Cigarette smoking, passive smoking, alcohol consumption and hearing loss

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ABSTRACT

The objective of this large population-based cross-sectional study was to evaluate the association between smoking, passive smoking, alcohol consumption and hearing loss. The study sample was a subset of the UK Biobank resource, 164,770 adults aged between 40 and 69 years who completed a speech-in-noise hearing test (the Digit Triplet Test). Hearing loss was defined as speech recognition in noise in the better ear poorer than 2 standard deviations below the mean with reference to young normally hearing listeners. In multiple logistic regression controlling for potential confounders, current smokers were more likely to have a hearing loss than non-smokers (OR 1.15 95%CI 1.09-1.21). Among non-smokers, those who reported passive exposure to tobacco smoke were more likely to have a hearing loss (OR 1.28 95%CI 1.21-1.35). For both smoking and passive smoking, there was evidence of a dose-response effect. Those who consume alcohol were less likely to have a hearing loss than lifetime teetotalers. The association was similar across three levels of consumption by volume of alcohol (lightest 25%; OR 0.61 95%CI 0.57-0.65; middle 50%; OR 0.62 95%CI 0.58-0.66; heaviest 25%; OR 0.65 95%CI 0.61-0.70). The results suggest that lifestyle factors may moderate the risk of hearing loss. Alcohol consumption was associated with a protective effect. Quitting or reducing smoking and avoiding passive exposure to tobacco smoke may also help prevent or moderate age-related hearing loss.

INTRODUCTION

Age-related hearing impairment is highly prevalent, with 36.7% of UK adults aged between 61 and 70 years having hearing loss (mean hearing threshold level >25dB HL over 500 to 4000 Hz in the better ear; Davis, 1989). Hearing loss has been viewed as an inevitable consequence of aging (Gates and Mills, 2005). Encouragingly, there is some evidence that this may not be the case; some older individuals have normal hearing (Cruickshanks et al., 1998b), and in younger generations the prevalence of hearing loss is lower than in older generations (Zhan et al., 2009; Hoffman et al., 2012). Further, hearing loss is associated with various modifiable risk factors, including noise exposure (Agrawal et al., 2008), cardiovascular disease (Gates et al., 1993; Helzner et al., 2005), exercise (Hull and Kerschen, 2010) and diabetes (Horikawa et al., 2013). Smoking and alcohol consumption (reviewed below) may represent additional modifiable risks, presenting opportunities to delay the onset and/or moderate the severity of hearing loss.

Smoking may impact upon the auditory system via direct ototoxic effects of nicotine or other ototoxic substances found in cigarette smoke (Maffei and MianiI, 1962) or vascular effects, such as increased blood viscosity and reduced available oxygen causing cochlear hypoxia (Lowe et al., 1980; Browning et al., 1986).

Several studies report an association between hearing loss and smoking (Siegelaub et al., 1974; Barone et al., 1987; Rosenhall et al., 1993; Cocchiarella et al., 1995; Cruickshanks et al., 1998a; Noorhassim and Rampal, 1998; Nakanishi et al., 2000; Itoh et al., 2001; Sharabi et al., 2002; Mizoue et al., 2003; Palmer et al., 2004; Burr et al., 2005; Helzner et al., 2005; Nomura et al., 2005; Uchida et al., 2005; Pouryaghoub et al., 2007; Fransen et al., 2008; Gopinath et al., 2010) but the evidence is not entirely consistent (Gates et al., 1993; Brant et al., 1996). A 2005 meta analysis concluded that there are moderate-to-large associations between smoking and hearing loss[1] (Nomura et al., 2005). Passive smoking may also be associated with hearing loss; Cruickshanks and colleagues (1998a) reported that non-smokers who lived with a smoker were

[1] This meta analysis reported an overall risk ratio of 1.33 (95% CI 1.24-1.44) over five cross-sectional studies, 1.97 (1.44, 2.70) over 4 cohort studies, and 2.89 (2.26, 3.70) in one case-control study [27].

more likely to have hearing loss than those who did not live with a household member who smokes.

Moderate alcohol consumption - typically defined as consumption of one to two drinks per day – is associated with protective effect against cardiovascular disease (Baum-Baicker, 1985; Moore and Pearson, 1986; Rimm et al., 1991; Ronksley et al., 2011), possibly via increasing levels of high density lipoprotein cholesterol (HDL) and reduced coagulation (Pearson, 1996). In contrast, high levels of alcohol consumption are associated with increased risk of cardiovascular disease (Criqui, 1987). High levels of alcohol consumption do not result in increased HDL, but are associated with increased levels of low density lipoprotein, increased blood clotting, histological changes in the myocardium and reduced threshold for ventricular fibrillation, all linked to adverse cardiovascular outcomes (McKee and Britton, 1998).

