Tobacco, but Neither Cannabis Smoking Nor Co-Drug Use, Is Associated With Hearing Loss in the National Health and Nutrition Examination Survey, 2011 to 2012 and 2015 to 2016

Rachael R. Baiduc,[1] Joshua W. Sun,[2] Christopher Spankovich,[3] and Eric A. Vance[2]

Introduction: A relationship between tobacco smoking and hearing loss has been reported; associations with cannabis smoking are unknown. In this cross-sectional population-based study, we examined relationships between hearing loss and smoking (tobacco, cannabis, or co-drug use).

Methods: We explored the relationship between hearing loss and smoking among 2705 participants [mean age = 39.41 (SE: 0.36) years] in the National Health and Nutrition Examination Survey (2011 to 12; 2015 to 16). Smoking status was obtained via questionnaire; four mutually exclusive groups were defined: nonsmokers, current regular cannabis smokers, current regular tobacco smokers, and co-drug users. Hearing sensitivity (0.5 to 8 kHz) was assessed, and two puretone averages (PTAs) computed: low- ($PTA_{0.5,1,2}$) and high-frequency ($PTA_{3,4,6,8}$). We defined hearing loss as threshold >15 dB HL. Multivariable logistic regression was used to examine sex-specific associations between smoking and hearing loss in the poorer ear (selected based on $PTA_{0.5,1,2}$) adjusting for age, sex, race/ethnicity, hypertension, diabetes, education, and noise exposure with sample weights applied.

Results: In the age-sex adjusted model, tobacco smokers had increased odds of low- and high-frequency hearing loss compared with non-smokers [odds ratio (OR) = 1.58, 95% confidence ratio (CI): 1.05 to 2.37 and OR = 1.97, 95% CI: 1.58 to 2.45, respectively]. Co-drug users also had greater odds of low- and high-frequency hearing loss [OR = 2.07, 95% CI: 1.10 to 3.91 and OR = 2.24, 95% CI: 1.27 to 3.96, respectively]. In the fully adjusted multivariable model, compared with non-smokers, tobacco smokers had greater odds of high-frequency hearing loss [multivariable adjusted odds ratio = 1.64, 95% CI: 1.28-2.09]. However, in the fully adjusted model, there were no statistically significant relationships between hearing loss ($PTA_{0.5,1,2}$ or $PTA_{3,4,6,8}$) and cannabis smoking or co-drug use.

Discussion: Cannabis smoking without concomitant tobacco consumption is not associated with hearing loss. However, sole use of cannabis was relatively rare and the prevalence of hearing loss in this population was low, limiting generalizability of the results. This study suggests that tobacco smoking may be a risk factor for hearing loss but does not support an association between hearing loss and cannabis smoking. More definitive evidence could be derived using physiological measures of auditory function in smokers and from longitudinal studies.

Key words: Cannabis smoking, Co-drug use, Epidemiology, Hearing loss, National Health and Nutrition Examination Survey, Tobacco smoking.

Abbreviations: MVOR = multivariable adjusted odds ratio; NCHS = National Center for Health Statistics; NHANES = National Health and Nutrition Examination Survey; OR = odds ratio; PTA = pure-tone average; SE = standard error of the mean.

(Ear & Hearing 2022;00;00–00)

[1]Department of Speech, Language, and Hearing Sciences, University of Colorado Boulder, Colorado, USA; [2]Department of Applied Mathematics, University of Colorado Boulder, Boulder, Colorado, USA; and [3]Department of Otolaryngology-Head and Neck Surgery Jackson, University of Mississippi Medical Center, Mississippi, USA.

INTRODUCTION

Hearing loss is a common chronic condition associated with potential consequences including depression (Kiely et al. 2013), social isolation (Shukla et al. 2020), and increased risk of cognitive decline (Golub et al. 2020). By 2050, approximately 900 million individuals worldwide are projected to have hearing loss (Davis & Hoffman 2019), posing a significant public health burden. Risk factors related to modifiable lifestyle choices [e.g., diet (Spankovich & Le Prell 2014) and tobacco smoking (Cruickshanks et al. 1998)] have been linked to auditory dysfunction.

Epidemiological research has associated tobacco smoking with hearing loss in cross-sectional (Cruickshanks et al. 1998; Fransen et al. 2008; Helzner et al. 2011; Hong et al. 2015) and longitudinal (e.g., Hu et al. 2019) studies, a relationship further bolstered by laboratory studies connecting cigarette smoke with spiral ganglion degeneration in mice (Paquette et al. 2018) and nicotine exposure with outer hair cell damage in guinea pigs (Abdel-Hafez et al. 2014). Cruickshanks et al. (1998) reported increased odds of hearing loss in current smokers vs. nonsmokers in a cross-sectional analysis of the Epidemiology of Hearing Loss Study. This finding held after adjustment for age, sex, history of cardiovascular disease, alcohol, education, and noise exposure. Cross-sectional National Health and Nutrition Examination Survey (NHANES) studies have associated hearing loss with smoking, most notably in long-term (Agrawal et al. 2008) and heavy smokers (Agrawal et al. 2009). The Korean NHANES also reported a relationship between tobacco smoking and hearing loss (Hong et al. 2015). Some reports support the possibility of a dose-dependence [i.e., greater tobacco consumption is associated with increased odds of hearing loss (e.g., Nakanishi et al. 2000; Fransen et al. 2008; Agrawal et al. 2009; Dawes et al. 2014)]. A meta-analysis reported an overall risk ratio for hearing loss of 1.33 [95% confidence interval (CI): 1.24 to 1.44] based on cross-sectional studies and 1.97 (95% CI: 1.44 to 2.70) based on cohort studies (Nomura et al. 2005).

Although there is a substantial body of literature supporting a link between smoking and hearing loss, these findings are equivocal. Some cross-sectional reports (Gates et al. 1993; Lin et al. 2011), primarily those in older adults, have failed to find a relationship between tobacco smoking and hearing loss. Moreover, temporal data from the Baltimore Longitudinal Study of Aging (Brant et al. 1996), Denmark's Ebeltoft Health Promotion Project (Karlsmose et al. 2000), Blue Mountains Hearing Study (Gopinath et al. 2010), and Rotterdam Study (Rigters et al. 2018) did not find evidence linking tobacco smoking to incident hearing loss.

<zdoi; 10.1097/AUD.0000000000001219>

The relationship between hearing loss and tobacco smoking has received substantial attention. Whether or not hearing loss is associated with smoking other drugs remains uncertain. While tobacco use has been declining since the 1960s (National Center for Chronic Disease Prevention and Health Promotion 2014), increased legalization and availability of recreational and medicinal cannabis has resulted in greater cannabis use among adults (Hasin et al. 2019). To date, there are no population-based studies describing the relationship between cannabis smoking and hearing loss although one recent report linked cannabis smoking to tinnitus in the NHANES (2011–12) after adjustment for hearing loss and other covariables (Qian & Alyono 2020). Research also suggests delta-9-tetrahydrocannabinol and cannabidiol binding to cannabinoid receptor 1 (CB_1) may exacerbate tinnitus (Zheng et al. 2015). Conversely, cannabinoid signaling may be otoprotective against cisplatin ototoxicity (Ghosh et al. 2018; Ghosh et al. 2021). Hearing loss as a factor relative to cannabis use and other forms of smoking is thereof of interest.

Scientific investigation of auditory function in cannabis users remains in its infancy. In this study, we sought to examine relationships between smoking (tobacco and cannabis) and hearing loss. Given the proclivity of cannabis consumers to use tobacco (Tsai et al. 2017), relationships with co-drug use (i.e., use of both substances) were also of interest. Therefore, we investigated the relationship between current smoking (cannabis, tobacco, and co-drug use) and hearing loss using a nationally representative sample of adults from the NHANES. We use a cutoff for normal hearing of 15 dB HL. Although more conservative than some previous reports, this approach is in line with clinical recommendations from the American Speech-Language-Hearing Association (Clark 1981) and allows us to capture slight hearing loss.

MATERIALS AND METHODS

Study Cohort

We report relationships between smoking and hearing loss among U.S. adults aged 20 to 59 years using data from the NHANES. The study design and sampling has been described in depth elsewhere (Johnson et al. 2014; Chen et al. 2020). In brief, NHANES is an ongoing cross-sectional study of United States civilians; approximately 10,000 individuals are selected each cycle for participation via multistage probability sampling. We combined data from two 2-year cycles (2011 to 2012, n=9338 and 2015 to 2016, n=9544). The intermediate 2013 to 2014 cycle was not used because audiological evaluations were not conducted. The National Center for Health Statistics Institutional Review Board approved the NHANES study and written consent was obtained from all participations. Local Institutional Review Board review was unnecessary as the dataset is publicly available and de-identified.

