringent criteria [i.e. PTA (0.5,1.2.4) > 40 dB HL]. (Popelka et al. 2000) A case-control study in Japan reported a U-shaped relation between alcohol consumption and hearing loss, with a 45% decreased risk of hearing loss for occasional drinkers (not defined), a 27% decreased risk for light drinkers (<30 g/d of alcohol), but no association for heavy drinkers (≥30 g/d of alcohol). (Itoh et al. 2001) In contrast, our findings are consistent with those from a prospective study of 531 men, based on data from the Baltimore Longitudinal Study of Aging (BLSA), which found no association between moderate alcohol use and hearing loss assessed by audiometry. (Brant et al. 1996)

Our findings suggest that the relation between alcohol, specifically liquor, and hearing loss may vary by level of vitamin B12 intake. A previous study in this cohort examined the relation between vitamin B12 intake and risk of hearing loss. (Shargorodsky et al. 2010) We found a lower risk of hearing loss among men with higher intake of vitamin B12 only among those with the highest alcohol consumption, suggesting an interaction between alcohol and vitamin B12 intake. The present study examined the association between alcohol consumption and risk of hearing loss and further examined whether the relation varied by vitamin B12 intake. The observation of higher risk among those with both higher alcohol intake and lower intake of vitamin B12 supports the likelihood of an interaction. Due to its impact on cellular metabolism, vascular function, and myelin synthesis, vitamin B12 deficiency has previously been implicated as an important factor in cochlear pathology. (Brant et al. 1996; Gates et al. 1993; Hall 1990; Shemesh et al. 1993) In a small cross-sectional study, women with hearing loss had lower serum levels of vitamin B12 (Houston et al. 1999). Possibly, as higher levels of alcohol consumption may lead to a depletion of hepatic vitamin B12 stores, (Halsted et al. 2002) greater vitamin B12 intake would be required to preserve cochlear functioning in those who consume higher levels of alcohol. Whether liquor in particular alters vitamin B12 metabolism differently than beer or wine has not been examined.

The lack of association between alcohol intake and the risk of hearing loss did not vary by folate intake. A previous investigation by Durga et al demonstrated that folic acid supplementation slowed low-frequency hearing decline in older adults. (Durga et al. 2007) However, this was limited to individuals with low levels of blood folate in a country without folate supplementation of the food supply. Thus, it is possible that the relation between alcohol intake and hearing loss may be modified by a level of folate intake lower than in our study population.

Our study differs from previous work in several ways. A particular strength is the long-term prospective updated measurement of alcohol consumption over the course of up to 18 years, with updated measurements every four years. In addition, we examined the relation between more finely defined categories of alcohol consumption than used previously. Further, participants in this study were younger than many of those examined in other studies. We also evaluated the intake of specific alcoholic beverages (beer, red wine, white wine, or liquor). Although we observed an increased risk of hearing loss among those who consumed white wine 2–4 times per week, this result is likely spurious as there was no dose response.

This study has limitations. Although the participants in this cohort may not be representative of the adult U.S. population, follow-up rates are high and information provided is reliable. Assessment of hearing loss was based on self-report of professionally diagnosed hearing

loss. Standard pure-tone audiometry is considered the gold standard for evaluation of hearing loss, however self-reported hearing loss has been demonstrated to be a reliable assessment. (Sindhusake et al. 2001) Moreover, participants were specifically asked whether they had been "professionally diagnosed" with hearing loss, a more objective measure than the commonly used single question, "Do you feel you have a hearing loss?" Nonetheless, given the high prevalence of hearing loss in men of this age group, (Agrawal et al. 2008) there was likely misclassification of outcome. Further, few participants in our cohort reported very high levels of alcohol consumption, thus our ability to examine the potentially detrimental effects of heavy alcohol use was limited. Assessment of alcohol consumption was based on self-report, however the measures of quantity and frequency of alcohol consumption used in this study were previously validated,(Giovannucci et al. 1991) and any misclassification in our instruments is unlikely to affect the rank order of alcohol consumption. Finally, it has been suggested that the protective role of alcohol may be to diminish or delay the progression of hearing loss once it has occurred, a process this study cannot examine.

We did not have information on lifetime noise exposure in the whole cohort, a common cause of hearing loss. Although noise exposure may increase the vulnerability to hearing loss related to age (Erway et al. 1996; Gates et al. 2000; Kujawa and Liberman 2006) or other causes, (Brown et al. 1981) it is not known whether the impact of noise is modified by alcohol. Previous studies of alcohol use and hearing loss have not addressed leisure time and occupational noise exposure in detail.

