Cardiovascular risk factors and hearing loss: The HUNT study

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Original Article

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Abstract

Objective: The purpose of the present paper was to examine the association between prospectively and cross-sectionally assessed cardiovascular risk factors and hearing loss. *Design*: Hearing was assessed by pure-tone average thresholds at low (0.25–0.5 kHz), middle (1–2 kHz), and high (3–8 kHz) frequencies. Self-reported or measured cardiovascular risk factors were assessed both 11 years before and simultaneously with the audiometric assessment. Cardiovascular risk factors were smoking, alcohol use, physical inactivity, waist circumference, body mass index, resting heart rate, blood pressure, triglycerides, total serum cholesterol, LDL cholesterol, HDL cholesterol, and diabetes. *Study sample*: A population-based cohort of 31 547 subjects. *Results*: After adjustment for age, sex, level of education, income, recurrent ear infections, and noise exposure, risk factors associated with poorer hearing sensitivity were smoking, diabetes, physical inactivity, resting heart rate, and waist circumference. Smoking was only associated with hearing loss at high frequencies. The effects were very small, in combination explaining only 0.2–0.4% of the variance in addition to the component explained by age and the other cofactors. *Conclusion*: This cohort study indicates that, although many cardiovascular risk factors are associated with hearing loss, the effects are small and of doubtful clinical relevance.

Key Words: Epidemiology, hearing loss, smoking, alcohol, physical activity, body mass index, blood pressure, blood lipids, diabetes

Hearing loss is probably one of the most common public health problems in the industrialized world. Age-related hearing loss is the most common type of hearing loss, and approximately one-third of people over 65 years of age are affected by disabling hearing loss (World Health Organization, 2015). Although hearing normally declines with age, there is great individual variation in the age of onset and severity. While the genetic contribution to hearing is substantial (Kvestad et al, 2012), a modest part of the variation is explained by known risk factors such as work-related noise exposure and ear diseases. This has motivated the search for other possible risk factors, such as systemic diseases and lifestyle factors like recreational noise exposure, smoking, alcohol, and diet. The size of the most affected older population is growing, which increases the burden of disease as well as the demand for preventive measures.

A normal cochlear blood flow is essential for the auditory transduction. For example, the stria vascularis, a highly vascularized region of the cochlea that produces the endolymph and the endocochlear potential, is highly susceptible to ischemic damage. Thus, it is reasonable to assume that factors influencing circulation also affect hearing. Age-related atrophy of the stria vascularis has been found in people with flat hearing loss (Schuknecht, 1964) suggesting that the effects of cardiovascular risk factors on hearing also have an effect at lower frequencies (Gates et al, 1993).

Hearing loss has been associated with several cardiovascular risk factors, including hypertension (Gates et al, 1993), smoking (Nomura et al, 2005), diabetes (Horikawa et al, 2013), being overweight (Fransen et al, 2008), inactivity (Loprinzi et al, 2014), cholesterol (Fuortes et al, 1995), triglycerides (Helzner et al, 2011), resting heart rate (Helzner et al, 2011), and unhealthy diet (Spankovich & Le Prell, 2013). Moderate alcohol intake has been associated with better hearing (Fransen et al, 2008). A healthy lifestyle has been suggested as a preventive measure to protect against age-related hearing impairment (Fransen et al, 2008; Dobie, 2008).

Prospective studies are scarce and often yield weak associations (Gopinath et al, 2011; Shargorodsky et al, 2010). It is therefore difficult to establish whether the associations are causal or confounded by underlying factors, such as general rate of aging or recall-bias, or if there is a reverse causality with hearing loss

Abbreviations	
BLM	Measurements and blood analyses
BMI	Body mass index
CI	Confidence interval
HDL	cholesterol: High density lipid cholesterol
HUNT	study: Nord-Trøndelag health study
LDL	cholesterol: Low density lipid cholesterol
NTHLS	Nord-Trøndelag hearing loss study
OR	Odds ratio
PTA	Pure-tone binaural average thresholds
Q1	Questionnaire 1
Q2	Questionnaire 2

being a stressor that increases the cardiovascular disease risk. In this large, general population sample of Norwegian adults, we assessed the risk factors both prospectively 11 years before and simultaneously with the assessment of hearing. The aim of the study was to investigate the relation between cardiovascular risk factors (smoking, alcohol use, physical inactivity, waist circumference, body mass index (BMI), resting heart rate, blood pressure, triglycerides, cholesterol, and diabetes) and hearing loss.

Methods

Study population

The Nord-Trøndelag health study (HUNT) is a large population-based study where all residents in the county of Nord-Trøndelag, Norway, aged ≥20 years were invited to participate in two cross-sectional surveys in 1984–86 (HUNT 1) and in 1995–97 (HUNT 2). A total of 77 212 subjects (89% of those invited) participated in HUNT 1, and 65 237 (69%) in HUNT 2 (Krokstad et al, 2013). HUNT 1 and HUNT 2 included several types of examinations, including blood measures (BLM) and questionnaires (Q1, completed by all participants, and Q2, completed by 85% of the participants included in our sample at both HUNT 1 and HUNT 2).