Exclusions

Survey participants who underwent audiological evaluation and completed a full drug questionnaire were considered for inclusion. Figure 1 shows the flow of participant exclusions. Based on audiological testing, the eligible sample size was 8277. Of those, participants were excluded if they met any of the following criteria: cold or sinus infection 24 hours before evaluation, loud noise exposure within 24 hour of audiometric testing (per Spankovich & Le Prell 2014), unreliable test-retest 1 kHz threshold(s), former smoking status, unclassifiable smoking status due to missing data, bilateral conductive pathology [i.e., non-Type A tympanogram (compliance ≤0.3 or pressure ≤−150 daPa), current pressure equalization tubes, abnormal otoscopy, and/or cerumen impaction], or audiometric issues

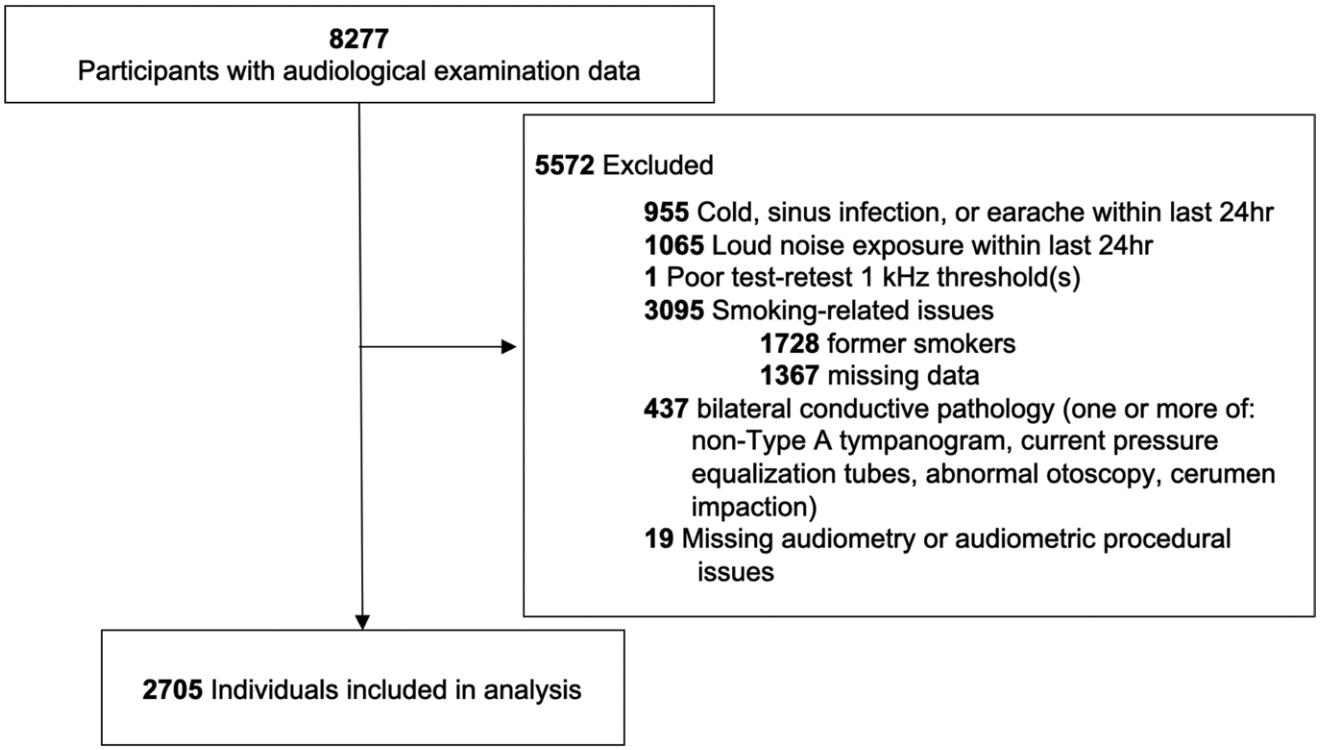

Fig. 1. Flowchart of participant exclusions.

(missing data or procedural issues). Individuals with unilateral conductive pathology were retained in the dataset and analysis was conducted on the nonpathologic ear. Included and excluded participants were similar in terms of race/ethnicity. Included participants were slightly older (39.4 versus 37.1 years) and more likely to be female (56.0% versus 50%).

Audiological Testing

Relevant audiological assessment included case history, otoscopy, puretone audiometry, and tympanometry. Sessions were conducted by trained examiners in sound-isolating rooms in a mobile examination center using an AD226 audiometer (Interacoustics AS, Assens, Denmark). Air conduction thresholds were obtained bilaterally at 0.5, 1, 2, 3, 4, 6, and 8 kHz using a modified Hughson Westlake procedure. Standard supra-aural (TDH-49P; Telephonics, Farmingdale, NY) or insert (EarTone 3A; Etymotic Research, Elk Grove Village, IL) earphones were used. Thresholds ranged from -10 to 120 dB HL (95 dB HL at 8 kHz) depending on transducer. For statistical analysis, nonresponses were coded as maximum ouput+10 dB. Additional details regarding audiometric examination are available online (2011-12 cycle: https://wwwn.cdc.gov/nchs/data/nhanes/2011-2012/manuals/Audiometry_Procedures_Manual.pdf and 2015-16 cycle: https://wwwn.cdc.gov/nchs/data/nhanes/2015-2016/manuals/2016_Audiometry_Procedures_Manual.pdf).

Consistent with previous reports (Spankovich & Le Prell 2013; Loprinzi & Joyner 2017; Spankovich et al. 2017) two puretone averages (PTA) were calculated: low- ($PTA_{0.5,1,2}$) and high-frequency ($PTA_{3,4,6,8}$). The worse ear was defined as that with a higher $PTA_{0.5,1,2}$ and hearing loss was defined as PTA >15 dB HL. Although more conservative than some previous reports, this approach is in line with clinical recommendations from the American Speech-Language-Hearing Association (Clark 1981) and allows us to capture slight hearing loss. Noise exposure history was determined via questionnaire regarding firearm use, Active-Duty military service, occupational noise exposure ≥3 months, and non-occupational loud noise exposure ≥10 hours/week (all Yes or No).

Determination of Smoking Status

Smoking status was ascertained from the 'Smoking – Cigarette Use', 'Smoking – Recent Tobacco Use', and 'Drug Use' questionnaires. Figure 2 is a decision tree that outlines criteria for the four smoking groups. To summarize, current regular tobacco smokers were participants who responded: (1) 'Yes' to "Have you smoked at least 100 cigarettes in your entire life?" (2) 'every day' or 'some days' to "Do you now smoke cigarettes?" and (3) 'No' to one or both of the following: "Have you ever smoked marijuana at least once a month for more than one year?" and "Have you ever, even once, used marijuana or hashish?" Current regular cannabis users were participants who responded: (1) 'Yes' to "Have you ever, even once, used marijuana or hashish?" (2) 'Yes' to "Have you ever smoked marijuana or hashish at least once a month for more than one year?" (3) '≤30 days' to "How long has it been since you last smoked marijuana or hashish at least once a month for one year?" and (4) 'No' to "Have you smoked at least 100 cigarettes in your entire life?" Co drug users were participants who met the first two criteria for current tobacco use and the first three criteria for current cannabis use. Finally, non-smokers were participants who responded: (1) 'No' to "Have you smoked at least 100 cigarettes in your entire life?" (2) 'No' to "Have you ever, even once, used marijuana or hashish?" and/or "Have you ever smoked marijuana or hashish at least once a month for more than one year?" Groups were mutually exclusive.

Model Covariates

We selected model covariates based on past reports. The following factors were considered: age (Agrawal et al. 2008; Goderie et al. 2019), race/ethnicity (Agrawal et al. 2008; Goman & Lin 2016), diabetes (Bainbridge et al. 2008; Akinpelu et al. 2014), hypertension (Lin et al. 2016), and education (Nash et al. 2011). Race/ethnicity was classified as non-Hispanic white, non-Hispanic black, non-Hispanic Asian, Mexican American, other Hispanic, and other (including multiracial). Diabetes was defined as self-reported physician diagnosis, use of diabetic medication, or fasting plasma glucose ≥126 mg/dL (as per Hoffman et al. 2017). Hypertension was defined as self-reported physician diagnosis, use of antihypertensives, or average of four blood pressure measurements ≥130 (systolic) or ≥80 mm Hg (diastolic) based on current guidelines (Whelton et al. 2018). We included four noise exposure variables in fully adjusted models: firearm use, Active-Duty military service, occupational noise exposure ≥3 months, and non-occupational loud noise exposure ≥10 hours/week.