These findings do not support an overall relation between low or moderate alcohol consumption and risk of hearing loss in older men. Additional studies are needed to examine the relation between alcohol intake and hearing loss in women, younger men, and other racial groups. The potential role of vitamin B12 in alcohol-related ototoxicity merits further investigation.

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Table 1

Baseline Characteristics of Men According to Alcohol Use (1986)

	Alcohol Use (grams/day)						
	None	**0.1–4.9**	**5.0–9.9**	**10.0–14.9**	**15.0–29.9**	**30.0–49.9**	**50.0+**
N	**5795**	**6481**	**3990**	**3406**	**3717**	**2163**	**721**
Variable							
Age, y	51.2	50.4	50.6	51.7	51.2	52.4	52.0
Race, %							
African-American	0.8	0.9	1.0	0.5	0.6	0.5	0.4
Asian	2.9	1.7	1.1	0.7	0.8	0.9	0.7
BMI, kg/m^2	25.5	25.4	25.2	25.2	25.2	25.4	25.7
Physical Activity, mets/wk	19.2	21.1	23.2	23.9	23.7	22.3	20.3
Hypertension, %	16.9	16.4	15.9	16.4	18.2	21.3	25.8
Diabetes, %	2.8	1.6	1.2	1.1	1.0	1.0	2.1
Gout, %	3.5	3.4	2.8	3.3	3.6	5.4	6.6
Smoking, never, %	62.8	53.5	48.6	43.4	38.0	28.8	26.1
Smoking, Past, %	28.0	35.8	41.0	44.5	50.0	52.1	51.1
Smoking, current, %	4.9	5.5	6.1	7.2	7.2	13.8	17.1
Elevated Cholesterol, %	10.7	11.2	11.2	11.1	11.7	11.8	14.1
Cardiovascular disease, %	4.2	4.1	4.2	3.5	3.5	3.9	3.4
Folate, mcg/d	478	481	487	473	481	454	417
Vitamin B12 mcg/d	13	12	13	12	12	12	12
Furosemide use, %	0.3	0.3	0.5	0.5	0.3	0.7	1.0
Aspirin, regular use %	24.4	24.3	26.5	28.3	30.4	32.8	32.2
Acetaminophen, regular use %	6.1	5.5	4.3	5.2	4.8	5.9	6.1
NSAIDs, regular use %	4.5	4.7	4.9	4.4	5.4	5.9	6.4

Values are means unless otherwise specified. Regular use of aspirin, acetaminophen or NSAIDs is defined as twice or more per week. BMI=body mass index mets/wk=metabolic equivalent tasks per week

Table 2

Age- and Multivariate-Adjusted Hazard Ratios for Alcohol Use and Incident Hearing Loss

Alcohol Use (grams/day)	Cases	Person-years	Age-adjusted Hazard Ratio (95% CI)	Multivariate-adjusted Hazard Ratio* (95% CI)
0	751	86768	1.00 (ref)	1.00 (ref)
0.1–4.9	782	92904	1.01 (0.91–1.12)	1.00 (0.91–1.11)
5.0–9.9	485	56460	1.01 (0.90–1.14)	1.00 (0.89–1.12)
10.0–14.9	489	50380	1.10 (0.98–1.23)	1.08 (0.96–1.21)
15.0–29.9	559	58211	1.07 (0.96–1.19)	1.09 (0.97–1.22)
30.0–49.9	283	31137	0.99 (0.86–1.14)	0.98 (0.85–1.13)
50.0+	98	10222	1.03 (0.84–1.27)	1.04 (0.84–1.30)
p-trend			0.31	0.56

*Adjusted for age, body mass index, physical activity, folate, vitamin B12, smoking, hypertension, diabetes, profession, race, hypercholesterolemia, cardiovascular disease, gout, furosemide use, aspirin use, nonsteroidal anti-inflammatory use, and acetaminophen use

Table 3

Age- and Multivariate-Adjusted Hazard Ratios for Specific Alcoholic Beverage Use and Incident Hearing Loss