In the Nord-Trøndelag hearing loss study (NTHLS), which was part of HUNT 2, 17 of the 24 municipalities in the county were offered and accepted a hearing examination, consisting of pure-tone audiometry and the completion of two questionnaires (Hearing Q1 and Q2), as part of the screening programme. The participation rate for NTHLS was about 67% except in one municipality in which the participation rate was 41%. Participation was much higher for persons 50–80 years of age. The subjects ranged in age from 20 to 101 years (median = 48.0 years; mean = 50.2, SD = 17.0). NTHLS collected valid audiometric data from 50 464 participants. The sample is described in more detail elsewhere (Tambs et al, 2003).

Altogether the present sample consists of 31 547 subjects that had valid HUNT 1 data (Q1, Q2, and BLM), HUNT 2 data (Q1 and BLM), and audiometric data in NTHLS.

Study variables
HEARING LOSS
Air conduction hearing threshold levels were obtained by pure-tone audiometry at eight frequencies from 0.25 to 8 kHz in accordance with ISO 8253–1 (1989) as described in an earlier publication in NTHLS (Tambs et al, 2003). We defined three outcome variables:

pure-tone binaural average thresholds (PTA) of low frequency 0.25 and 0.5 kHz, middle frequency 1 and 2 kHz, and high frequency 3, 6, and 8 kHz.

CARDIOVASCULAR RISK FACTORS
We studied the following cardiovascular risk factors from questionnaire data and measurements in HUNT 1 and 2: smoking, alcohol use, physical inactivity, body mass index (BMI), resting heart rate, systolic and diastolic blood pressure, and diabetes. In order to obtain a reliable estimate of exposure over time, we used the measures from both HUNT 1 and HUNT 2 on these risk factors. The following risk factors were only measured in HUNT 2, simultaneously with the assessment of hearing: waist circumference, triglycerides, total serum cholesterol, LDL cholesterol, and HDL cholesterol.

Smoking status was measured by two items on daily smoking and previous daily smoking in HUNT 1 (Q2) and by three items on daily smoking (cigarettes, cigar, and pipe) and one item on previous daily smoking in HUNT 2 (Q1). Smoking was categorized in three categories for HUNT 1 and HUNT 2, representing never smoking daily, previous daily smoking, and daily smoking. The measures for HUNT 1 and 2 were summed into five levels representing levels from never having smoked daily (0), either in HUNT 1 or in HUNT 2, to daily smoking in both HUNT 1 and HUNT 2 (4).

Alcohol use was measured by three items in HUNT 1 (Q2) and five items in HUNT 2 (Q1). In HUNT 1, one item related to frequency of use, and the other two related to drunkenness and overuse. In HUNT 2, one item related to frequency of use, three items related to quantity, and one related to being teetotal. Alcohol use was categorized into three categories: (1) teetotal; (2) not drinking in the last two weeks (HUNT 1) or last month (HUNT 2), but not teetotal; (3) drinking not more than four times in the last two weeks (HUNT 1) or not more than eight times in the last month (HUNT 2); or (4) drinking more than four times in the last two weeks (HUNT 1) or more than eight times in the last month (HUNT 2). The two variables were summed into a seven category variable representing levels from teetotal (0) to drinking more than eight times last month in both HUNT 1 and HUNT 2 (6).

Physical activity was measured by three items in HUNT 1 (Q2) (frequency, intensity, and duration of activities) and two variables in HUNT 2 (Q1) (hours of light and heavy activity during leisure time). An index as the product of frequency, intensity, and duration scales was weighted according to Kurtze et al (Kurtze et al, 2008) into a scale ranging from 1–15. The scale was categorized into four categories (no, low, medium, and high activity) with cut-offs at 0.01, 0.76 and 1.88 corresponding to lower 10%, median value and upper 25%. From HUNT 2, the subjects were also classified into four groups; inactive (no activity); low (<3 hours light activity and/or <1 hour heavy activity per week); medium (≥3 hours light activity and/or <1 hours heavy activity per week), and high (any light activity and ≥1 hour heavy activity per week). The two variables were summed into a seven category variable representing levels from being inactive in both HUNT 1 and HUNT 2 (0) to being highly active in both HUNT 1 and HUNT 2 (6). Reversing the scale measured the level of physical inactivity.

Diabetes was measured by the question 'Do you have or have you had diabetes?' (yes, no) with no distinction between type 1 or 2 diabetes in both HUNT 1 (Q1) and HUNT 2 (Q1). Diabetes was assessed as three levels representing no diabetes, diabetes in HUNT 2 only, and diabetes in HUNT 1 and HUNT 2.

BMI was calculated as the weight in kilograms divided by squared height in metres. The mean value across HUNT 1 and HUNT 2 was used as a predictor variable. Waist circumference was measured manually to the nearest centimetre in HUNT 2 only. Resting heart rate was measured in HUNT 1 by palpating the radial pulse, if necessary with the aid of a stethoscope placed over the heart. In HUNT 2, resting heart rate was measured three times in parallel with the measurement of blood pressure. Resting heart rate was assessed as the mean of the HUNT 1 measure and the mean of the second and third measures of HUNT 2. Systolic and diastolic blood pressure (SBP and DBP) were measured twice in HUNT 1 and three times in HUNT 2 at 1-minute intervals. The mean of the two measures (HUNT 1) and the mean of the second and third measures (HUNT 2) were used in the analyses.