Statistical Analysis

We combined data from NHANES 2011 to 2012 and 2015 to 2016. We performed logistic regression to determine multivariable adjusted odds ratios [MVOR (95% CI)] of low- and high-frequency hearing loss ($PTA_{0.5,1,2}$ and $PTA_{3,4,6,8}$ >15 dB HL, respectively) by smoking status (current regular tobacco smoker, current regular cannabis smoker, co-drug user, or non-smoker). Fully adjusted multivariable models included age, race/ethnicity, hypertension, diabetes, education, and all noise exposure variables as covariates. We used NHANES sample weights, which reflect the differential probability of selection, in analyses per National Center for Health Statistics guidelines (2018). Data from these 2705 participants represent 63.7 million people in the United States. Variance estimation accounted for the complex survey design. We used residual degrees of freedom calculated from design degrees of freedom in our models. Models were generated using the svyglm function (Lumley & Scott 2017) in R [R Core Team (2019) v. 3.6.1].

RESULTS

In Table 1, we present demographic data. Most participants (75.85%) were nonsmokers. Only 2.20% of the study population reported smoking cannabis without co-use of tobacco. Cannabis and co-drug use were more common in males than females; tobacco use was comparable between males and females. Table 2 displays demographic data for the four smoking groups. Of the four groups, tobacco smokers were the oldest and had the highest prevalence of diabetes and hypertension. The tobacco smoking group also reported the greatest occupational noise exposure, firearm use, and military service.

In Table 1 in Supplemental Digital Content 1, http://links.lww.com/EANDH/B10, we show the frequency of tobacco

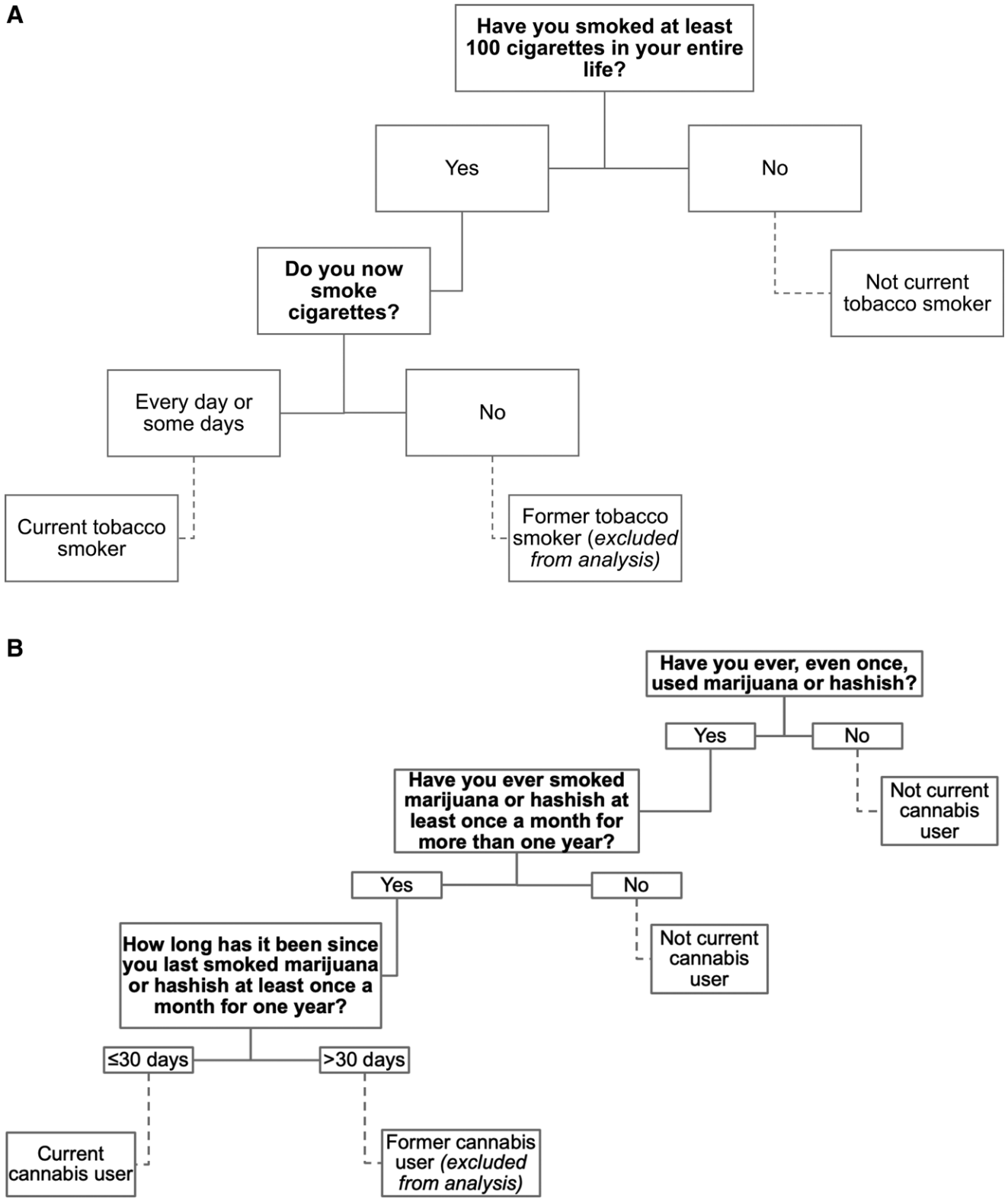

Fig. 2. Decision tree showing classification of smoking groups. A, Tobacco smoking classification, (B) cannabis smoking classification, (C) final determination of smoking Status. Questions from 'Smoking – Cigarette Use' (A), 'Smoking – Recent Tobacco Use' (A), and 'Drug Use' (B and C) National Health and Nutrition Examination Survey questionnaires.

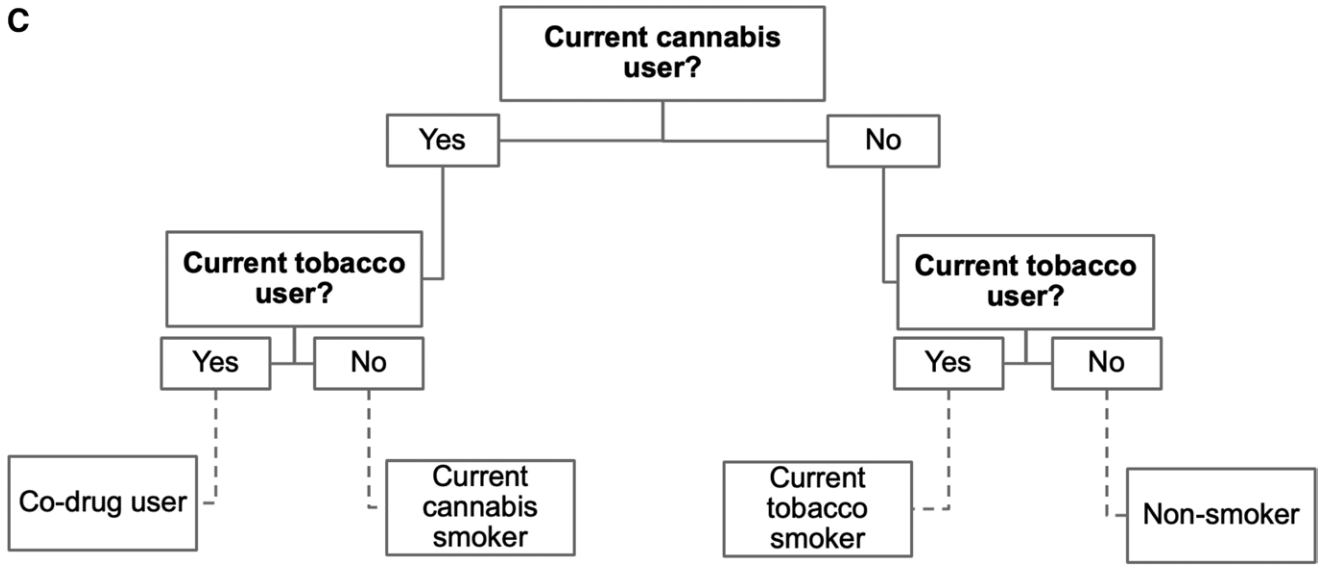

Fig. 2. Continued.

smoking (days smoked in last 30 days), quantity of cigarettes smoked per day over the last 30 days, and years of smoking. For males, tobacco smokers smoked more frequently [26.75 (0.86) versus 22.82 (1.18) days] and consumed a greater number of cigarettes in the last 30 days [14.05 (1.37) versus 12.04 (1.39) days] than co-drug users. In contrast, amongst females, these two metrics were comparable between smoking groups. For both sexes, tobacco smokers reported more years of smoking than co-drug users. Table 3 shows the weighted prevalence of hearing loss by smoking group. In the overall sample, the prevalence of low-frequency hearing loss was the highest among co-drug users and the lowest in cannabis smokers (24.72% and 8.14%, respectively). For males, the prevalence of low-frequency hearing loss was highest in co-drug users (31.65%) and lowest in cannabis smokers (5.35%). Similar trends were observed for high-frequency hearing loss although co-drug users and tobacco smokers had close prevalence estimates (60.88% and 61.57%, respectively). For females, tobacco smokers had the highest prevalence of low- and high-frequency hearing loss (28.30% and 55.84%, respectively). Low-frequency hearing loss was nearly twice as prevalent in female tobacco smokers than male tobacco smokers (28.30% vs. 15.76%, respectively). Low-frequency hearing loss was also more prevalent in female cannabis smokers than male cannabis smokers (12.92% versus 5.35%). For all other comparisons, males had higher prevalence of hearing loss than females.