Beverage and Frequency of Use	Cases	Person-years	Age-adjusted Hazard Ratio (95% CI)	Multivariate-adjusted Hazard Ratio* (95% CI)
Beer				
<1/month	1629	175029	1.00 (ref)	1.00 (ref)
1/mo–1/wk	1089	118953	1.04 (0.96–1.12)	1.01 (0.92–1.10)
2–4/wk	386	47893	0.98 (0.88–1.10)	0.94 (0.83–1.06)
5/wk–1/d	204	26935	0.95 (0.82–1.10)	0.92 (0.79–1.08)
>1/d	84	10995	0.99 (0.80–1.23)	0.98 (0.78–1.23)
Red Wine				
<1/month	1741	197492	1.00 (ref)	1.00 (ref)
1/mo–1/wk	1018	119240	0.98 (0.91–1.06)	0.96 (0.87–1.06)
2–4/wk	408	39503	1.10 (0.98–1.22)	1.02 (0.90–1.16)
5/wk–1/d	178	19048	0.94 (0.80–1.09)	0.93 (0.78–1.10)
>1/d	45	4960	0.91 (0.67–1.22)	0.89 (0.66–1.21)
White Wine				
<1/month	1455	166156	1.00 (ref)	1.00 (ref)
1/mo–1/wk	1301	148984	1.04 (0.96–1.12)	1.04 (0.95–1.14)
2–4/wk	438	43222	1.19 (1.07–1.32)	1.19 (1.05–1.35)
5/wk–1/d	146	16803	1.07 (0.79–1.45)	1.01 (0.84–1.21)
>1/d	43	4553	1.02 (0.80–1.81)	1.07 (0.78–1.46)
Wine, combined				
<1/month	1225	140550	1.00 (ref)	1.00 (ref)
1/mo–1/wk	1251	145216	1.02 (0.94–1.10)	1.01 (0.93–1.10)
2–4/wk	584	58478	1.12 (1.02–1.24)	1.14 (1.02–1.27)
5/wk–1/d	280	30357	0.98 (0.86–1.12)	0.99 (0.86–1.14)
>1/d	83	9079	0.97 (0.78–1.22)	0.97 (0.77–1.22)
Liquor				
<1/month	1658	196097	1.00 (ref)	1.00
1/mo–1/wk	804	92300	1.07 (0.98–1.17)	1.06 (0.97–1.17)
2–4/wk	388	42152	1.07 (0.95–1.19)	1.02 (0.91–1.15)
5/wk–1/d	356	32819	1.14 (1.02–1.28)	1.09 (0.96–1.23)
>1/d	205	18063	1.15 (0.99–1.33)	1.09 (0.93–1.27)

*Adjusted for age, body mass index, physical activity, folate, vitamin B12, smoking, hypertension, diabetes, profession, race, hypercholesterolemia, cardiovascular disease, gout, furosemide use, aspirin use, nonsteroidal anti-inflammatory use, and acetaminophen use

Table 4

Alcohol Use and the Multivariate-adjusted* Hazard Ratios for Incident Hearing Loss Stratified by Level of B12 Intake

		B12 Intake Below Median		B12 Intake Median or Above
Alcohol Use (grams/day)	**# cases**	**Multivariate-adjusted HR (95% CI)**	**# cases**	**Multivariate-adjusted HR (95% CI)**
0	330	1.00 (ref)	421	1.00 (ref)
0.1–4.9	336	1.02 (0.87–1.20)	446	0.99 (0.86–1.13)
5.0–9.9	208	1.03 (0.86–1.24)	277	0.95 (0.82–1.12)
10.0–14.9	217	1.18 (0.98–1.41)	272	1.02 (0.87–1.19)
15.0–29.9	259	1.19 (1.00–1.41)	300	0.99 (0.85–1.16)
30.0–49.9	156	1.26 (1.03–1.54)	127	0.75 (0.61–0.92)
50.0+	46	1.12 (0.81–1.54)	52	0.97 (0.72–1.31)
	p-interaction=0.005			

*Adjusted for age, body mass index, physical activity, folate, smoking, hypertension, diabetes, profession, race, hypercholesterolemia, cardiovascular disease, gout, furosemide use, aspirin use, nonsteroidal anti-inflammatory use, and acetaminophen use

Table 5

Liquor (Spirits) Use and the Multivariate-adjusted* Hazard Ratios for Incident Hearing Loss Stratified by Level of B12 Intake

	# cases	B12 Intake Below Median	# cases	B12 Intake Median or Above
Liquor Use (servings)		**Multivariate-adjusted HR (95% CI)**		**Multivariate-adjusted HR (95% CI)**
<1 month	736	1.00 (ref)	922	1.00 (ref)
1/mo – 1/wk	360	1.14 (0.99–1.31)	444	1.01 (0.89–1.14)
2–4 /wk	172	1.14 (0.95–1.36)	216	0.95 (0.81–1.12)
5/wk – 1/day	160	1.22 (1.01–1.47)	196	1.00 (0.84–1.18)
>1 /day	105	1.36 (1.09–1.70)	100	0.89 (0.71–1.11)
	p-interaction=0.003			

*Adjusted for age, body mass index, physical activity, folate, smoking, hypertension, diabetes, profession, race, hypercholesterolemia, cardiovascular disease, gout, furosemide use, aspirin use, nonsteroidal anti-inflammatory use, acetaminophen use, and use of other individual beverages (beer, red wine, white wine)