Triglycerides, total serum cholesterol and high density lipid (HDL) cholesterol were measured in nonfasting serum in HUNT 2 only. Low density lipid (LDL) cholesterol was calculated using the Friedewald equation (Friedewald et al, 1972) without restrictions on the triglyceride levels.

Metabolic syndrome was defined in HUNT 2 only according to the following cut-off points: waist circumference ≥ 88 cm in females and ≥ 102 cm in males; triglycerides ≥ 1.7 mmol·L^{-1}; HDL cholesterol <1.3 mmol·L^{-1} in females and <1.0 mmol·L^{-1} in males; systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or use of anti-hypertensive medication; and glucose ≥ 5.6 mmol·L^{-1} at ≥ 4 hours since last meal (serum measurements were nonfasting) or self-reported diabetes. The presence of three or more of these criteria defined metabolic syndrome.

COVARIATES

We collected information on covariates from national registers and from questionnaires. From national registers, we had information on level of education (primary and secondary school, vocational school, high school, undergraduate and graduate school), and income in 1998.

Noise exposure and recurrent ear infections were determined from questions in NTHLS Q1 as described in detail elsewhere (Engdahl et al, 2005). Occupational noise exposure was measured by questionnaire items on the duration of exposure to loud noise at work in general (scored 0–3) and from specific noise sources: staple gun/hammering, metal hammering/riveting, circular saw/machine planing, chain saw operation, tractor/construction machines, sledgehammer operation, blasting, machine room noise, and other factory noise ('yes' or 'no'). Non-occupational exposure was measured by questionnaire items about impulse noise (i.e. explosions, shootings, etc.) ('yes', 'perhaps/don't know', or 'no'); playing in a band ('yes' or 'no'), going to discotheques, rock concerts, or similar loud events ('yes' or 'no'), using Walkman or other type of personal stereo player with ear phones (scored 0–3); recurrent ear infections (in childhood or later) ('yes', 'perhaps/don't know', or 'no').

STATISTICAL ANALYSIS

The effect of the cardiovascular risk factors on hearing loss was assessed by multivariate linear regression (GLM-Multivariate) in SPSS version 20.0 (IBM Corp.). Dependent and correlated hearing loss variables were the three PTA variables at low, middle, and high frequency. The hearing loss was first regressed separately on each

risk factor adjusted initially only for sex and age (model 1), and as a second step also for level of education, income, noise, and recurrent ear infections (model 2). In subsequent analyses, all risk factors were adjusted for each other (model 3). In the latter analysis the total serum cholesterol was discarded because of its close dependence on HDL cholesterol, LDL cholesterol, and triglycerides. A general index based on all cardiovascular risk factors was generated in order to estimate the total overall effect of cardiovascular risk. The index was calculated by weighting the score of each item by its respective regression coefficients estimated in the initial regression analyses. Preliminary analyses with predictor variables from both HUNT 1 and HUNT 2 showed little or no differential effect of the prospective predictors compared to the predictors observed simultaneously with the outcome measure. These preliminary results justified collapsing the predictor variables observed 11 years apart, giving maximally reliable and broadly comprising exposure variables. Multivariate effects were tested with Pillai's trace test (with significance level of 0.01) and regression coefficients, and partial eta square coefficients were estimated for each of the dependent variables. The three variables smoking (five levels), alcohol (seven levels), and physical activity (seven levels) were tested for non-linear effects by dummy-coding. SPSS Multiple Imputation was used to impute values for the questionnaire data using the conditional specification by the Markov chain Monte Carlo method. All risk factors measured in HUNT 1 and HUNT 2 plus a few additional items on alcohol and smoking not used in the present analysis were used in the multiple imputation model. Estimates of parameters of interest were averaged across five copies of the data to give a single estimate. Standard errors were computed according to the 'Rubin rules' (Rubin, 1987). Data were missing mainly for physical activity (4% missing in HUNT 1 and 36% missing in HUNT 2), smoking (1% in HUNT 1 and 4% in HUNT 2), and alcohol use (2% in HUNT 1 and 6% in HUNT 2). For the other risk factors, there was less than 1% missing data.

Results

Table 1 shows characteristics of the study participants. The subjects in the final sample ranged in age from 32 to 99 years (median = 55, mean = 56.8, SD = 14.1). The association between cardiovascular risk factors and hearing loss is shown in Table 2. Except for systolic and diastolic blood pressure and triglycerides, there were statistical significant multivariate associations with all cardiovascular risk factors (model 1), but all associations were weak and the associations were reduced by controlling for other covariates (model 2). Estimates were generally in the hypothesized direction: the effect of smoking, that was a positive association at high frequencies only, was maintained also after controlling for the other cardiovascular risk factors (model 3); higher levels of physical activity slightly decreased the level of hearing loss; diabetes increased hearing loss at high frequency; high waist circumference increased the level of hearing loss at the median frequency and also at high frequency when controlling for other risk factors; and metabolic syndrome resulted in a hearing shift of about 1 dB at high frequencies. HDL cholesterol was negatively associated with hearing loss at all frequencies, an effect that was maintained after controlling for the other cardiovascular risk factors. Also LDL cholesterol and total serum cholesterol was negatively associated with hearing loss. Systolic blood pressure was positively associated with low frequency hearing loss but only after controlling for the

Table 1. Descriptive statistics for the sample in the study ($N = 31\,547$)[a].