Age-sex-adjusted odds ratios for low- and high-frequency hearing loss are shown in Table 4. Tobacco smokers had significantly increased odds of low- and high-frequency hearing loss (OR = 1.58, 95% CI: 1.05 to 2.37 and OR = 1.97, 95% CI: 1.58 to 2.45, respectively). Co-drug use was also associated with low- and high-frequency hearing loss (OR = 2.07, 95% CI: 1.10 to 3.91 and OR = 2.24, 95% CI: 1.27 to 3.96, respectively). In the fully adjusted multivariable model, only one association between smoking and hearing loss remained significant: that between tobacco smoking and high-frequency hearing loss (MVOR = 1.64, 95% CI: 1.28 to 2.09). Relationships between hearing loss and co-drug use were not statistically significant although MVORs for both low- and high-frequency loss were above 1.5.

DISCUSSION

This is the first population-based study to explore the relationship between cannabis and co-drug (cannabis and tobacco) use and hearing. In this nationally representative cross-sectional study of 2705 US adults, we identified a relationship between tobacco smoking and high-frequency hearing loss. This observation persisted after adjustment for potential confounders including age, race/ethnicity, hypertension, diabetes, education, and noise exposure.

In the overall sample, the prevalence of low-frequency hearing loss was highest amongst co-drug users (24.72%) and current regular tobacco smokers (22.78%; Table 3). Similarly, high-frequency hearing loss was most prevalent amongst tobacco smokers (58.36%) and co-drug users (54.63%). Previous studies, including those from the NHANES, have described similar findings in terms of tobacco smoking. For example, the NHANES 1999 to 2004 reported higher prevalence of hearing loss in tobacco smokers vs. non-smokers (Agrawal et al. 2008). Relatedly, the Korean NHANES identified a higher prevalence of hearing loss in smokers compared to non-smokers amongst participants in their 40s, 50s, and 60s (Chang et al. 2016). An analysis of Epidemiology of Hearing Loss Study participants aged 48 to 79 years is also in agreement with these collective findings (Cruickshanks et al. 1998).

In the current study, the distribution of hearing loss across smoking groups differed by sex. The prevalence of low-frequency hearing loss was approximately twice as high in male co-drug users than males who used tobacco alone. This was not the case in female participants. This finding is likely related to tobacco smoking dose: male co-drug users reported smoking more cigarettes per day and more days of smoking within the past 30 days than males who smoked tobacco exclusively (see Table 1 in Supplemental Digital Content 1, http://links.lww.com/EANDH/B10). However, male tobacco smokers reported more years of smoking than co-drug users (22.19 versus 20.57 years, respectively). Evidence of a dosage effect has been reported in previous studies (Fransen et al. 2008; Dawes et al. 2014; Hu et al. 2019). Our findings may also relate to

TABLE 1. Characteristics among participants in the NHANES 2011–2012 and 2015–2016, United States

	Male (*n*=1178)			Female (*n*=1527)			Combined (*n*=2705)		
Characteristic	Mean or %	SE	*N*	Mean or %	SE	*N*	Mean or %	SE	*N*
Age, years	38.84	0.45	1178	39.86	0.47	1527	39.41	0.36	2705
Race/ethnicity									
Mexican American	10.23%	0.02	168	10.56%	0.02	266	10.42%	0.02	434
Other Hispanic	8.22%	0.01	136	7.68%	0.01	193	7.92%	0.01	329
Non-Hispanic White	62.03%	0.03	379	61.76%	0.03	483	61.88%	0.03	862
Non-Hispanic Black	10.03%	0.02	243	11.59%	0.02	342	10.90%	0.02	585
Non-Hispanic Asian	6.87%	0.01	210	5.55%	0.01	200	6.13%	0.01	410
Other race (including multiracial)	2.61%	0.01	42	2.85%	0.01	43	2.75%	0.00	85
Smoking status									
Nonsmoker	73.52%	0.02	832	77.68%	0.02	1230	75.85%	0.01	2062
Current regular cannabis	3.16%	0.01	39	1.45%	0.00	25	2.20%	0.00	64
Current regular tobacco	15.89%	0.02	204	15.88%	0.01	208	15.89%	0.01	412
Co-drug user	7.44%	0.01	103	4.98%	0.01	64	6.06%	0.01	167
Educational level									
Less than 9th grade	5.03%	0.01	94	4.08%	0.01	108	4.50%	0.01	202
9–11th grade (includes 12th grade with no diploma)	10.09%	0.01	146	7.15%	0.01	154	8.44%	0.01	300
High school graduate/GED or equivalent	19.36%	0.02	246	18.18%	0.02	291	18.70%	0.01	537
Some college or AA degree	26.18%	0.01	309	32.96%	0.02	498	29.97%	0.01	807
College graduate or above	39.34%	0.03	383	37.63%	0.03	476	38.39%	0.03	859
Diabetes, yes	7.78%	0.01	111	7.32%	0.01	149	7.52%	0.01	260
Hypertension, yes	43.18%	0.02	532	32.74%	0.01	535	37.34%	0.01	1067
Noise exposure									
Occupational									
No	59.17%	0.03	728	82.10%	0.02	1278	72.00%	0.02	2006
Yes	40.83%	0.03	450	17.90%	0.02	249	28.00%	0.02	699
Other noise exposure									
No	82.64%	0.02	999	93.26%	0.01	1440	88.58%	0.01	2439
Yes	17.36%	0.02	179	6.74%	0.01	87	11.42%	0.01	266
Firearm use									
No	39.46%	0.02	618	68.77%	0.02	1194	55.86%	0.02	1812
Yes	60.54%	0.02	560	31.23%	0.02	333	44.14%	0.02	893
Military service									
No	90.00%	0.01	1074	98.31%	0.01	1505	94.65%	0.01	2579
Yes	10.00%	0.01	104	1.69%	0.01	22	5.35%	0.01	126
Puretone average, dB HL									
Low-frequency*									
Better ear	7.22	0.32	1178	7.06	0.33	1527	7.13	0.24	2705
Worse ear	10.09	0.38	1178	9.84	0.35	1527	9.95	0.27	2705
Hearing loss, yes	15.69%	0.02	183	16.44%	0.02	246	16.11%	0.01	429
High-frequency†									
Better ear	19.08	0.71	1178	14.46	0.46	1527	16.50	0.46	2705
Worse ear	21.40	0.84	1178	15.54	0.47	1527	18.12	0.51	2705
Hearing loss, yes‡	50.54%	0.02	577	38.52%	0.02	564	43.81%	0.02	1141

Sample weights applied.
**Defined as average threshold in dB HL at 0.5, 1, 2 kHz in the worse ear*
†Defined as average threshold in dB HL at 3, 4, 6, 8 kHz in the worse ear
‡Defined as PTA > 15 dB HL
PTA, pure-tone average; SE, standard error of the mean.

other health and lifestyle differences between the two groups. As shown in Table 2, compared with co-drug users, tobacco smokers have higher prevalence of diabetes and hypertension and report greater noise exposure for three of the four noise exposure categories.