Since cardiovascular disease may be associated with hearing loss (Johnsson, 1973; Rubinstein et al., 1977; Makishima, 1978; Susmano and Rosenbush, 1988; Gates et al., 1993; Brant et al., 1996), an effect of alcohol consumption on hearing may be via a cardiovascular causal pathway. The small amount of research in this area appears partly to bear this out; heavy drinking was associated with increased risk of hearing loss (Rosenhall et al., 1993; Popelka et al., 1998), or no increased risk versus nondrinkers (Itoh et al., 2001). Moderate alcohol consumption was associated with a protective effect on hearing (Popelka et al., 1998; Itoh et al., 2001; Helzner et al., 2005; Fransen et al., 2008; Gopinath et al., 2010). Findings are not consistent, however, as some studies have not detected any significant association between moderate or heavy alcohol consumption and hearing (Brant et al., 1996; Curhan et al., 2011).

In summary, smoking and passive smoking may be associated with hearing loss. There is some evidence for a protective effect of alcohol consumption against hearing loss. High levels of alcohol consumption are associated with reduced benefit compared to moderate levels of consumption, or with an increased risk of hearing loss. The aim of the present study was to test for associations between smoking, passive smoking, alcohol consumption and hearing loss, independent of age, sex, socio-economic status, ethnicity and other known risks for hearing loss (including cardiovascular factors, diabetes, ototoxic medications and noise exposure

(Cruickshanks et al., 2010)). The expectation was that smoking and passive smoking would be associated with greater risk of hearing loss. Moderate alcohol consumption would be associated with reduced risk, while higher levels of alcohol consumption would be associated with less benefit.

METHODS

This research was conducted using the UK Biobank (Collins, 2012), which contains data from over 500,000 people. The very large sample size was designed to facilitate research into the environmental and genetic causes of disease in middle and older age. Additional measures were added to the UK Biobank protocol throughout the duration of data collection, and so the present study focused on a subsample of 164,770 participants who completed a hearing test (the Digit Triplet Test, described below). Participants were aged between 40 to 69 years at the time of testing. UK Biobank recruitment took place between March 2007 and July 2010 via the UK National Health Service, and aimed to be as representative and inclusive as possible of the general UK population. Recruitment was via postal invitation with a telephone follow-up, and the overall response rate was 5.47%. Table 1 shows the sex, ethnicity and Townsend deprivation index score[2] (Norman, 2010) for the subset of the UK Biobank sample included in the present study versus the corresponding section of the UK population aged 40 to 69 years.

(Table 1 here)

The study sample contains a slightly higher proportion of females and people living in more affluent areas than in the general population. The proportion of White ethnicity is similar to that in the general population. Participants attended a UK Biobank assessment centre and provided written informed consent. They completed a 'whole body' assessment of 90 minutes duration that included a computerized questionnaire on lifestyle and medical history as well as physical measures, including hearing testing, BMI assessment and pulse wave arterial stiffness

[2] The Townsend deprivation scheme is a proxy measure of socioeconomic status that is widely used in health studies. It comprises four input variables on unemployment, non-car ownership, non-home ownership and household overcrowding based on area of residence, each of which is expressed as a z-score relative to the national level which are then summed to give a single deprivation score. Lower Townsend scores represent areas associated with less deprived (i.e. more affluent) socioeconomic status.

assessment. Detailed information about the assessment procedure and the additional data collected (not reported in the present study) may be found elsewhere (http://www.ukbiobank.ac.uk/).

Assessments

Hearing - Digit Triplet Test

The Digit Triplet Test (DTT) is a speech-in-noise test developed for reliable large-scale hearing screening (Smits et al., 2004; Vlaming et al., 2011). The DTT correlates strongly with measures of hearing sensitivity (PTA; $r = 0.77$ (Smits et al., 2004)) and with other speech-in-noise tests (for example, Sentences-in-Noise (Plomp and Mimpen, 1979); $r = 0.85$ (Smits et al., 2004)). The DTT is therefore a reliable measure of hearing impairment. As listening in noise is a key function of hearing and difficulty hearing in noise is the most common complaint by people with hearing loss, speech recognition testing in noise arguably provides a more ecologically valid measure than detection of tones in a quiet environment (Arlinger et al., 2009). In the version of the DTT used in the UK Biobank, fifteen sets of three monosyllabic digits were presented via circumaural headphones (Sennheiser HD-25). Left and right ears were tested separately with the order of testing randomized across participants. Participants first set the volume of stimuli to a comfortable listening level. Digits were then presented in background noise shaped to match the spectrum of the speech stimuli. Noise levels varied contingent on correct identification of the three digits via a touchscreen interface, with the SNR for 50% correct recognition threshold estimated adaptively. The recognition threshold was taken as the mean SNR for the last eight triplets. Lower (more negative) scores correspond to better performance. In the present study, hearing loss was based on performance of the better ear (i.e. the ear with the lower recognition threshold). Hearing loss was identified if the better ear recognition threshold was more than two standard deviations poorer with respect to a reference group of participants aged 18 to 29 years with normal hearing (defined as pure tone audiometric thresholds <25 dB HL between 250 Hz and 8,000 Hz bilaterally) (Dawes et al., 2014), i.e. a threshold greater than or equal to -5.5 dB.