	HUNT 1	HUNT 2
Low frequency PTA, mean dB (SD)		18.5 (11.8)
Middle frequency PTA, mean dB (SD)		17.6 (15.7)
High frequency PTA, mean dB (SD)		33.1 (23.4)
Age, mean years (SD)	45.4 (14.1)	56.9 (14.1)
Sex, N (%)		
Men	14 704 (46.6)	14 704 (46.6)
Women	16 843 (53.4)	16 843 (53.4)
Smoking, N (%)[b]		
No	13 479 (42.7)	14 397 (45.6)
Previous	8001 (25.4)	8975 (28.4)
Present	10 067 (31.9)	8175 (25.9)
Alcohol consumption, N (%)[b]		
Teetotal	2787 (8.8)	4698 (14.9)
Not drinking last 14 days/month	14 005 (44.4)	9187 (29.1)
1–8 times per month	12 954 (41.1)	16 048 (50.9)
≥ 8 times per month	1801 (5.7)	1151 (3.6)
Physical activity, N (%)[b]		
No	3053 (9.7)	2890 (9.2)
Low	13 550 (43.0)	13 921 (44.1)
Medium	6699 (21.2)	5912 (18.7)
Hard	8245 (26.1)	8824 (28.0)
Diabetes, N (%)		
No	31 196 (98.9)	30 351 (96.2)
Yes	351 (1.1)	1196 (3.8)
BMI, mean kg/m^2 (SD)	25.0 (3.7)	26.8 (4.1)
Resting heart rate, mean bpm (SD)	73.8 (12.0)	72.3 (12.9)
Systolic blood pressure, mean mmHg (SD)	133.6 (20.0)	141.6 (22.7)
Diastolic blood pressure, mean mmHg (SD)	83.4 (11.1)	82.6 (12.2)
Waist circumference, mean cm (SD)		87.7 (11.4)
Triglyserides, mean mmol/L (SD)		1.8 (1.1)
Total serum cholesterol, mean mmol/L (SD)		6.1 (1.2)
HDL cholesterol, mean mmol/L (SD)		1.4 (0.4)
LDL cholesterol, mean mmol/L (SD)		4.4, (1.2)
Metabolic syndrome, N (%)		
No		21 101 (66.9)
Yes		10 445 (33.1)

[a]Continuous variables are expressed with mean (standard deviations) and category variables with frequency (%).
[b]Measured with different items in HUNT 1 and HUNT 2.

other cardiovascular risk factors including diastolic blood pressure. Diastolic blood pressure was negatively associated with low and middle frequency hearing loss in the fully adjusted model only. BMI was also positively associated with hearing loss at the middle frequency, but negatively associated at low-frequency hearing loss, and, when controlled for other risk factors, BMI was negatively associated with hearing loss at all frequencies. Finally, we found a small protective effect of alcohol.

The variables smoking, alcohol, and physical activity were also entered as factors testing for nonlinear effects over categories. The effects increased incrementally between each category for all these variables. The background covariates (age, sex, education, level of education, income, noise exposure, and recurrent ear infections) explained 29.4%, 42.4%, and 60.9% of the variance in hearing loss at low, middle, and high frequencies, respectively (adjusted R squared), of which age alone explained the major part (26.1%, 39.5%, and 52.4%). Adding all cardiovascular risk factors increased the explained variance by only 0.4% at low, 0.4% at middle, and 0.2% at high frequencies. Partial eta squared estimates for the summary indexes were 0.6%, 0.8%, and 0.7%, respectively.

Discussion

Principal findings
After adjustment for other important covariates, we found small effects of cardiovascular risk factors on hearing loss. The cardiovascular risk factors explained only a trivial fraction of the variance in hearing loss in the general population. Estimates were generally in the hypothesized direction confirming previous studies, except for cholesterol, which was associated with better hearing. Smoking was associated with hearing loss at high frequencies only.

Strengths and weaknesses of the study
The major advantages of our study are that most risk factors were measured prospectively, that its population was representative of the general adult population of Nord-Trøndelag County, and that the large sample gives precise estimates of the effect sizes. The county is fairly representative of Norway in terms of geography, economy, industry, sources of income, age distribution, morbidity, and mortality. But the county has no large cities and the average

Table 2. Mean bilateral hearing loss at low, middle and high frequencies in NTHLS. Results from multivariate regression models of cardiovascular risk factors measured in HUNT 1 and 2. (N = 31 547).

