








Association Between Speech Reception Threshold in Noise and Multimorbidity: The UK Biobank Study

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Abstract

Objective. To investigate the association between hearing function, as approached with the functional auditory capacity, and multimorbidity.

Study Design. Cross-sectional study.

Setting. The UK Biobank was established from 2006 to 2010 in the United Kingdom. This cross-sectional analysis included 165,524 participants who provided baseline information on hearing function.

Methods. Functional auditory capacity was measured with a digit triplet test. Three categories were defined according to the speech reception threshold in noise (SRTn): normal (SRTn < −5.5 dB signal-to-noise ratio [SNR]), insufficient (SRTn ≥ −5.5 to ≤ −3.5 dB SNR) and poor hearing function (SRTn > −3.5 dB SNR). To define multimorbidity, 9 chronic diseases were considered, including chronic obstructive pulmonary disease, dementia, Parkinson's disease, stroke, cancer, depression, osteoarthritis, coronary heart disease, and diabetes; multimorbidity was defined as the coexistence of 2 or more in the same individual. Analyses were conducted using logistic models adjusted for relevant confounders.

Results. Among the study participants, 54.5% were women, and the mean (range) age was 56.7 (39–72) years. The prevalence of insufficient and poor hearing function and multimorbidity was 13% and 13.2%, respectively. In comparison with having a normal SRTn, the odds ratio (95% confidence interval) of multimorbidity associated with insufficient SRTn was 1.13 (1.08–1.18), and with poor SRTn was 1.25 (1.14–1.37).

Conclusion. Insufficient and poor hearing function was associated with multimorbidity. This association suggests common biological pathways for many of the considered morbidities.

Keywords

cross-sectional studies, multimorbidity, speech in noise, UK Biobank

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Life expectancy has followed an upward trajectory in most countries.¹ Simultaneously, the prevalence of noncommunicable diseases has been increasing, accounting for more than 70% of deaths worldwide nowadays.² Owing to improvements in health care and living conditions, many individuals survive their first chronic condition, which increases the likelihood of multimorbidity, defined as the coexistence of 2 or more chronic diseases in an individual.³ Multimorbidity has been associated with disability,⁴ which directly impacts the quality of life,⁵ increases the risk of depression,⁶ lowers self-rated health,⁷ and leads to greater health care utilization.⁸ However, not all people develop multimorbidity, and the determinants of this outcome are insufficiently known.

Hearing loss (HL) is one of the most prevalent chronic diseases in older adults.⁹ Some studies have associated HL with a higher prevalence of individual chronic diseases, including chronic obstructive pulmonary disease (COPD), dementia, Parkinson's disease, stroke, depression, osteoarthritis, coronary heart disease, and diabetes.^{10–16} Other studies have found that HL is also associated with

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impaired physical function, frailty, and disability.¹⁷⁻²¹ Research to better characterize the association between hearing capacity and multimorbidity may contribute to a better understanding of the burden of disease related to HL as well as to identify common mechanisms subjacent to age-related degenerative conditions since hearing impairment might be an early physiologic marker of unhealthy aging^{22,23} and the number of coexisting diseases is a major proxy of biological aging.²⁴ Therefore, we examined the association between speech reception threshold in noise (SRTn), a measure of functional auditory capacity, and multimorbidity in a cohort of middle-aged and older adults.

Methods

Study Design and Participants

The UK Biobank study is a large population-based cohort study, established in 2006 to 2010 in the United Kingdom.²⁵ The study recruited more than 500,000 participants aged 39 to 72 years, with information on their health status, demographics, and lifestyle. In addition, participants provided several types of biological samples and underwent a physical examination. Recruitment of participants was carried out through a centrally coordinated identification, using information from the National Health Service (NHS) registers of potentially eligible people living within a reasonable distance of each of the 22 UK Biobank centers located in England, Scotland, and Wales. Each of the participants agreed to have their health monitored. The sample size and age range allow investigation of common causes of morbidity, premature mortality and also allow event determination at an age where cause-specific outcomes are generally well recorded, with less comorbidity than results at older ages.²⁶

This study was performed under generic ethical approval obtained by the UK Biobank from the NHS National Research Ethics Service (reference 11/NW/0382, June 17, 2011). All study participants signed written informed consent.