Our age-sex-adjusted logistic regression analysis revealed a significant relationship between smoking (tobacco and co-drug) and hearing loss (Table 4). However, the fully adjusted multivariable model shows that only tobacco smoking is associated with hearing loss, specifically $PTA_{3,4,6,8}$. This finding agrees with earlier reports (Fransen et al. 2008; Agrawal et al. 2009; Engdahl et al. 2015) including one from the NHANES (Agrawal et al. 2009) that identified significant relationships between tobacco smoking and hearing loss, most notably at high frequencies. The Health Aging, and Body Composition study found that tobacco smoking was associated with hearing loss in males (Helzner et al. 2011) but their participants were considerably older than ours (~78 years versus ~39 years) limiting direct comparisons. Longitudinal data provide additional insight. Hu et al. (2019), in a study of 50195 predominantly male Japanese employees aged similarly to participants in our study, identified increased risk of low- and high-frequency hearing loss in tobacco smokers compared with non-smokers. However, support for the tobacco-hearing loss link remains inconsistent, even amongst NHANES investigations. For example, an NHANES (2005 to 2006) analysis restricted to participants aged ≥70 years failed to

TABLE 2. Characteristics among participants in the NHANES 2011–12 and 2015–16, United States by smoking group

	Non-Smokers (*n*=2062)			Cannabis Smokers (*n*=64)			Tobacco Smokers (*n*=412)			Co-Drug Users (*n*=167)		
Characteristic	Mean or %	SE	*N*	Mean or %	SE	*N*	Mean or %	SE	*N*	Mean or %	SE	*N*
Age, years	39.21	0.47	2062	31.80	2.24	64	41.71	0.66	412	38.71	1.52	167
Sex, male	42.69%	0.01	832	63.13%	0.09	39	44.06%	0.03	204	54.02%	0.06	103
Race/ethnicity												
Mexican American	10.96%	0.02	350	7.59%	0.04	7	9.59%	0.02	62	6.80%	0.02	15
Other Hispanic	8.26%	0.01	262	11.31%	0.05	8	7.33%	0.02	49	3.90%	0.01	10
Non-Hispanic White	60.48%	0.03	591	53.09%	0.10	18	68.11%	0.05	180	66.36%	0.04	73
Non-Hispanic Black	10.73%	0.02	435	21.55%	0.06	25	8.17%	0.02	72	16.28%	0.03	53
Non-Hispanic Asian	7.25%	0.01	365	1.31%	0.01	2	3.11%	0.01	36	1.85%	0.01	7
Other race (including multiracial)	2.31%	0.00	59	5.14%	0.03	4	3.71%	0.01	13	4.81%	0.01	9
Educational level												
Less than 9th grade	4.49%	0.01	155	1.99%	0.02	2	5.11%	0.01	35	3.98%	0.01	10
9–11th grade (includes 12th grade with no diploma)	5.73%	0.01	174	10.49%	0.04	9	17.06%	0.02	80	19.05%	0.03	37
High-school graduate/GED or equivalent	14.87%	0.01	350	18.73%	0.06	15	28.13%	0.03	108	41.81%	0.05	64
Some college or AA degree	28.52%	0.01	595	46.66%	0.07	30	36.11%	0.04	136	26.02%	0.04	46
College graduate or above	46.39%	0.03	788	22.11%	0.09	8	13.59%	0.03	53	9.14%	0.04	10
Diabetes, yes	7.67%	0.01	206	4.12%	0.03	4	8.23%	0.01	43	5.07%	0.03	7
Hypertension, yes	35.70%	0.01	777	30.01%	0.09	18	45.80%	0.04	200	38.30%	0.04	72
Noise exposure												
Occupational												
No	76.21%	0.02	1611	64.37%	0.06	46	58.02%	0.04	258	58.69%	0.04	91
Yes	23.79%	0.02	451	35.63%	0.06	18	41.98%	0.04	154	41.31%	0.04	76
Other noise exposure												
No	90.33%	0.01	1904	81.09%	0.05	50	87.15%	0.02	361	73.17%	0.04	124
Yes	9.67%	0.01	158	18.91%	0.05	14	12.85%	0.02	51	26.83%	0.04	43
Firearm use												
No	56.83%	0.02	1436	64.68%	0.08	44	50.84%	0.03	238	53.64%	0.04	94
Yes	43.17%	0.02	626	35.32%	0.08	20	49.16%	0.03	174	46.36%	0.04	73
Military service												
No	94.79%	0.01	1969	100.00%	0.00	64	93.52%	0.02	386	93.85%	0.03	160
Yes	5.21%	0.01	93	0.00%	0.00	0	6.48%	0.02	26	6.15%	0.03	7
Puretone average, dB HL												
Low-frequency*												
Better ear	6.61	0.23	2062	5.39	0.68	64	9.25	0.55	412	8.78	0.91	167
Worse ear	9.37	0.25	2062	7.69	0.87	64	12.17	0.72	412	12.17	1.13	167
High-frequency†												
Better ear	15.68	0.50	2062	11.27	1.06	64	19.68	0.82	412	20.30	1.68	167
Worse ear	17.28	0.59	2062	12.47	1.24	64	21.42	0.95	412	22.13	1.95	167

Sample weights applied.
**Defined as average threshold in dB HL at 0.5, 1, 2 kHz in the worse ear.*
†Defined as average threshold in dB HL at 3, 4, 6, 8 kHz in the worse ear.
PTA, pure-tone average; SE, standard error of the mean.

TABLE 3. Weighted prevalence [% (SE)] of hearing loss (worse ear) stratified by sex

	Male		Female		Combined	
Smoking status	%	SE	%	SE	%	SE
Low-frequency hearing loss*						
Non-smoker	14.50%	1.33%	14.08%	1.52%	14.26%	1.01%
Current regular cannabis	5.35%	2.68%	12.92%	6.34%	8.14%	2.63%
Current regular tobacco	15.76%	3.92%	28.30%	5.14%	22.78%	3.10%
Co-drug user	31.65%	8.98%	16.58%	6.49%	24.72%	6.00%
High-frequency hearing loss†						
Non-smoker	47.93%	2.69%	34.73%	1.81%	40.36%	1.73%
Current regular cannabis	31.46%	9.82%	21.83%	9.21%	27.91%	7.71%
Current regular tobacco	61.57%	3.59%	55.84%	3.24%	58.36%	2.27%
Co-drug user	60.88%	6.95%	47.29%	6.16%	54.63%	5.34%

NHANES 2011–12 and 2015–16, United States. Sample weights applied.
**Defined as average threshold in dB HL at 0.5, 1, 2 kHz > 15 dB HL.*
†Defined as average threshold in dB HL at 3, 4, 6, 8 kHz > 15 dB HL.

TABLE 4. Age-sex-adjusted OR (95% CI) and MVOR* (95% CI) for associations between smoking and hearing loss (PTA >15 dB HL, worse ear), NHANES 2011–12 and 2015–16

	Age- and Sex-Adjusted Model			Multivariable-Adjusted Model*		
	OR	95% CI	*P*	MVOR	95% CI	*P*
Low-frequency hearing loss†						
Current regular cannabis‡	0.87	(0.33–2.28)	0.771	0.84	(0.31–2.27)	0.713
Current regular tobacco	1.58	(1.05–2.37)	0.030	1.32	(0.87–2)	0.169
Co-drug user	2.07	(1.1–3.91)	0.027	1.57	(0.79–3.13)	0.176
High-frequency hearing loss§						
Current regular cannabis‡	0.98	(0.38–2.53)	0.963	0.92	(0.34–2.49)	0.854
Current regular tobacco	1.97	(1.58–2.45)	0.000	1.64	(1.28–2.09)	0.001
Co-drug user	2.24	(1.27–3.96)	0.007	1.85	(0.92–3.71)	0.079

Reference, non-smokers. Sample weights applied. Bold, statistically significant at the P≤0.05 level.
**Adjusted for age, sex, race/ethnicity, hypertension, diabetes, education, and noise exposure.*
†Defined as average threshold in dB HL at 0.5, 1, 2 kHz > 15 dB HL in the worse ear.
‡ Number of cannabis smokers with hearing loss is <10.
§Defined as average threshold in dB HL at 3, 4, 6, 8 kHz > 15 dB HL in the worse ear.
CI, confidence interval; MVOR, multivariable-adjusted odds ratio; OR, odds ratio.

find an association between tobacco smoking and hearing loss (Lin et al. 2011). Other population-based analyses including the Framingham Study (Gates et al. 1993) and a report from the all-male Health Professionals Follow-up Study (Shargorodsky et al. 2010) also suggest that tobacco smoking is not a significant risk factor for hearing loss. This may be further explained by confounding variables included in statistical models. For example, Spankovich & Le Prell (2013; 2014) found tobacco smoking was related to hearing status when adjusting for similar variables to the current study, however, the relationship was no longer statistically significant when dietary quality was added to the model. Some longitudinal examinations suggest significant relationships between tobacco smoking and prevalent, but not incident, hearing loss (Karlsmose et al. 2000; Gopinath et al. 2010; Rigters et al. 2018). Overall, this suggests that smoking by itself may be of minimal consequence for hearing loss, but rather overall health status including cardiovascular health, dietary health, and lifestyle factors including smoking may be of relevance. Further, though the relationship between these combined factors in general appear small in effect size, these variables are modifiable, unlike age, sex, and race/ethnicity.