Risk factor	Dependent variable	Model 1[a]			Model 2[b]			Model 3[c]		
		Regression coefficients (dB/unit)	[95% CI]	Partial eta squared (%)	Regression coefficients (dB/unit)	[95% CI]	Partial eta squared (%)	Regression coefficients (dB/unit)	[95% CI]	Partial eta squared (%)
Smoking daily (five levels from no smoking to smoking in both HUNT 1 and 2)	LF	0.07	[0.00, 0.14]	0.01	0.00	[−0.07, 0.07]	0.00	0.00	[−0.08, 0.07]	0.00
	MF	0.17	[0.09, 0.26]	0.05	0.07	[−0.01, 0.16]	0.01	0.08	[−0.05, 0.20]	0.01
	HF	0.59	[0.48, 0.69]	0.38	0.43	[0.33, 0.53]	0.21	0.45	[−0.83, 1.72]	0.20
Alcohol (seven levels from teetotal to ≥8 times per month in both HUNT 1 and 2)	LF	−0.41	[−0.50, −0.32]	0.26	−0.21	[−0.30, −0.12]	0.07	−0.19	[−0.38, 0.01]	0.05
	MF	−0.42	[−0.53, −0.31]	0.18	−0.16	[−0.27, −0.05]	0.03	−0.14	[−0.31, 0.03]	0.02
	HF	−0.34	[−0.47, −0.20]	0.08	−0.07	[−0.21, 0.06]	0.00	−0.20	[−0.46, 0.06]	0.03
Physical activity (seven levels from inactive to highly active in both HUNT1 and 2)	LF	−0.33	[−0.41, −0.26]	0.26	−0.22	[−0.30, −0.15]	0.12	−0.21	[−0.56, 0.13]	0.11
	MF	−0.36	[−0.44, −0.27]	0.21	−0.23	[−0.31, −0.14]	0.09	−0.17	[−0.41, 0.08]	0.04
	HF	−0.30	[−0.41, −0.19]	0.10	−0.15	[−0.26, −0.05]	0.03	−0.11	[−0.37, 0.14]	0.00
Diabetes (no, HUNT 2 only, HUNT 1 and HUNT 2)	LF	0.90	[0.47, 1.34]	0.05	0.63	[0.20, 1.06]	0.03	0.47	[−0.62, 1.56]	0.01
	MF	1.05	[0.52, 1.58]	0.05	0.70	[0.19, 1.22]	0.02	0.32	[−0.50, 1.13]	0.00
	HF	1.75	[1.10, 2.40]	0.09	1.43	[0.79, 2.06]	0.06	1.24	[−3.96, 6.45]	0.05
BMI (kg/m2)	LF	−0.02	[−0.05, 0.01]	0.01	−0.05	[−0.08, −0.02]	0.03	−0.08	[−0.15, −0.01]	0.03
	MF	0.06	[0.02, 0.10]	0.03	0.03	[0.00, 0.07]	0.01	−0.09	[−0.17, 0.00]	0.02
	HF	0.02	[−0.03, 0.07]	0.00	−0.02	[−0.07, 0.02]	0.00	−0.15	[−0.30, 0.00]	0.05
Resting heart rate (10•beats/min)	LF	0.30	[0.19, 0.41]	0.10	0.17	[0.06, 0.27]	0.03	0.20	[0.08, 0.33]	0.04
	MF	0.36	[0.23, 0.49]	0.09	0.20	[0.07, 0.32]	0.03	0.21	[0.06, 0.36]	0.03
	HF	0.39	[0.23, 0.55]	0.07	0.22	[0.07, 0.38]	0.03	0.18	[0.00, 0.35]	0.01
Systolic blood pressure (10•mmHg)	LF	0.01	[−0.04, 0.07]	0.00	−0.03	[−0.09, 0.03]	0.00	0.27	[0.15, 0.39]	0.09
	MF	0.05	[−0.02, 0.11]	0.01	0.00	[−0.07, 0.07]	0.00	0.23	[0.10, 0.36]	0.05
	HF	−0.01	[−0.10, 0.07]	0.00	−0.06	[−0.15, 0.02]	0.01	0.04	[−0.11, 0.18]	0.00
Diastolic blood pressure (10•mmHg)	LF	−0.14	[−0.23, −0.04]	0.02	−0.11	[−0.20, −0.01]	0.02	−0.58	[−0.86, −0.31]	0.14
	MF	−0.08	[−0.20, 0.03]	0.01	−0.02	[−0.13, 0.09]	0.00	−0.47	[−0.74, −0.19]	0.06
	HF	−0.07	[−0.21, 0.07]	0.00	−0.01	[−0.15, 0.12]	0.00	−0.07	[−0.33, 0.18]	0.00
Waist circumstance (dm)	LF	0.04	[−0.07, 0.15]	0.00	−0.08	[−0.19, 0.03]	0.01	0.13	[−0.07, 0.33]	0.01
	MF	0.44	[0.31, 0.58]	0.13	0.29	[0.16, 0.43]	0.06	0.51	[0.20, 0.82]	0.06
	HF	0.37	[0.20, 0.53]	0.06	0.17	[0.01, 0.33]	0.01	0.61	[0.21, 1.00]	0.06
Triglyserid (mmol/L)	LF	−0.03	[−0.13, 0.07]	0.00	−1.09	[−2.06, −0.11]	0.02	−0.09	[−0.22, 0.05]	0.01
	MF	0.09	[−0.03, 0.21]	0.01	0.01	[−1.17, 1.18]	0.00	−0.10	[−0.27, 0.06]	0.01
	HF	0.04	[−0.11, 0.19]	0.00	−0.72	[−2.16, 0.72]	0.00	−0.14	[−0.37, 0.09]	0.01
HDL cholesterol (mmol/L)	LF	−0.33	[−0.43, −0.24]	0.15	−0.34	[−0.44, −0.25]	0.16	−0.45	[−1.38, 0.48]	0.02
	MF	−0.65	[−0.77, −0.54]	0.38	−0.66	[−0.78, −0.55]	0.41	−1.31	[−6.73, 4.12]	0.13
	HF	−0.62	[−0.76, −0.48]	0.23	−0.67	[−0.81, −0.53]	0.28	−1.11	[−5.25, 3.02]	0.06
LDL cholesterol (mmol/L)	LF	−0.56	[−0.85, −0.26]	0.04	−0.26	[−0.55, 0.03]	0.01	−0.30	[−0.66, 0.07]	0.10
	MF	−1.50	[−1.86, −1.15]	0.22	−1.16	[−1.51, −0.81]	0.13	−0.67	[−2.10, 0.76]	0.35
	HF	−1.24	[−1.68, −0.80]	0.10	−0.90	[−1.32, −0.47]	0.05	−0.68	[−2.18, 0.82]	0.23