Assessment of Functional Auditory Capacity

At baseline, a total of 165,524 participants completed the hearing function assessment. Functional auditory capacity was measured with a digit triplet test (DTT) to determine their STRn, which quantifies the ability to understand speech in noise. It was carried out at the UK Biobank evaluation center with the same headphones (Sennheiser HD-25) for all participants without sound-treated booths. However, the staff kept ambient noise to a minimum to reduce the possibility of distraction by participants. Before starting the test, participants were asked to remove their hearing aids if they had them. In addition, the volume of the speech was set to the individual's most comfortable level for each ear. Then,

the participant listened to 15 sets of 3 digits presented with background noise and had to enter each triplet on a keyboard on the touch screen. If the triplet was correctly identified, the noise level was increased for the next triplet; otherwise, the noise level was decreased. Each ear was tested separately, and SRTn was defined as the signal-to-noise ratio (SNR) at which half of the presented digits could be recognized correctly. The SNR could range between -12 and $+8$ dB. In our analyses, we used the SRTn for the best ear for each participant, and if the SRTn was only available for 1 ear, we assumed that it was the best one. Three cutoff points were established to categorize participants in UK Biobank according to their performance on the DTT: (1) normal (SRTn < -5.5 dB SNR); (2) insufficient (SRTn ≥ -5.5 to ≤ -3.5 dB SNR); and (3) poor functional auditory capacity (SRTn > -3.5 dB SNR). The DTT has shown a good correlation with pure-tone audiometry ($r = .77$), which suggests that about 60% of the performance on DTT is explained by standardized audiometric data.²⁷

Assessment of Multimorbidity

To define multimorbidity, 9 chronic diseases previously used in the Whitehall II study were selected²⁸: COPD, dementia, Parkinson's disease, stroke, cancer, depression, osteoarthritis, coronary heart disease, and diabetes. Multimorbidity was defined as the coexistence of 2 or more of these diseases in the same individual.²⁹

The information on COPD, dementia, Parkinson's disease, and stroke was algorithmically defined by combining information from the baseline assessment data, which included participants' self-reported medical conditions, along with linked data from hospital admission records (diagnoses and procedures).³⁰ COPD was defined through hospital diagnoses (International Classification of Diseases [ICD]-10 codes J43-J44, or ICD-9 codes 4920, 4928, 4929, 4969) or self-report. Dementia was defined through hospital diagnoses (ICD-10 codes A81.0, F00-F03, F05.1, F10.6, G30-G30.9, G31.1, G31.2, G31.8, I67.3, or ICD-9 codes 2902-2904, 2912, 2941, 3310-3312, 3315). Parkinson's disease was defined through hospital diagnoses (ICD-10 codes G20-G23, G25.9, G26, G90.3, or ICD-9 codes 3320, 3321, 3330). Stroke was defined through hospital diagnoses (ICD-10 codes I60-I61, I63-I64, or ICD-9 codes 4309, 4319, 4349, 4369). Cancer diagnoses were obtained through linkage with national cancer registries (cancer registry with malignant cancer, ICD-10 codes C00-C97, or ICD-9 codes 1401-2089). Depression was defined as hospital diagnoses (ICD-10 codes F32-33, or ICD-9 codes 7150-7159), use of antidepressants (fluoxetine, citalopram, escitalopram, sertraline, lustral, paroxetine, or bupropion) and self-report. Osteoarthritis was defined through hospital diagnoses (ICD-10 codes M15-19 or ICD-9 code 7150) and self-report. Coronary heart disease was defined through hospital diagnoses (ICD-10 codes I20-25, or

ICD-9 codes 4140, 4292, 4129, 4139, 4140, 4141, 4148, 4149, 4150, 4151, 4160, 4161, 4168, 4169), operative procedures according to the office of Population Censuses and Surveys Classification of Interventions and Procedures version 4 (K40-49, K50, K75, U19) and self-report. Lastly, diabetes was defined as hospital diagnoses (ICD-10 codes E10-14), or HbA1c ≥ 48 mmol/mol in those not using diabetes medication; or use of diabetes medication (insulin, nateglinide, repaglinide, glipizide, glimepiride, metformin, rosiglitazone, pioglitazone, or acarbose) or self-report. We considered the information on multimorbidity until the date of the hearing function assessment to determine prevalent cases.