Age, sex, ethnicity and socioeconomic status

Data on sex, age at time of assessment, ethnicity (2001 UK Census categories) and the Townsend deprivation score corresponding to area of residence were recorded for each participant. For the regression analyses, Townsend scores were categorized into quartiles from the least to the most deprived sections of the sample. Ethnicity was coded according to 'White' or 'Non-white' ethnic background.

Smoking

Smoking status was based on responses to two questions "Do you smoke tobacco now?" and "In the past, how often have you smoked tobacco?" Current smokers are those who reported currently smoking occasionally or on most or all days. Ex- smokers are those who reported previously smoking occasionally or on most or all days. Non-smokers are those who reported never smoking or who reported just having tried smoking once or twice. Current and ex-smokers were asked "About how many cigarettes do/did you smoke on average each day?" Pack-years were calculated according to daily consumption of cigarettes divided by 20 (to index the number of packs per day) and multiplied by the duration of smoking in years. Pack-year category was then assigned based on the bottom 25^{th} percentile (defined as greater than 0 and less than or equal to 10 pack-years), the middle range between the 25^{th} percentile and 75^{th} percentile (greater than 10 and less than or equal to 33 pack-years) and the top 25^{th} percentile (greater than 33 pack-years).

Non-smokers were asked the additional questions "At home, about how many hours per week are you exposed to other people's tobacco smoke?" and "Outside of your home, about how many hours per week are you exposed to other people's tobacco smoke?" Participants were identified as being exposed to tobacco smoke if they reported any weekly exposure either at home or outside the home. Exposure was quantified further by summing the weekly hours of exposure in and outside the home, then grouped according to three levels of exposure; no exposure, 1 hour or less per week, 2-9 hours per week and 10 or more hours per week.

Alcohol consumption

Alcohol drinkers and non-drinkers were identified on the basis of responses to the question "About how often do you drink alcohol?" Non-drinkers were identified on the basis of the response 'Never', while drinkers were identified on the basis of the remaining response options ('Special occasions only', 'One to three times a month', 'One or twice a week', 'Three or four times a week', 'Daily or almost daily'). Those answered 'Never' were asked the additional question "Did you previously drink alcohol?" ('Yes'/'No'). If participants had previously drunk alcohol, they were asked about the reason for giving up drinking[3].

The number of drinks per week was calculated on the basis of the summed total of reported weekly consumption of red wine, champagne or white wine, beer or cider, spirits, fortified wine or other alcoholic drinks. These frequencies were then transformed into grams of ethanol by multiplying by a conversion factor (18.4 for red white, champagne or white wine; 20 for beer or cider; 8 for fortified wine or spirits; 12 for other alcoholic drinks (House Of Commons Science and Technology Committee, 2012)[4]. Grams of ethanol for each type of drink were summed to provide the overall total grams of ethanol consumed per week. The total grams of ethanol consumed per week was then classified according to five categories: never drinkers (i.e. those who have never regularly drunk alcohol), ex-drinkers (those who have given up consumption alcohol), the lowest 25% of alcohol drinkers (the first 25th percentile; 1 to 118.4 grams of ethanol per week), the middle 50% (middle range between the 25th percentile and 75th percentile; 118.4 to 196.8 grams of ethanol per week) and highest 25% (the top 25 percentile; greater than 196.8 grams of ethanol per week). The 'highest' range includes levels of alcohol consumption that are considered 'hazardous' to general health (The Royal College of Psychiatrists, 2011).

Cardiovascular disease, cholesterol, hypertension and diabetes.

[3] Ex-drinkers were asked the question "Why did you stop drinking alcohol?" ('Illness or ill health', 'Doctor's advice', 'Health precaution', 'Financial reasons', 'Other reason', 'Do not know' or 'Prefer not to answer'). 48.6% reported stopping drinking for reasons of illness, doctor's advice or as a health precaution.

[4] There are 8 grams (10 ml) of alcohol in a standard drink in the UK, equal to one 'unit'. A medium sized glass of wine or champagne is 2.3 units. One pint of full-strength beer or cider is 3 units, while light beer or cider is 2 units. In the present study, one serve of beer or cider was taken as being equal to 2.5 units. One shot of spirits or fortified wine is 1 unit. Alcopops and other forms of alcohol count as 1.5 units [52]. The alcohol content in grams of each type of drink was calculated by multiplying the number of units by 8. One unit or standard drink is 14 grams of alcohol in the US, 10 grams in Australia, and 19.75 grams in Japan.