(continued)

Table 2. Continued

Risk factor	Dependent variable	Model 1[a]			Model 2[b]			Model 3[c]		
		Regression coefficients (dB/unit)	[95% CI]	Partial eta squared (%)	Regression coefficients (dB/unit)	[95% CI]	Partial eta squared (%)	Regression coefficients (dB/unit)	[95% CI]	Partial eta squared (%)
Total serum cholesterol (mmol/L)	LF	−0.29	[−0.39, −0.19]	0.10	−0.32	[−0.42, −0.22]	0.13	na		
	MF	−0.56	[−0.68, −0.44]	0.25	−0.59	[−0.71, −0.47]	0.29	na		
	HF	−0.54	[−0.69, −0.39]	0.16	−0.62	[−0.76, −0.47]	0.21	na		
Metabolic syndrome (yes/no)	LF	0.00	[−0.26, 0.25]	0.00	−0.19	[−0.44, 0.06]	0.01	na		
	MF	0.89	[0.58, 1.19]	0.10	0.68	[0.37, 0.98]	0.06	na		
	HF	1.11	[0.73, 1.49]	0.10	0.84	[0.47, 1.21]	0.06	na		
Index of all cardiovascular risk factors (SD)	LF	1.08	[0.96, 1.19]	1.07	0.77	[0.66, 0.88]	0.57	na		
	MF	1.41	[1.27, 1.55]	1.29	1.09	[0.95, 1.22]	0.76	na		
	HF	1.61	[1.44, 1.78]	1.10	1.30	[1.12, 1.47]	0.69	na		

[a] Adjusted for covariates age and sex.
[b] Adjusted for covariates age, sex, level of education, income, noise exposure, and recurrent ear infections.
[c] Adjusted for all covariates plus all other cardiovascular risk factors. LF = low frequency PTA (0.25–0.5 kHz), MF = middle frequency PTA (1–2 kHz), HF = high frequency PTA (3–8 kHz). na = not available (redundant measure).

income, the prevalence of higher education, and the prevalence of current smokers are a little lower than the average for Norway (Holmen et al, 2003). Since the audiometric test was part of a general health survey, in which hearing was only one of many health outcomes to be studied, and the participation rate in the population survey was relatively high (67% for the vast majority of the county), a notable selection bias is unlikely. It might be a slight selection towards lower prevalence of the cardiovascular risk-factors, but the prevalence in smoking among responders (30%) was only slightly lower than among non-responders (35%) (Langhammer et al, 2000). Most of the risk factors were averaged over two periods separated by 11 years, so their effects represent long term risks. Possible short term effects may thus have been somewhat underestimated if they are stronger than the long term effects.

Having had data on hearing at baseline would have been an advantage in order to reduce the option for a reverse causality. With our available data we cannot completely exclude the possibility of stress associated with hearing loss causing cardiovascular disease risk such as smoking or blood pressure. However, previous analyses of the present data show that the effect of hearing loss on well-being and mental health is, at the most, quite moderate (Tambs, 2004).

Although we have controlled for several important covariates in model 2, we cannot rule out that unmeasured confounding accounts for these small observed effects. Controlling for covariates may bias the risk estimates if the covariates are in reality colliders or mediators. A collider is a variable that is the outcome of two (or more) variables. Adjusting for a covariate that is the outcome of both the dependent and the independent variable may induce collider bias. Although income and education may be descendants of both hearing loss and cardiovascular risk, we believe this to be a minor problem. The same applies for noise exposure and recurrent ear infections. We therefore consider controlling for these covariates (model 2) to be a more valid model for estimating the effects of the cardiovascular risk than not controlling for these (model 1), although the unadjusted model is relevant for comparison with other studies without adjustment. Model 3, in which all cardiovascular risk factors were adjusted for each other, estimates independent direct effects of the risk factors. While the different cardiovascular risk factors are related in a complex way it is not straightforward to interpret this model as the factors may not be pure confounders, but mediators or colliders. It is however useful for interpreting the overall effect of the cardiovascular risk factors.