Other Variables

Participants reported their baseline age, sex, ethnicity, educational level, and total household income,³¹ and the Townsend deprivation index (TDI) was calculated based on the preceding national census output areas.³² In addition, participants reported their smoking status. Weight and height were measured under standardized conditions, and the body mass index (BMI) was calculated as weight (kilograms) divided by height (meters) squared. Physical activity (in metabolic equivalent tasks, METs-h/week) was evaluated with the Short International Physical Activity Questionnaire.³³ To determine the hours of sedentary time, we summed the hours that participants spent watching television, using the computer, and driving on a typical day (ranging between 0 and 16 hours).³⁴ The number of hours of sleep per day, having hypercholesterolemia or hypertension were self-reported. Cognitive function was assessed with the reaction time test; a longer time indicated worse cognitive.³⁵ The exposure to a noisy workplace or loud music, tinnitus, and the use of ototoxic medication (aspirin and ibuprofen) were also reported by the participants. Diet information was assessed with up to five 24-hour recalls (Oxford Web-Q)³⁶ to obtain the average food consumption reflecting habitual diet, and then, nutrient intakes were derived from food composition tables specific to the United Kingdom.³⁷ Among participants who completed at least 2 dietary 24-hour recalls, we calculated the Dietary Approaches to Stop Hypertension (DASH) score, to define diet quality. This healthy diet index scores positively the consumption of foods or nutrients that provide health benefits and negatively those that increase the risk of chronic diseases. Of note, the sodium item was not calculated because this information had not been derived from the available data set.³⁸

Statistical Analysis

Among the participants with hearing function assessment, we found that some had missing information for the following variables: 268 for the TDI, 1144 for the calculation of BMI, 30,237 for physical activity, and

1588 for the reaction time test. We imputed these missing values through multiple imputations by chained equations. Therefore, statistical analyses were conducted with 165,524 participants. Participants who did not undergo hearing assessment have a similar prevalence of multimorbidity, are similar in age and with a similar percentage of women and British ethnicity, have a slightly lower educational level, have lower income, and are fewer smokers.

We assessed differences in sociodemographic characteristics, lifestyle, and cognitive function between the categories of SRTn, by means of the analysis of variance and χ^2 test, for continuous and categorical variables, respectively. Next, we used logistic regression models to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between SRTn and multimorbidity. We built 3 sequentially adjusted models to observe the effect of each of the main confounders on the association between HL and multimorbidity, since each of the adjustment variables are closely related to hearing function and chronic diseases that were included in the definition of multimorbidity: (1) adjusted for age and sex; (2) additionally adjusted for ethnic background (British, other ethnic group), educational level (primary or less, secondary, and university), TDI as a continuous variable, average total household income (less than £18,000, £18,000 to £30,999, £31,000 to £51,999, £52,000 to £100,000, greater than £100,000, prefer not answer, do not know), smoking status (current, former, or never), BMI (< 25.0 , $25.0-29.9$, ≥ 30.0 kg/m²), physical activity (tertiles of METs-h/week), sedentary time (tertiles of h/day), hours of daily sleep (< 7 , $7-8$, > 8), hypercholesterolemia (no or yes), and hypertension (no or yes); and (3) further adjusted for poor cognitive performance (reaction time greater than or equal to the 75th percentile of the cohort), noisy workplace (no or yes), loud music exposure (no or yes), tinnitus (no or yes), and use of ototoxic drugs (no or yes). In addition, we analyzed the SRTn as a continuous variable (per 2-dB SNR increment) and calculated its association with multimorbidity.

Also, we analyzed the association between STRn categories and individual chronic diseases with additional adjustments for the other diseases, to understand the impact of each of them on this association. In addition, stratified analyses by sex, age group, TDI, physical activity, and cognitive function levels were run; interactions were assessed with the likelihood ratio test that compared models with and without cross-product interaction terms. Finally, we performed sensitivity analyses to understand the role of diet in the association between SRTn and multimorbidity in the analytical sample with additional information on diet, and main analyses were adjusted for the DASH score since there is a well-established relationship with a robust body of evidence showing that having a high-quality diet significantly reduces the risk of developing multiple chronic diseases.³⁹ In addition, diet⁴⁰ and specific nutrients⁴¹ have been shown to have effects in reducing the risk of HL. All tests

were 2-sided, with P less than .05 considered to be statistically significant. Analyses were performed with Stata (version 16.1; Stata Corp).