The average participant age in our study was ~40 years old, which is considerably younger than participants evaluated in some earlier reports (e.g., Gates et al. 1993; Fransen et al. 2008; Gopinath et al. 2010; Helzner et al. 2011; Lin et al. 2011; Rigters et al. 2018) but close to others (Agrawal et al. 2009; Engdahl et al. 2015; Hu et al. 2019). On one hand, the relatively young age of NHANES participants is a strength of this study because any effect of smoking would not be overshadowed by aging. On the other hand, younger age effectively limits lifetime smoking dose. As such, auditory function might not have been affected to an extent that is identifiable using puretone audiometry. Hu et al. (2019) evaluated longitudinal changes in hearing sensitivity of tobacco smokers in the Japan Epidemiology Collaboration on Occupational Health Study. Average participant age in their study varied by smoking group (non-smokers, 43.3 years; past smokers, 46.3 years; current smokers, 42.8 years) and was close to the average age of participants in the present study. They reported a hazard ratio of unilateral high-frequency (4 kHz) hearing loss for smokers of 1.6 (95% CI: 1.5-1.7). Risk of high-frequency hearing loss was dose-dependent. There are important distinctions between Hu et al.'s study and ours. First, we used a different definition of high-frequency hearing loss ($PTA_{3,4,6,8}$ >15 dB HL). Using this definition, we identified significantly increased odds of high-frequency hearing loss in current tobacco smokers. However, frequency-specific analysis (*data not shown*) did not reveal an association between tobacco smoking and threshold elevation at 4 kHz. Second, Hu et al observed the greatest risk of high-frequency hearing loss in persons who smoked ≥21 cigarettes/day. This smoking dose is nearly twice the average dose reported by current tobacco smokers in our study. Last, there are notable demographic differences. Participants in Hu et al.'s study were Japanese, the majority (95%) of smokers were male, and the study took place in an occupational setting. It is therefore not representative of the general Japanese population.

The pathogenesis of acquired hearing loss in smokers is complex. Cigarette smoke contains upwards of 4000 chemical constituents (Burns 1991). Toxicants including carcinogens and carbon monoxide are present in both cannabis and tobacco smoke (Meier & Hatsukami 2016) although the Δ9-tetrahydrocannabinol in cannabis smoke may be protective against pro-carcinogens (Melamede 2005). Fechter et al. (1997) showed that carbon monoxide exposure results in high-frequency hearing loss in the guinea pig. Based on electrophysiological findings, the authors hypothesized the site of involvement is the junction between inner hair cells and Type 1 spiral ganglion cells. Moreover, their work suggests that carbon monoxide hypoxia gives rise to free radicals in the cochlea. In mice experimentally exposed to chronic cigarette smoke, spiral ganglion neurons exhibit increased oxidative stress compared to control neurons (Paquette et al. 2018). Further, nicotine administration in guinea pigs induces topographic changes to outer hair cell stereocilia (e.g., bending, disorganization, loss of stereocilia tip and side links), most markedly in the cochlear base (Abdel-Hafez et al. 2014).

In humans, the effects of smoking on auditory function may be direct (e.g., nicotine ototoxicity) and/or indirect (e.g., by increasing cardiovascular disease risk, which may then promote auditory dysfunction). It is well established that tobacco smoking can initiate atherogenesis [reviewed by Messner & Bernhard (2014)]. A high atherogenic index (defined as the ratio between non-high-density lipoprotein cholesterol and high-density lipoprotein cholesterol) was recently associated with hearing

loss in a study of Chinese adults (Zhang et al. 2020). Tobacco smokers also exhibit increased levels of C-reactive protein (Tracy et al. 1997; Ohsawa et al. 2005), a systemic inflammatory biomarker that has been associated with incident hearing loss (Nash et al. 2014). Numerous otoacoustic emission studies describe impaired cochlear function in cigarette smokers (e.g., Mustafa 2014) but few studies have been conducted to assay cochlear health in cannabis smokers. We previously reported subtle cochleopathology in young (18- to 29-year-old) cannabis smokers (Brumbach et al. 2019). Torre and Reed (2020) found reduced low-frequency otoacoustic emission amplitudes in cannabis smokers compared to non-users, but this finding was restricted to males. Future studies are needed to determine the extent to which tobacco and cannabis toxicant exposure in humans may lead to auditory dysfunction.

There are several notable strengths of our study. A diverse nationally representative population was studied and, with application of NHANES sample weights, the results can be generalized to the non-institutionalized U.S. adult population. We defined hearing loss using a strict cutoff of 15 dB HL thereby permitting identification of slight losses. Although population-based studies frequently employ a 25 dB cutoff, use of a lower cutoff is advantageous in several respects. Recently, subclinical hearing loss (defined using a 15 dB HL cutoff) was linked to cognitive decline in two nationally representative datasets, one of which was the NHANES (Golub et al. 2020). It has been argued that 15 dB HL should constitute the upper limit of normal hearing and in fact, persons with hearing in the clinically normal range of 15-25 dB HL have sought amplification (Martin & Champlin 2000). Finally, early evidence of cochlear dysfunction can be observed in persons with behavioral thresholds above 15 dB HL (Ohlms et al. 1991).

This study also has several limitations. First, cross-sectional analysis prohibits conclusions regarding causality. For example, the higher smoking prevalence among those with hearing loss may be explained by smoking activity in response to stress related to existing hearing loss or related tinnitus due to other factors. The smoking groups were carefully defined and mutually exclusive. However, the NHANES drug questionnaire does not query participants for specifics regarding their ingested cannabis products. Cannabis consumption can occur via numerous modalities such as smoking, vaping, ingestion, and topical application. The design of the NHANES drug questionnaire neither allows disambiguation between these consumption modalities nor provides specific information in terms of cannabis product potency. Despite use of two NHANES data cycles for this analysis, the sample size of cannabis smokers was low, as was the prevalence of hearing loss in this group, resulting in wide confidence intervals, between-group imbalances, and limiting interpretation of results from the cannabis smoking group. Cannabis use was determined via self-report which is potentially subject to under-reporting. It is therefore possible the prevalence of cannabis smokers in this study is an underestimate. Though possible, the literature suggests considerable underreporting of cannabis consumption is unlikely and is more common for drugs with greater stigma (e.g., cocaine; Harrison et al. 1997). A study of young adults [~21 years (range, 17 to 35 years)] found a high concordance (sensitivity of 91.8%; specificity of 89.6%) between self-reported cannabis use and urinalysis-detected cannabis metabolites (Zaldívar Basurto et al. 2009). The validity of self-reported cannabis consumption specific to survey research was assessed by Harrison et al. (1997) who compared self-report and urinalysis data finding congruence between the two indicators of drug use in 83.5% of cases. Harrison et al. also concluded that self-administered surveys generate higher prevalence estimates (and presumably, more valid data) than interviews that require participants to verbally respond. Participants in the NHANES self-report their drug use. Whether or not this study underestimated the prevalence of cannabis use, the low number of cannabis smokers remains a limitation. Finally, although we adjusted for numerous established covariates (e.g., sex, age, noise exposure, etc.), we did not adjust for all possible confounders. For example, other modifiable lifestyle factors such as dietary quality have been linked to hearing loss (Spankovich & Le Prell 2014) and, although beyond the scope of this study, might be considered in future investigations.

In conclusion, our study adds to the inconclusive body of evidence on the relationship between tobacco smoking and hearing loss and to the small but growing body of literature on auditory outcomes in cannabis users. We found an association between tobacco smoking and high-frequency hearing loss. Neither cannabis smoking in isolation nor co-drug use were associated with hearing loss. Additional research is warranted to determine if the relationships observed here also hold for incident hearing loss.

ACKNOWLEDGMENTS

Portions of this work were presented at the American Auditory Society conference, 6 March 2021 (virtual). Author contributions are as follows: R. R. B. designed the study, critically reviewed the results of statistical analysis, and drafted the article; J. W. S. performed statistical analysis, created tables and figures, interpreted results, and provided critical manuscript revisions; C. S. provided critical review of the data analysis plan, interpretative analysis, and critical article revisions; E. A. V. co-designed the statistical analysis plan, oversaw statistical analysis, provided interpretative analysis, and provided critical article revisions.