Cardiovascular disease was identified on the basis of self-report of any cardiovascular problem, including angina, heart attack, heart failure, stroke, transient ischemic attack, intermittent claudication, arterial embolism or deep venous thrombosis. High cholesterol was identified if the participant reported that they had high cholesterol, or that they were currently taking medication for high cholesterol. Hypertension was identified if the participant reported that they had hypertension, currently took medication for high blood pressure, or had a measured systolic blood pressure greater than 140 mm Hg or diastolic pressure greater than 90 mm Hg. Diabetes was identified if the participant reported that they had Type 1 or Type 2 diabetes, or that they currently look insulin for diabetes.

Pulse wave arterial stiffness index and BMI

Pulse wave arterial stiffness index was calculated as the time between peaks of the pulse waveform measured at the finger via infrared sensor divided by the participant's height. Pulse wave measurement was performed with a PulseTrace PCA2 (CareFusion, USA). For details of pulse wave measurement, see http://biobank.ctsu.ox.ac.uk/crystal/field.cgi?id=21021). Body mass index (BMI) was calculated as the participants weight (in kilograms) divided by height squared (in metres).

Physical activity, ototoxic medication, occupation- and music-related noise exposure

Participants were classified as active if they reported doing over 30 minutes of moderate physical activity on the day prior to assessment, in response to the question "Yesterday, about how long did you spend doing activities that needed moderate effort, making you somewhat short of breath? For example walking upstairs, going to the gym, jogging, energetic dancing, aerobics, most sports, using heavy power tools and other physically demanding DIY & gardening." Participants were classified as 'inactive' if they reporting doing less than 10 minutes or no physical activity. Work noise exposure was identified on the basis of any reported noise exposure in response to the question "Have you ever worked in a noisy place where you had to shout to be heard?" Music noise exposure was identified on the basis of any reported exposure in response to the question "Have you ever listened to music for more than 3 hours per week at a volume which you would need to shout to be heard or, if wearing headphones, someone else

would need to shout for you to hear them?" The criterion for work and music related noise roughly corresponds to exposure exceeding 85 dB(A) (Health and Safety Executive, 1989). All medications that were currently being taken regularly (daily, weekly, or monthly) were recorded, not including short-term medications (e.g. a 1 week course of antibiotics) or prescribed medications that were not taken. All medications with known ototoxicity were coded as ototoxic, including loop diuretics, aminoglycoside antibiotics, quinine derivatives, non-steroidal anti-inflammatories and salicylates.

Data analysis

Analyses were performed with IBM SPSS version 20. Logistic regression was used to model the effects of alcohol and smoking and other covariates on hearing loss. As shown in Table 2, for some measures such as Pulse wave stiffness and Physical activity there were missing data. The primary reason for these missing data is that measures were added to the study protocol at different time points over the course of data collection. As the reason for missing data was not systematically related to hearing or to any other variable, it was assumed that data are missing completely at random. Missing variable analysis did not identify any pattern to the missing data.

Potential confounders (Table 2) were selected on the basis of having been implicated with hearing loss in previous research (Gates and Mills, 2005; Cruickshanks et al., 2010). Variables included SES (Townsend index; First, Second, Third and Fourth quartile), BMI, Pulse wave stiffness index, ethnicity (White/non-White), hypertension (Yes/No), cardiovascular disease (Yes/No), high cholesterol (Yes/No), ototoxic medication (Yes/No), diabetes (Yes/No), physical activity (Yes/No), occupational noise exposure (Yes/No), music noise exposure (Yes/No), alcohol consumption (Never drinker/Ex drinker/Lowest/Middle/Highest drinkers) and smoking status (Never/Ex smoker/Current). To evaluate the main effects of smoking and alcohol consumption, all variables were entered simultaneously. Non-significant contributors from that multi-variable regression were excluded, and the regression re-run retaining only those variables that were important effect modifiers. The variables that were excluded from the multi-variable final

model were pulse wave stiffness index, BMI, hypertension, music noise exposure and physical activity.

In order to evaluate dose-response effects for smoking, current and ex-smokers were selected. Regression with all covariates was re-run for this subset of participants with the pack-year categorical variable (Lowest/Middle/Highest number of pack-years) substituted for smoking status. To test for effects of passive exposure to tobacco smoke and dose-response effects of passive exposure in non-smokers, a regression model was re-run with all covariates and the passive exposure variables were substituted for the smoking status variable. For these analyses, non-significant contributing variables were dropped from the final regression model. The final models for each analysis differed slightly from the model for all participants since those variables not significantly contributing to the model were excluded.

RESULTS

Table 2 shows the characteristics of normal hearing and hearing impaired participants, according to demographic variables age, sex, SES and ethnicity as well as alcohol consumption and smoking status and covariates. Each variable was entered into a logistic regression along with age and sex with hearing status as the dependent measure to provide a *p*-value for its association with hearing loss independent of age and sex. Significant *p* values in Table 2 suggest that the variable is a potential confounder. All variables were significantly associated with hearing loss except sex.