Some risk factors (smoking, alcohol consumption, physical inactivity, and diabetes) were based on self-reporting. Imprecise reporting may have attenuated their effects. Often, reporting bias may also produce systematic errors, for instance subjects who know they have a hearing loss may attribute the loss to noise and may over-report noise exposure. Such bias is hardly likely for cardiovascular factors.

The amount of missing data was low with the exception of data on physical activity in HUNT 2 (36% missing). One explanation for the low response to the particular question on physical activity in HUNT 2 might be that it was somewhat vaguely formulated. However, it is reasonable to assume that the data are randomly missing as subjects with missing data on physical activity in HUNT 2 scored similar to others on the physical activity index in HUNT 1 (mean = 1.22, SD = 1.79, and mean = 1.54, SD = 2.21, p <.001). In any case, the uncertainty associated with the missing data was reflected in standard errors estimated by the use of multiple imputation.

Because of the large number of risk factors, some statistically significant results may have occurred by chance, but the large sample size makes the estimated size of the associations highly precise. The reliability of the hearing thresholds at low frequencies was somewhat lower (Engdahl et al, 2005). Measurement error may thus have deflated the estimated effects slightly more at this frequency range.

Comparisons of the results with other studies

SMOKING

A meta-analysis, based on five cross-sectional studies on the effect of smoking on hearing loss, found an increased risk of hearing loss among current smokers versus non-smokers (odds ratio (OR) = 1.3 (95% confidence interval (CI) 1.2–1.4)) (Nomura et al, 2005). Similar effect sizes have also been found in later studies (Dawes et al, 2014; Agrawal et al, 2009; Gopinath et al, 2010; Nash et al, 2011; Sung et al, 2013) although one recent study reported no effects (Lin et al, 2011). We found an effect of smoking on high-frequency hearing loss only after controlling for other covariates (model 2). Stronger effects for high frequency than for lower frequency hearing have also been found by others (Fransen et al, 2008; Nakanishi et al, 2000; Agrawal et al, 2009; Mizoue et al, 2003). Our estimated difference in mean hearing thresholds between current long-time smokers (level 4) and non-smokers (level 0) (4×0.43 dB/unit = 1.7 dB at 3–8 kHz adjusted for covariates) is similar to that reported by Sung et al (2013) (0.6, 0.8, 1.5, 1.8 dB at 1, 2, 3, 4 kHz respectively). Agrawal et al (2009) reported larger effects for subjects smoking more than 20 pack-years of cumulative exposure exposure (1–2 dB at 0.5–3 kHz, and 4–5 dB at 4–8 kHz).

ALCOHOL CONSUMPTION

Several studies have found small to medium protective effects of moderate alcohol consumption on hearing loss (Gopinath et al, 2010; Dawes et al, 2014; Fransen et al, 2008; Popelka et al, 2000). There was a protective effect also in our data, but the effect was negligible. Moderate alcohol consumption has been reported to be positively associated with socioeconomic status, and being an abstainer is often related to reduced health in the first place (Rundberg et al, 2014). Thus, different levels of controlling for socioeconomic status and health may explain some of the discrepancy with previous studies. Observed protective effects of alcohol consumption should therefore be interpreted with caution. Gopinath et al (2011) did not show any protective effect of alcohol consumption on new cases of hearing impairment at a follow-up five years later, and low or moderate alcohol consumption did not influence the risk of self-reported hearing loss in a longitudinal study of older men (Curhan et al, 2011).

BLOOD PRESSURE

We found the effect of systolic and diastolic blood pressure to be negligible (model 2). Previous findings also report small or no effects. Gates et al (1993) found a positive association between systolic blood pressure and hearing loss at low frequencies and reported an effect of about 0.5 dB per 10 mmHg, which is similar to ours. Rosenhall and Sundh (2006) found an effect in the low frequency range for old women only. Negative findings have been reported for self-reported history of hypertension on hearing loss (OR = 1.1, 95% CI 0.7–1.5) (Agrawal et al, 2009), and for self-reported history of hypertension on self-reported hearing loss (HR = 1.0; 95% CI 0.9–1.0) (Shargorodsky et al, 2010). In the fully adjusted model (model 3) we found a small effect of systolic blood pressure (0.3 dB per 10 mmHG increase) at low frequencies and, somewhat unexpectedly, a small protective effect of diastolic blood pressure at low and middle frequencies.