The data that support the findings of the study are openly available in the National Health and Nutrition Examination Survey data repository offered through the Centers for Disease Control and Prevention. Accessible here: https://wwwn.cdc.gov/nchs/nhanes/Search/DataPage.aspx?Component=Demographics&CycleBeginYear=2015

The authors have no relevant financial disclosures or conflicts of interest.

Address for correspondence: Rachael R. Baiduc, University of Colorado Boulder, Department of Speech, Language, and Hearing Sciences, 2501 Kittredge Loop Drive, 409 UCB, Boulder, CO, USA. E-mail: rachael.baiduc@colorado.edu

Received April 16, 2021; accepted February 3, 2022

REFERENCES

Abdel-Hafez, A. M., Elgayar, S. A., Husain, O. A., Thabet, H. S. (2014). Effect of nicotine on the structure of cochlea of guinea pigs. *Anat Cell Biol, 47*, 162–170.

Agrawal, Y., Platz, E. A., Niparko, J. K. (2008). Prevalence of hearing loss and differences by demographic characteristics among US adults: data from the National Health and Nutrition Examination Survey, 1999-2004. *Arch Intern Med, 168*, 1522–1530.

Agrawal, Y., Platz, E. A., Niparko, J. K. (2009). Risk factors for hearing loss in US adults: data from the National Health and Nutrition Examination Survey, 1999 to 2002. *Otol Neurotol, 30*, 139–145.

Akinpelu, O. V., Mujica-Mota, M., Daniel, S. J. (2014). Is type 2 diabetes mellitus associated with alterations in hearing? A systematic review and meta-analysis. *Laryngoscope, 124*, 767–776.

Bainbridge, K. E., Hoffman, H. J., Cowie, C. C. (2008). Diabetes and hearing impairment in the United States: audiometric evidence from the National Health and Nutrition Examination Survey, 1999 to 2004. *Ann Intern Med, 149*, 1–10.

Brant, L. J., Gordon-Salant, S., Pearson, J. D., Klein, L. L., Morrell, C. H., Metter, E. J., Fozard, J. L. (1996). Risk factors related to age-associated hearing loss in the speech frequencies. *J Am Acad Audiol, 7*, 152–160.

Brumbach, S., Goodman, S. S., Baiduc, R. R. (2019). Behavioral hearing thresholds and distortion product otoacoustic emissions in cannabis smokers. *J Speech Lang Hear Res, 62*, 3500–3515.

Burns, D. M. (1991). Cigarettes and cigarette smoking. *Clin Chest Med, 12*, 631–642.

Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey: Analytic Guidelines, 2011-2014 and 2015-2016. 2018. Hyattsville, MD: U.S. Department of Health and Human Services, CDC, (https://wwwn.cdc.gov/nchs/data/nhanes/analyticguidelines/11-16-analytic-guidelines.pdf).

Chang, J., Ryou, N., Jun, H. J., Hwang, S. Y., Song, J. J., Chae, S. W. (2016). Effect of Cigarette Smoking and Passive Smoking on Hearing Impairment: Data from a Population-Based Study. *PLoS One, 11*, e0146608.

Chen, T. C., Clark, J., Riddles, M. K., Mohadjer, L. K., Fakhouri, T. (2020). National Health and Nutrition Examination Survey, 2015-2018: Sample design and estimation procedures. *Vital Health Stat 2*, 184, 1–35.

Clark, J. G. (1981). Uses and abuses of hearing loss classification. *ASHA, 23*, 493–500.

Cruickshanks, K. J., Klein, R., Klein, B. E., Wiley, T. L., Nondahl, D. M., Tweed, T. S. (1998). Cigarette smoking and hearing loss: the epidemiology of hearing loss study. *JAMA, 279*, 1715–1719.

Davis, A. C. & Hoffman, H. J. (2019). Hearing loss: rising prevalence and impact. *Bull World Health Organ,* 97, 646–646A.

Dawes, P., Cruickshanks, K. J., Moore, D. R., Edmondson-Jones, M., McCormack, A., Fortnum, H., Munro, K. J. (2014). Cigarette smoking, passive smoking, alcohol consumption, and hearing loss. *J Assoc Res Otolaryngol, 15*, 663–674.

Engdahl, B., Aarhus, L., Lie, A., Tambs, K. (2015). Cardiovascular risk factors and hearing loss: The HUNT study. *Int J Audiol, 54*, 958–966.

Fransen, E., Topsakal, V., Hendrickx, J. J., Van Laer, L., Huyghe, J. R., Van Eyken, E., Lemkens, N., Hannula, S., Mäki-Torkko, E., Jensen, M., Demeester, K., Tropitzsch, A., Bonaconsa, A., Mazzoli, M., Espeso, A., Verbruggen, K., Huyghe, J., Huygen, P. L., Kunst, S., Manninen, M., et al. (2008). Occupational noise, smoking, and a high body mass index are risk factors for age-related hearing impairment and moderate alcohol consumption is protective: a European population-based multicenter study. *J Assoc Res Otolaryngol, 9*, 264–76; discussion 261.

Fechter, L. D., Liu, Y., Pearce, T. A. (1997). Cochlear protection from carbon monoxide exposure by free radical blockers in the guinea pig. *Toxicol Appl Pharmacol, 142*, 47–55.

Gates, G. A., Cobb, J. L., D'Agostino, R. B., Wolf, P. A. (1993). The relation of hearing in the elderly to the presence of cardiovascular disease and cardiovascular risk factors. *Arch Otolaryngol Head Neck Surg, 119*, 156–161.

Ghosh, S., Stansak, K., Walters, B. J. (2021). Cannabinoid Signaling in Auditory Function and Development. *Front Mol Neurosci, 14*, 678510.

Ghosh, S., Sheth, S., Sheehan, K., Mukherjea, D., Dhukhwa, A., Borse, V., Rybak, L. P., Ramkumar, V. (2018). The Endocannabinoid/Cannabinoid Receptor 2 System Protects Against Cisplatin-Induced Hearing Loss. *Front Cell Neurosci, 12*, 271.

Goderie, T. P. M., Stam, M., Lissenberg-Witte, B. I., Merkus, P., Lemke, U., Smits, C., Kramer, S. E. (2020). 10-Year Follow-Up Results of The Netherlands Longitudinal Study on Hearing: Trends of Longitudinal Change in Speech Recognition in Noise. *Ear Hear, 41*, 491–499.

Golub, J. S., Brickman, A. M., Ciarleglio, A. J., Schupf, N., Luchsinger, J. A. (2020). Association of Subclinical Hearing Loss With Cognitive Performance. *JAMA Otolaryngol Head Neck Surg, 146*, 57–67.

Goman, A. M., Lin, F. R. (2016). Prevalence of Hearing Loss by Severity in the United States. *Am J Public Health, 106*, 1820–1822.

Gopinath, B., Flood, V. M., McMahon, C. M., Burlutsky, G., Smith, W., Mitchell, P. (2010). The effects of smoking and alcohol consumption on age-related hearing loss: the Blue Mountains Hearing Study. *Ear Hear, 31*, 277–282.

Harrison, L. (1997). The validity of self-reported drug use in survey research: an overview and critique of research methods. *NIDA Res Monogr, 167*, 17–36.

Hasin, D. S., Shmulewitz, D., Sarvet, A. L. (2019). Time trends in US cannabis use and cannabis use disorders overall and by sociodemographic subgroups: a narrative review and new findings. *Am J Drug Alcohol Abuse, 45*, 623–643.

Helzner, E. P., Patel, A. S., Pratt, S., Sutton-Tyrrell, K., Cauley, J. A., Talbott, E., Kenyon, E., Harris, T. B., Satterfield, S., Ding, J., Newman, A. B. (2011). Hearing sensitivity in older adults: associations with cardiovascular risk factors in the health, aging and body composition study. *J Am Geriatr Soc, 59*, 972–979.

Hoffman, H. J., Dobie, R. A., Losonczy, K. G., Themann, C. L., Flamme, G. A. (2017). Declining Prevalence of Hearing Loss in US Adults Aged 20 to 69 Years. *JAMA Otolaryngol Head Neck Surg, 143*, 274–285.

Hong, J. W., Jeon, J. H., Ku, C. R., Noh, J. H., Yoo, H. J., Kim, D. J. (2015). The prevalence and factors associated with hearing impairment in the Korean adults: the 2010-2012 Korea National Health and Nutrition Examination Survey (observational study). *Medicine (Baltimore), 94*, e611.