Results

Of the total study participants, 54.5% were women and had a mean (SD) age of 56.7 (8.2) years (range, 39-72 years). The mean (SD) number of chronic diseases at baseline was 0.58 (0.85). Arthrosis was the most prevalent condition, followed by coronary heart disease and diabetes. The prevalence of all examined conditions increased in the categories of insufficient and poor SRTn with respect to normal hearing function (**Table 1**).

In the analytical sample, 87% of the participants had a normal hearing function, 11% insufficient, and 2% had poor hearing function, according to the SRTn category. The prevalence of multimorbidity was 13.2%. Participants' characteristics according to SRTn categories are presented in **Table 2**. In comparison with participants with normal SRTn, those with insufficient and poor SRTn were more frequently male, older, of non-British ethnicity, and with lower socioeconomic level; also, they were more often current smokers, with higher BMI, but more physically active, with higher prevalence of hypercholesterolemia, hypertension, and poor cognitive performance. Regarding the auditory variables, they were more exposed to noise at work, had more tinnitus, and used more frequently ototoxic drugs.

The association between hearing function and multimorbidity is presented in **Table 3**. We observed an association between impaired hearing and multimorbidity in the models adjusted for age and sex. The estimates were slightly modified after further adjustment for sociodemographic and lifestyle characteristics, risk factors of chronic diseases, and variables related to hearing impairment: in comparison with having a normal SRTn, the OR (95% CI) associated with insufficient SRTn was 1.13 (1.08-1.18), and

with poor SRTn was 1.25 (1.14-1.37). Each 2-dB SNR increment in the SRTn was associated with a 6% (5%-8%) increased likelihood of multimorbidity.

When we examined the association between categories of SRTn and each chronic disease considered, hearing impairment was associated with a higher prevalence of COPD, dementia, Parkinson's disease, stroke, depression, and diabetes (Supplemental Table S1, available online). In the analyses among subgroups of participants, no differences were observed in the association between categories of SRTn and multimorbidity by strata of sex, age, TDI, physical activity, or impaired cognitive function (**Figure 1**). In a separate analysis among participants with information on habitual diet, the association between hearing function and multimorbidity remained after additional adjustment for diet quality (OR and 95% CI) for insufficient SRTn: 1.12 (1.02-1.22) and for poor SRTn: 1.38 (1.10-1.72) (Supplemental Table S2, available online).

Discussion

In this large study, insufficient and poor hearing function was associated with prevalent multimorbidity. Each 2-dB SNR increment in the SRTn was associated with a 6% (5%-8%) increased likelihood of multimorbidity. No differences were observed in the study association by strata of sex, age, TDI, physical activity, and impaired cognitive function. The associations observed could place people with HL as a population at special risk for the development of geriatric syndromes such as multimorbidity.

The causes of HL are multiple, including degenerative processes associated with aging, genetic mutations, and exposure to high-intensity noise or ototoxic drugs.⁴² HL can be caused by damage to both the central and peripheral auditory systems and shares biological mechanisms with many chronic diseases, particularly inflammation and oxidative stress.⁴²⁻⁴⁴ There is a strong body of evidence

Table 1. Chronic Diseases at Baseline Among the Study Participants in the UK Biobank, According to Categories of Hearing Function (N = 165,524)

Hearing function	Normal	Insufficient SRTn	Poor	P value
	SRTn < -5.5 dB SNR	to -3.5 dB SNR	SRTn > -3.5 dB SNR	
COPD, % (n = 3126)	1.7	3.0	4.1	<.001
Dementia, % (n = 76)	0.04	0.09	0.2	<.001
Parkinson's disease, % (n = 295)	0.2	0.3	0.5	<.001
Stroke, % (n = 2420)	1.3	2.4	3.8	<.001
Cancer, % (n = 12,176)	7.2	8.7	8.4	<.001
Depression, % (n = 15,582)	9.2	10.6	14.1	<.001
Osteoarthritis, % (n = 32,657)	19.0	24.8	28.7	<.001
Coronary heart disease, % (n = 15,807)	8.8	13.8	17.7	<.001
Diabetes, % (n = 14,379)	7.9	13.1	18.3	<.001

Abbreviations: COPD, chronic obstructive pulmonary disease; SNR, signal-to-noise ratio; SRTn, speech reception threshold in noise in the better ear.