(Table 2 here)

Smoking and alcohol consumption

To evaluate the main effects of smoking and alcohol consumption, all variables were entered simultaneously into a multi-variable logistic regression model. Non-significant contributors from the initial model were excluded, and the regression model re-run retaining only those variables that were important effect modifiers in the multi-variable model. The variables that were excluded from the final model were pulse wave stiffness index, BMI, hypertension, music noise exposure and physical activity. Table 3 shows the final multi-variable regression model for

hearing loss. Nagelkerke[5] r^2 for the model was 0.10. Both alcohol consumption status and smoking status were significantly associated with hearing loss. Current smokers were at higher odds[6] of hearing loss than never smokers, although ex-smokers were at slightly less odds of hearing loss than never smokers. Compared to lifetime non-drinkers, all categories of current drinkers were similarly less likely to have hearing loss.

(Table 3)

Smoking dose-response analysis

Compared to the bottom 25% of smokers by pack-year, those in the middle 50% and top 25% had greater odds of hearing loss in a final regression model (Table 4) that included age, cholesterol, occupation-related noise exposure, ethnicity, alcohol consumption and SES. Higher ORs for those with a higher 'dose' of smoking (represented by pack-years) indicates that higher doses of smoking are associated with increased odds of hearing loss. This is consistent with a dose-response effect for smoking.

Passive exposure to tobacco smoke

Non-smokers who were exposed to tobacco smoke were more likely to have hearing loss than non-smokers with no exposure in a final regression model (Table 5) that included age, sex, ethnicity, cardiovascular disease, diabetes, hypertension, occupation-related noise exposure and alcohol consumption. Regression modeling of dose effects revealed that those who reported 1 hour or less weekly passive exposure to tobacco smoke were at no additional risk compared to non-smokers with no exposure (OR 1.00 95% CI 0.94-1.07), while those that reported between 2-9 hours of weekly exposure and over 10 hours per week were at progressively higher odds of hearing loss (OR 1.28 95% CI 1.18-1.39; OR 1.39 95% CI 1.19-1.61).

[5] In linear regression models, the coefficient of determination r^2 indicates the proportion of the variance in the outcome variable that is associated with the predictor variable(s). Larger r^2 values suggest more variation is explained by the model. For logistic regression models, it is not possible to compute an r^2 statistic that is directly comparable to the r^2 in a linear regression model, and a pseudo- r^2 such as Nagelkerke r^2 are calculated as an approximation. Pseudo r^2 measures tend to be lower than the r^2 statistic used with linear regression models.

[6] Odds ratios (OR) are measures of association between an exposure (e.g. smoking) and an outcome (e.g. hearing loss). The OR is the odds that the outcome will occur given the exposure compared to the odds of the outcome occurring without the exposure. An OR greater than 1 for an exposure indicates increased odds of the outcome, while an OR less than 1 indicates reduced odds of the outcome. If the 95% confidence interval for the OR crosses the 0 point, this indicates that the OR is not statistically significantly different from 0 at a level of α= 0.05.

Increasing odds of hearing loss with increasing amounts of passive exposure to tobacco smoke was consistent with a dose-dependent effect.

(Table 4 and 5)

DISCUSSION

Smoking

In the present study, current smokers were at 15.1% higher odds of hearing loss than non-smokers. The most recent survey estimated the proportion of smokers in the UK adult population at 20% (Office for National Statistics, 2012), and rates of up to 60% are reported in other countries (World Health Organisation, 2013). Given such high levels of exposure and evidence of a substantial association between smoking and hearing loss, smoking may represent a significant contributor to hearing loss worldwide. Note that the association between smoking and hearing loss was observed in a regression model that included cardiovascular disease. This might suggest that smoking has an impact on hearing via causal pathways in addition to cardiovascular ones, such as via direct ototoxic effect of tobacco smoke (Maffei and MianiI, 1962; Guth and Norris, 1996). Alternatively, the measures of cardiovascular disease in the present study may not have been sensitive to microvascular changes that could impact on hearing and not have fully captured the variance due to cardiovascular factors on hearing.

In addition to elevated risk associated with smoking, there was evidence of a dose-response effect, with the risk of hearing loss higher for those with higher dose, measured in pack-years of smoking. The present study provided the novel finding that passive exposure to tobacco smoke among non-smokers was associated with a 28% elevated risk of hearing loss, and that this association was dose-dependent. Note that the association between hearing loss and passive smoking appears stronger than the association between hearing loss and smoking. This may be partly because the odds for smoking were determined by comparing smokers with non-smokers. Some non-smokers may be exposed to tobacco smoke, and so the association between smoking and hearing loss may be underestimated.