Hu, H., Sasaki, N., Ogasawara, T., Nagahama, S., Akter, S., Kuwahara, K., Kochi, T., Eguchi, M., Kashino, I., Murakami, T., Shimizu, M., Uehara, A., Yamamoto, M., Nakagawa, T., Honda, T., Yamamoto, S., Hori, A., Nishiura, C., Okazaki, H., Imai, T., et al; Japan Epidemiology Collaboration on Occupational Health Study Group. (2019). Smoking, smoking cessation, and the risk of hearing loss: Japan epidemiology collaboration on occupational health study. *Nicotine Tob Res, 21*, 481–488.

Johnson, C. L., Dohrmann, S. M., Burt, V. L., Mohadjer, L. K. (2014). National Health and Nutrition Examination Survey: sample design, 2011-2014. *Vital Health Stat 2*, *162*, 1–33.

Karlsmose, B., Lauritzen, T., Engberg, M., Parving, A. (2000). A five-year longitudinal study of hearing in a Danish rural population aged 31-50 years. *Br J Audiol, 34*, 47–55.

Kiely, K. M., Anstey, K. J., Luszcz, M. A. (2013). Dual sensory loss and depressive symptoms: the importance of hearing, daily functioning, and activity engagement. *Front Hum Neurosci, 7*, 837.

Lin, B. M., Curhan, S. G., Wang, M., Eavey, R., Stankovic, K. M., Curhan, G. C. (2016). Hypertension, Diuretic Use, and Risk of Hearing Loss. *Am J Med, 129*, 416–422.

Lin, F. R., Thorpe, R., Gordon-Salant, S., Ferrucci, L. (2011). Hearing loss prevalence and risk factors among older adults in the United States. *J Gerontol A Biol Sci Med Sci, 66*, 582–590.

Loprinzi, P. D., & Joyner, C. (2017). Relationship between objectively measured physical activity, cardiovascular disease biomarkers, and hearing sensitivity using data from the national health and nutrition examination survey 2003-2006. *Am J Audiol, 26*, 163–169.

Lumley, T. & Scott, A. (2017). Fitting regression models to survey data. *Stat Sci*, *32*, 265–278.

Martin, F. N., & Champlin, C. A. (2000). Reconsidering the limits of normal hearing. *J Am Acad Audiol, 11*, 64–66.

Meier, E., & Hatsukami, D. K. (2016). A review of the additive health risk of cannabis and tobacco co-use. *Drug Alcohol Depend, 166*, 6–12.

Melamede, R. (2005). Cannabis and tobacco smoke are not equally carcinogenic. *Harm Reduct J, 2*, 21.

Messner, B., & Bernhard, D. (2014). Smoking and cardiovascular disease: mechanisms of endothelial dysfunction and early atherogenesis. *Arterioscler Thromb Vasc Biol, 34*, 509–515.

Mustafa, M. W. (2014). Transient evoked otoacoustic emissions and vestibular evoked myogenic potentials in cigarette and water pipe smokers. *Eur Arch Otorhinolaryngol, 271*, 2669–2673.

Nakanishi, N., Okamoto, M., Nakamura, K., Suzuki, K., Tatara, K. (2000). Cigarette smoking and risk for hearing impairment: a longitudinal study in Japanese male office workers. *J Occup Environ Med, 42*, 1045–1049.

Nash, S. D., Cruickshanks, K. J., Zhan, W., Tsai, M. Y., Klein, R., Chappell, R., Nieto, F. J., Klein, B. E., Schubert, C. R., Dalton, D. S., Tweed, T. S. (2014). Long-term assessment of systemic inflammation and the cumulative incidence of age-related hearing impairment in the epidemiology of hearing loss study. *J Gerontol A Biol Sci Med Sci, 69*, 207–214.

Nash, S. D., Cruickshanks, K. J., Klein, R., Klein, B. E., Nieto, F. J., Huang, G. H., Pankow, J. S., Tweed, T. S. (2011). The prevalence of hearing impairment and associated risk factors: the Beaver Dam Offspring Study. *Arch Otolaryngol Head Neck Surg, 137*, 432–439.

National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. (2014). *The Health Consequences of Smoking–50 Years of Progress: A Report of the Surgeon General*. Centers for Disease Control and Prevention (US).

Ohlms, L. A., Lonsbury-Martin, B. L., Martin, G. K. (1991). Acoustic-distortion products: separation of sensory from neural dysfunction in

sensorineural hearing loss in human beings and rabbits. *Otolaryngol Head Neck Surg, 104*, 159–174.

Ohsawa, M., Okayama, A., Nakamura, M., Onoda, T., Kato, K., Itai, K., Yoshida, Y., Ogawa, A., Kawamura, K., Hiramori, K. (2005). CRP levels are elevated in smokers but unrelated to the number of cigarettes and are decreased by long-term smoking cessation in male smokers. *Prev Med, 41*, 651–656.

Shargorodsky, J., Curhan, S. G., Eavey, R., Curhan, G. C. (2010). A prospective study of cardiovascular risk factors and incident hearing loss in men. *Laryngoscope, 120*, 1887–1891.

Nomura, K., Nakao, M., Morimoto, T. (2005). Effect of smoking on hearing loss: quality assessment and meta-analysis. *Prev Med, 40*, 138–144.

Paquette, S. T., Dawes, R. P., Sundar, I. K., Rahman, I., Brown, E. B., White, P. M. (2018). Chronic cigarette smoke exposure drives spiral ganglion neuron loss in mice. *Sci Rep, 8*, 5746.

Qian, Z. J., & Alyono, J. C. (2020). An association between marijuana use and tinnitus. *Am J Otolaryngol, 41*, 102314.

Rigters, S. C., van der Schroeff, M. P., Papageorgiou, G., Baatenburg de Jong, R. J., Goedegebure, A. (2018). Progression of Hearing Loss in the Aging Population: Repeated Auditory Measurements in the Rotterdam Study. *Audiol Neurootol, 23*, 290–297.

Shukla, A., Harper, M., Pedersen, E., Goman, A., Suen, J. J., Price, C., Applebaum, J., Hoyer, M., Lin, F. R., Reed, N. S. (2020). Hearing Loss, Loneliness, and Social Isolation: A Systematic Review. *Otolaryngol Head Neck Surg, 162*, 622–633.

Spankovich, C., Bishop, C., Johnson, M. F., Elkins, A., Su, D., Lobarinas, E., Le Prell, C. G. (2017). Relationship between dietary quality, tinnitus and hearing level: data from the national health and nutrition examination survey, 1999-2002. *Int J Audiol, 56*, 716–722.

Spankovich, C., & Le Prell, C. G. (2014). Associations between dietary quality, noise, and hearing: data from the National Health and Nutrition Examination Survey, 1999-2002. *Int J Audiol, 53*, 796–809.

Spankovich, C., & Le Prell, C. G. (2013). Healthy diets, healthy hearing: National Health and Nutrition Examination Survey, 1999-2002. *Int J Audiol, 52*, 369–376.

Torre, P. 3rd, & Reed, M. B. (2020). Self-Reported Drug Use and Hearing Measures in Young Adults. *J Speech Lang Hear Res, 63*, 885–895.

Tsai, J., Rolle, I. V., Singh, T., Boulet, S. L., McAfee, T. A., Grant, A. M. (2017). Patterns of marijuana and tobacco use associated with suboptimal self-rated health among US adult ever users of marijuana. *Prev Med Rep, 6*, 251–257.

Whelton, P. K., Carey, R. M., Aronow, W. S., Casey, D. E. Jr, Collins, K. J., Dennison Himmelfarb, C., DePalma, S. M., Gidding, S., Jamerson, K. A., Jones, D. W., MacLaughlin, E. J., Muntner, P., Ovbiagele, B., Smith, S. C. Jr, Spencer, C. C., Stafford, R. S., Taler, S. J., Thomas, R. J., Williams, K. A. Sr, Williamson, J. D., et al. (2018). 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol, 71*, 2199–2269.

Zaldívar Basurto, F., García Montes, J.M., Flores Cubos, P., Sánchez Santed, F., López Ríos, F., Molina Moreno, A. (2009). Validity of the self-report on drug use by university students: correspondence between self-reported use and use detected in urine. *Psicothema*, 21, 213–219.

Zhang, H., Wang, D., Ma, H., Ren, Y., Li, C., Zheng, Y., Dai, X., Yang, L., Xu, L. (2020). Increased atherogenic index in the general hearing loss population. *Open Med (Wars), 15*, 349–357.

Zheng, Y., Reid, P., Smith, P.F. (2015). Cannabinoid CB1 receptor agonists do not decrease, but may increase acoustic trauma-induced tinnitus in rats. *Front Neurol*, *18*, 6–60.