Table 2. Baseline Participants' Characteristics According to Categories of Hearing Function in the UK Biobank (N = 165,524)

	Normal SRTn < -5.5 dB SNR	Insufficient SRTn -5.5 to -3.5 dB SNR	Poor SRTn > -3.5 dB SNR	P value
N	144,030	18,269	3225	
%	87.0	11.0	2.0	
Age, y	56.2 (8.1)	59.9 (7.4)	60.6 (7.4)	<0.001
Female, %	54.6	54.4	47.2	<.001
British ethnicity, %	86.4	75.0	67.0	<.001
Educational level; primary or less, %	14.1	25.5	36.6	<.001
Townsend deprivation index	-1.2 (2.9)	-0.7 (3.1)	-0.02 (3.3)	<.001
Total household income, <£18,000, %	17.6	27.2	35.4	<.001
Current smoker, %	9.9	10.8	11.2	.001
Body mass index, kg/m ²	27.4 (4.8)	27.7 (4.9)	28.2 (5.0)	<.001
Physical activity, METs-h/week	42.7 (41.4)	43.5 (42.4)	43.5 (43.9)	.03
Sedentary time ^a , h/day	4.9 (2.4)	4.9 (2.6)	4.9 (2.7)	.36
Hours of daily sleep	7.1 (1.2)	7.1 (1.5)	7.0 (1.7)	<.001
Hypercholesterolemia, %	17.2	25.6	30.5	<.001
Hypertension, %	23.4	28.6	29.8	<.001
Poor cognitive performance ^b , %	24.1	34.4	40.9	<.001
Noisy workplace, %	21.9	26.9	35.4	<.001
Loud music exposure, %	13.9	12.4	15.5	<.001
Tinnitus, %	16.1	22.7	32.7	<.001
Use of ototoxic drugs ^c , %	1.6	1.8	2.7	<.001
Number of chronic diseases ^d	0.55 (0.8)	0.77 (1.0)	0.96 (1.1)	<.001
Multimorbidity ^e , %	12.2	19.3	24.9	<.001

Values are means (SD) unless otherwise indicated. *P* values based on analysis of variance test for continuous variables or χ^2 test for qualitative variables. Abbreviations: COPD, chronic obstructive pulmonary disease; MET, metabolic equivalent task; SNR, signal-to-noise ratio; SRTn, speech reception threshold in noise in the better ear.

^aTotal number of hours spent watching television, using the computer, or driving.

^bDefined as reaction time (ms) \geq 75th percentile of the cohort.

^cAspirin and ibuprofen.

^dIncludes COPD, dementia, Parkinson's disease, stroke, cancer, depression, osteoarthritis, coronary heart disease, and diabetes.

^eDefined as having 2 or more chronic diseases.

Table 3. Odds Ratios (95% Confidence Interval) for the Association Between Categories of Hearing Function and Multimorbidity in the UK Biobank (N = 165,524)

Hearing function	Normal (SRTn < -5.5 dB SNR)	Insufficient (SRTn -5.5 to -3.5 dB SNR)	Poor (SRTn > -3.5 dB SNR)	<i>P</i> for trend	Per 2-dB SNR increment in SRTn
N	144,030	18,269	3225		165,524
Cases	17,566	3518	803		21,887
Age- and sex- adjusted	1.00	1.35 (1.30-1.41)	1.80 (1.66-1.96)	<.001	1.16 (1.15-1.18)
Model 1	1.00	1.16 (1.11-1.21)	1.33 (1.21-1.45)	<.001	1.08 (1.06-1.10)
Model 2	1.00	1.13 (1.08-1.18)	1.25 (1.14-1.37)	<.001	1.06 (1.05-1.08)

Model 1: Additionally adjusted for ethnic background (British, other ethnic groups), educational level (primary or less, secondary, and university), Townsend deprivation index (continuous), average total household income (<£18,000, £18,000 to £30,999, £31,000 to £51,999, £52,000 to £100,000, greater than £100,000, prefer not to answer, do not know), smoking status (current, former, or never), BMI (<25.0, 25.0-29.9, \geq 30.0 kg/m²), physical activity (tertiles of METs-h/week), sedentary time (tertiles of h/day), hours of daily sleep (<7, 7-8, >8), hypercholesterolemia (no or yes), and hypertension (no or yes).