One unexpected result not reported in previous research was that ex- smokers had slightly reduced risk of hearing loss than non-smokers. If this is a reliable result, it could perhaps be a reflection of a tendency for ex-smokers to adopt healthier lifestyles; the decision to stop smoking may be only one of several healthy lifestyle changes that may also impact upon hearing. With respect to cardiovascular disease, there is inconsistent evidence for residual risks for ex-smokers; some studies suggest little or no residual risk of smoking while others show some residual risk (Critchley and Capewell, 2003). The overall pattern identified by Critchley and Capewell's (2003) review was that there is a substantial and reliable reduction in risk for cardiovascular disease associated with quitting smoking. The present study suggests that the benefit of quitting or reducing smoking may extend to a reduction in the risk of hearing loss.

Alcohol consumption

Compared to those who have never consumed alcohol, all three levels of alcohol consumption were associated with around 40% reduced risk of hearing loss. The finding supports the small body of research to date (Popelka et al., 1998; Itoh et al., 2001; Fransen et al., 2008; Gopinath et al., 2010). Previous studies have shown either less or no association with very high levels of alcohol consumption (Itoh et al., 2001), or that very heavy drinking was associated with increased odds of hearing loss (Rosenhall et al., 1993; Popelka et al., 1998). The present study included levels of alcohol consumption that are considered 'hazardous' to general health (The Royal College of Psychiatrists, 2011). One may therefore have expected a U-shaped effect, with moderate levels of consumption associated with a protective effect and higher levels of consumption with less or no benefit compared to non-drinkers. In the studies by Rosenhall et al (1993) and Popelka et al (1998) cited above, 'very heavy drinking' was based on a historic measure; a record of having received two or more reports to the Swedish temperance board and a history of consuming more than 4 drinks per day, for Rosenhall et al and Popelka et al, respectively. Note that in the study by Popelka et al, all levels of *current* alcohol consumption were associated with a reduction in risk of hearing loss, similar to the present study. This discrepancy may be due to differences in patterns of alcohol consumption, in addition to the overall volume of consumption. In studies of cardiovascular disease, binge drinking (consuming

a whole week's healthy allowance of alcohol in one or two sittings) was associated with either no benefit or an increased risk of disease (Kauhanen et al., 1997; Murray et al., 2002). No data on binge drinking were available in the UK Biobank, so we were unable to test this possibility in the present study. Extrapolating from previous literature, one would expect that binge drinking would be associated with increased risk of hearing loss.

One variable relating to patterns of alcohol consumption that was available in the UK Biobank dataset was "alcohol usually taken with meals". In the present study, drinking alcohol with meals was associated with marginally reduced risk of hearing loss, compared to those who usually drink alcohol outside meals (data not reported here). A similar association has previously been observed in relation to risk for cardiovascular disease (Rehm et al., 2003), although this finding is difficult to interpret. Hypothesised casual mechanisms for beneficial effects of drinking alcohol with meals include a reduction in blood pressure (Foppa et al., 2002), increased fibrinolysis (Hendriks et al., 1994), increased HDL cholesterol (Veenstra et al., 1990), reduced absorption and/or increased elimination of alcohol (Lin and Li, 1998; Ramchandani et al., 2001). Alternatively, drinking alcohol with meals or drinking outside meals may be a marker of lifestyle, which may include a range of other risk and protective effects. Rehm, Sempos and Trevisan (2003) suggested that drinking wine with meals is characteristic of middle- and upper-class socio-economic status, and socio-economic status is strongly related to a wide range of health outcomes. It is therefore unclear whether drinking alcohol with meals represents a reduced risk of hearing loss, or whether it is merely a marker of a lifestyle associated with better hearing.

A strength of the present study was that associations between alcohol consumption and hearing loss were measured with reference to lifetime teetotalers. To our knowledge, all previous research to date has utilized current non-drinkers as the comparison group. This may have resulted in a bias because some non-drinkers may abstain from alcohol due to poor health and so have poorer hearing due to health-related factors that are unrelated to alcohol consumption (Hines and Rimm, 2001). The inclusion of 'sick-quitters' (referring to those who abstain from alcohol because of poor health) in the non-drinker comparison groups may have

resulted in over-estimates of the benefit associated with alcohol consumption. In the present study, the protective effect of alcohol consumption was evident based on comparisons with lifetime teetotalers, and so provides evidence that the protective association between alcohol consumption and hearing loss is reliable. Note that this conclusion rests on the assumption that lifetime teetotalers represent an unbiased comparison group. However, biases may still remain (Wannamethee and Shaper, 1998). Life-time teetotalers are a minority group within society, and may have unknown differences in lifestyle that result in increased risk of hearing loss. The benefits of alcohol consumption may therefore be over-estimated.

A further novel aspect of the present study was that hearing was measured with a test of speech recognition in noise. The measures in previous studies were predominantly tests of hearing sensitivity. Speech recognition tests arguably provide a more ecologically valid measure of hearing than does detection of tones in a quiet environment (Arlinger et al., 2009). The associations reported in the present study are therefore likely to relate strongly to real life hearing difficulties.