DIABETES

A meta-analysis of the effect of diabetes in general (type 1 or 2) on hearing loss reported an increased risk of hearing loss among diabetic compared with non-diabetic participants with an OR of 2.2 (95% CI 1.7–2.7) based on 13 studies with 20 194 participants and 7377 cases (Horikawa et al, 2013). A similar medium effect was found also in another meta-analysis restricted to diabetes type 2 with an OR of 1.9 (95% CI 1.5–2.5) based on 18 studies (Akinpelu et al, 2014). The latter study also compared mean hearing thresholds provided by seven studies resulting in a pooled difference between diabetics and controls of 4–8 dB depending on frequency. Our results, differences in mean hearing thresholds between long-time diabetics (in at least 11 years) and non-diabetics of 1.2, 1.4, and 2.7 dB at low, medium, and high frequencies respectively (model 2), are thus considerably weaker. Most of the effect disappeared after adjusting for other cardiovascular risk factors, probably partly because cardiovascular risk factors may mediate some of the effect of diabetes.

OVERWEIGHT

We found both BMI and waist circumference to be weakly positively associated with hearing loss, although at the median frequency only (model 2). BMI was negatively associated with hearing loss at low frequencies. When both variables were included in the same model, waist circumference was positively associated and BMI was negatively associated with hearing loss at all frequencies. Positive associations between hearing loss and high BMI (Fransen et al, 2008; Hwang et al, 2009; Helzner et al, 2011), and waist circumference (Hwang et al, 2009) has been reported. When both waist circumference and BMI were taken into account, they found a significant positive association with waist circumference only. BMI and waist circumference were both associated with increased risk of self-reported hearing loss in a prospective study of older women (Curhan et al, 2013), while BMI was not related to self-reported hearing loss in the prospective Health Professionals Follow-up Study of older men (Shargorodsky et al, 2010). A recent study of adolescents found an association between obesity and unilateral SNHL at low frequencies when controlling for age group, sex, race/ethnicity, SHS exposure, and poverty status (OR = 1.8, 95% CI 1.1–3.3) (Lalwani et al, 2013).

PHYSICAL ACTIVITY

We found that highly physically active subjects had slightly better hearing than physically inactive subjects (unadjusted effects of 1.1 dB, 1.9 dB, and 1.5 dB respectively at low, medium, and high frequencies). The small effect was reduced but still significant after controlling for covariates and other cardiovascular risk factors. Similarly, small effects were reported from another study of a smaller group of subjects with diabetes, in which the level of physical activity measured by actimetry was negatively associated with hearing loss (Loprinzi et al, 2014). Higher physical activity

was also weakly associated with reduced risk of self-reported hearing loss in a prospective large study of older women (Curhan et al, 2013).

RESTING HEART RATE

In agreement with Helzner et al (2011), we found that high resting heart rate was associated with hearing loss. Whereas Helzner et al reported standardized betas in the range of 0.05–0.09, our effect estimates in terms of standardized betas were generally much smaller and in the range of 0.01–0.02 (high and low frequencies respectively). The small effects sizes remained after adjusting for other cardiovascular risk factors.

BLOOD LIPIDS

We found total serum cholesterol, HDL cholesterol, and LDL cholesterol to be associated with better hearing. Although the protective effect of the 'good' HDL cholesterol may be reasonable, it is surprising that the effect of the 'bad' LDL, and total, cholesterol were in the same direction. This is also in contrast to previous studies that show either no or weak positive associations with hearing loss (Helzner et al, 2011; Axelsson & Lindgren, 1985; Simpson et al, 2013; Fuortes et al, 1995). Small positive associations between self-reported elevated cholesterol levels and self-reported hearing loss were also found in the Health Professionals Follow-up Study with OR of 1.1 (95% CI 1.0–1.2) (Shargorodsky et al, 2010). We did not control for confounding by lipid-lowering medication, which might explain some of the discrepancy with previous studies. Nevertheless, our findings support the conclusion by Simpson et al that the association between blood lipids and hearing loss is either spurious or too small to be of consequence in the assessment and treatment of hearing loss.

FREQUENCY SPECIFIC EFFECTS

The cardiovascular risk factors appeared to explain slightly more of the variance in hearing loss at low and medium frequencies than at high frequencies. This is in accordance with the hypotheses that cardiovascular risk factors affect the whole frequency range. Stronger associations with low-frequency hearing thresholds are found previously for cardiovascular risk factors (Frederiksen et al, 2014; Friedland et al, 2009) and for cardiovascular disease (Gates et al, 1993; Friedland et al, 2009).

Conclusions

After adjustment for age, sex, level of education, income, recurrent ear infections, and noise exposure, we observed a risk of reduced hearing sensitivity associated with smoking, diabetes, physical inactivity, resting heart rate, and waist circumference. Smoking was only associated with hearing loss at high frequencies. Higher levels of total serum cholesterol, LDL cholesterol, and HDL cholesterol were associated with better hearing. The effects were all small, increasing the explained variance altogether by only 0.2%–0.4%. Our effect estimates are based on a large and representative data material and are therefore valid and highly precise in terms of small confidence intervals. Therefore they serve as correctives to previous results in general, which tend to show stronger effects. A possible explanation of the discrepancy with previous results is publication bias of positive results. Our findings indicate that there is little to gain in increased hearing protection by reducing cardiovascular risk factors.

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