Limitations

This study utilized a cross-sectional correlational design, and it was not possible to establish causal associations. Nor was it possible to examine the time course of exposure to risks and development of hearing loss. A prospective cohort design may provide more convincing evidence of causal links. It is possible that an unmeasured confounder may be responsible for the effects observed in this study, or that the results are due to an effect specific to this sample. However, similar associations have been observed in previous studies in different countries and with different age cohorts. Smoking is associated with other risks for hearing loss (e.g. noise exposure), and so the apparent association between smoking and hearing loss may be explained by these other risks. However, the association between smoking and hearing loss was significant in a model that accounted for alcohol, cardiovascular disease, work-related noise exposure and SES. This suggests that smoking is not merely a marker for these other risks but rather represents a distinct risk in itself. Goodness-of-fit statistics suggested that there was variance in hearing loss that was not explained by the model. Some variance may not have

been adequately captured by the predictor measures (as described in the next paragraph) or the measure of hearing loss used in this study. Additionally, hearing loss is known to have a strongly heritable component (Uchida et al., 2011) and there may be interactions between genetic and environmental effects on susceptibility to hearing loss that were not accounted for in the present study.

Measures of alcohol consumption and smoking were based on self-report. There may be a tendency for participants to under-report smoking and drinking (Del Boca and Darkes, 2003; Gorber et al., 2009). The effect of this would be to bias results towards the null, and so associations between actual levels of smoking and drinking and hearing loss may therefore be larger than reported here. Occupation- and music-related noise exposure was based on a self-report measure which corresponds to noise levels above 85 dB(A) (Health and Safety Executive, 1989), but does not account for noise levels that may substantially exceed this level nor for the use or non-use of ear protection. There was no measure of leisure-related noise exposure (such as use of firearms or power tools). Some variance associated with noise exposure may not therefore be adequately measured. The UK Biobank utilized a proxy measure of socioeconomic status based on the participant's area of residence. This neighborhood-based estimate may have resulted in an ecological fallacy, i.e. that erroneous inferences about individual participant's socioeconomic status were made based on their area of residence. This procedure may have decreased the standard error of the estimated regression coefficient resulting in over estimation of the significance of socioeconomic status as a correlate of hearing loss.

Some previous studies (utilizing pure tone audiometric measures) suggested a stronger effect of alcohol consumption and smoking on high frequency than on low frequency hearing (Popelka et al., 2000; Mizoue et al., 2003), though other studies have not found such frequency-related effects (Fransen et al., 2008). Specific patterns of association with either high or low frequency hearing loss could provide evidence from which to infer causal mechanisms. We were not able to distinguish associations with particular patterns of high versus low frequency hearing loss with the hearing measure used in the present study.

The response rate in the present study was low, and this may represent a source of bias. However, this bias would only explain the association between smoking and hearing loss if smokers with hearing loss participated more readily than smokers without hearing loss. Likewise for alcohol, if alcohol drinkers without hearing loss participated more readily than alcohol drinkers with hearing loss. Neither of these possibilities seems likely. The UK Biobank suggests that as long as there are sufficiently large numbers of participants with different levels of relevant risk factors (as there seem to be in the present study), generalizable associations between risk factors and health outcomes can be made with confidence (Allen et al., 2012). Further reassurance of the generalizability of the associations reported in the present study is that they accord with those reported by other studies with close to 100% response rates (Nakanishi et al., 2000; Mizoue et al., 2003). The associations between smoking, alcohol consumption and hearing loss reported in the present study are unlikely to be the result of recruitment bias.

CONCLUSION

In this cross-sectional analysis alcohol consumption was associated with reduced odds of hearing loss, while smoking and passive smoking was associated with increased odds of hearing loss, all in a dose-dependent manner. Ex-smokers were not associated with increased odds of hearing loss compared to non-smokers. Giving up or reducing smoking and avoiding passive exposure to tobacco smoke may be beneficial in reducing the risk of hearing loss.

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Table
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Table 1. Participants in the study sample versus 2001 UK Census data for sex, ethnicity and socio-economic status. Sex and ethnicity are shown as percentages while socio-economic status is reported as average Townsend deprivation index score (with standard deviation).

		UK Biobank	UK Census 2001
Sex	Male	45.5	49.2
Ethnicity	White	91.5	91.3
Socioeconomic status	Mean Townsend score* (SD)	-1.1 (2.9)	0.7 (4.2)

*Lower Townsend scores indicate less deprivation

Table
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Table 2. Characteristics of normal hearing and hearing impaired participants.

	N participants	Normal hearing (N=143510)	Impaired hearing (N=21260)	*p* - logistic regression
Age	164770	56.1 (SD 8.1)	59.8 (SD 7.4)	<0.001
Pulse wave stiffness index	158899	9.3 (SD 3.82)	9.6 (SD 5.1)	0.010
BMI	158899	27.4 (SD 4.8)	27.8 (SD 4.9)	<0.001
Sex (male)	164770	45.3%	46.6%	0.310
Ethnicity (white)	164770	92.8%	82.7%	<0.001
SES (Townsend Index)	164770			
First quartile (most affluent)		25.6%	20.8%	<0.001
Second quartile		25.3%	24.1%	<0.001
Third quartile		25.2%	24.1%	<0.001
Fourth quartile (most deprived)		23.9%	32.1%	<0.001
Hypertension (yes)	164770	55.1%	64.6%	<0.001
Cardiovascular disease (yes)	164770	8.1%	13.0%	<0.001
High cholesterol (yes)	164770	18.4%	28.0%	<0.001
Ototoxic medication (yes)	164770	39.6%	45.2%	<0.001
Diabetes (yes)	164770	4.9%	9.1%	<0.001
Physical activity (inactive)	105846	42.5%	42.5%	0.028
Occupational noise exposure (yes)	163144	22.1%	28.5%	<0.001
Music noise exposure (yes)	162310	12.7%	11.2%	<0.001
Alcohol consumption	164770			
Never-drinker		4.1%	9.1%	<0.001
Ex-drinker		3.5%	5.0%	<0.001
Lowest 25%		23.0%	21.3%	<0.001
Middle 50%		46.2%	42.3%	<0.001
Highest 25%		23.1%	22.2%	<0.001
Smoking status	164208			
Never		55.4%	54.2%	<0.001
Ex-smoker		34.7%	34.9%	<0.001
Current		10.0%	10.9%	<0.001
Passive smoking (yes)	90658	4.3%	5.9%	<0.001

Notes: Shaded rows show continuous variables. Summary statistics for continuous variables are mean and standard deviation (in brackets). Unshaded rows show categorical variables. The summary statistic for categorical variables is the percentage of participants in each hearing category (normal/impaired).
The *p* – logistic regression statistic is the *p* value for the single variable in a logistic regression including age and sex only.

Table
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Table 3. Final multi-variable model for hearing loss showing odds ratios derived from a logistic regression model for hearing loss

	Odds Ratio (OR)	95% C.I. for OR	
Age	1.08	1.07	1.08
Sex (Male)	0.93	0.90	0.96
Ethnicity (Nonwhite)	3.08	2.94	3.23
SES			
First quartile; most affluent			
Second quartile	1.09	1.05	1.14
Third quartile	1.13	1.08	1.18
Fourth quartile; (most deprived	1.46	1.40	1.52
Cardiovascular Disease (Yes)	1.16	1.10	1.22
Cholesterol (Yes)	1.06	1.02	1.10
Diabetes (Yes)	1.18	1.12	1.26
Ototoxic Medication (Yes)	1.08	1.05	1.12
Occupation-related noise exposure (Yes)	1.37	1.32	1.42
Smoking Status			
Never smoker	-	-	-
Current smoker	1.15	1.09	1.21
Ex-smoker	0.95	0.92	0.98
Alcohol consumption			
Never drinker	-	-	-
Ex-drinker	0.79	0.72	0.86
Lowest 25%	0.62	0.58	0.66
Middle 50%	0.61	0.57	0.65
Highest 25%	0.65	0.61	0.70

Table
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Table 4. Final multi-variable model for smoking dose-response effects on hearing loss showing odds ratios derived from a logistic regression model for hearing loss

	Odds Ratio (OR)	95% C.I. for OR	
Age	1.07	1.07	1.08
Ethnicity (Nonwhite)	2.34	2.08	2.64
SES			
First quartile; most affluent	-	-	-
Second quartile	1.11	1.01	1.22
Third quartile	1.14	1.04	1.25
Fourth quartile; most deprived	1.43	1.31	1.56
Cholesterol (Yes)	1.11	1.04	1.18
Occupation-related noise exposure (Yes)	1.46	1.37	1.55
Alcohol consumption (Drinker)	0.78	0.73	0.84
Smoking – pack year			
Bottom 25%	-	-	-
Middle 50%	1.11	1.03	1.19
Top 25%	1.30	1.19	1.41

Table
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Table 5. Final multi-variable model for passive smoking effects on hearing loss showing odds ratios derived from a logistic regression model for hearing loss

	Odds Ratio (OR)	95% C.I. for OR	
Age	1.08	1.07	1.08
Sex (Male)	0.92	0.88	0.96
Ethnicity (Nonwhite)	3.27	3.07	3.48
SES			
First quartile; most affluent	-	-	-
Second quartile	1.11	1.05	1.19
Third quartile	1.11	1.06	1.20
Fourth quartile; most deprived	1.46	1.37	1.56
Cardiovascular Disease (Yes)	1.17	1.08	1.26
Diabetes (Yes)	1.26	1.15	1.37
Hypertension (Yes)	1.09	1.04	1.14
Occupation-related noise exposure (Yes)	1.28	1.21	1.35
Alcohol consumption (Drinker)	0.68	0.65	0.71
Passive Smoking (Yes)	1.28	1.21	1.35