Model 2: Additionally, adjusted for poor cognitive performance (no or yes), noisy workplace (no or yes), loud music exposure (no or yes), tinnitus (no or yes), and use of ototoxic drugs (no or yes).

Abbreviations: BMI, body mass index; MET, metabolic equivalent task; SNR, signal-to-noise ratio; SRTn, speech reception threshold in noise in the better ear.

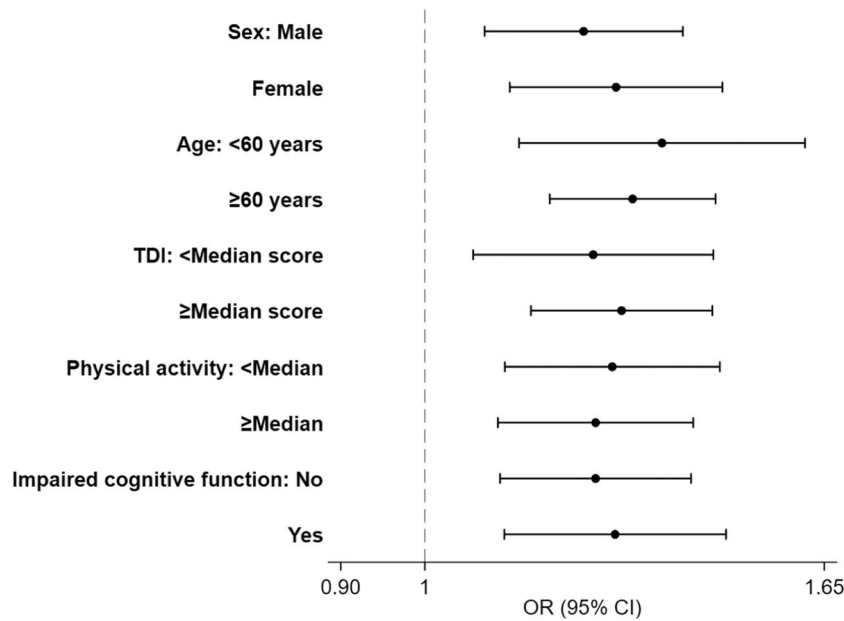


Figure 1. Odds ratios (ORs) (95% confidence interval [CI]) for the association between poor hearing function versus normal function among subgroups of participants in the UK Biobank. Estimates are adjusted as in model 2 in **Table 3**. TDI, Townsend deprivation index.

that associates inflammatory markers such as interleukine-6 and C-reactive protein with cardiovascular events, cancer, and mortality.⁴⁵ In addition, inflammation markers are strongly associated with cognitive impairment⁴⁶ and Alzheimer's disease.⁴⁷ Also, high concentrations of inflammatory markers are related to an increased risk of diabetes.⁴⁸ Although the inflammatory mechanisms of multimorbidity have been less studied,⁴⁹ low-grade inflammation has been postulated as one of the hallmarks of biological aging.²⁴ On the other hand, it has been observed that oxidative stress is associated with multimorbidity,⁴⁹ mainly due to reactive oxygen species that could increase the rate of cellular apoptosis.⁵⁰

To our knowledge, this is the first study examining the association between hearing function and multimorbidity. Previous studies have examined the association between HL and some of the specific chronic diseases included in the definition of multimorbidity.¹⁰⁻¹⁶ For example, Sharma et al,¹⁰ in a cross-sectional analysis of the National Health and Nutrition Examination Survey (NHANES), observed that COPD was directly associated with HL. A plausible explanation is that an inadequate supply of oxygen to the cochlea could cause ischemic lesions, hindering the conversion process of a mechanical signal to an electrical signal.⁵¹ We observed a strong association between poor SRTn and dementia, which is consistent with the Report of the Lancet Commission on Dementia, which places HL as the most important modifiable risk factor in mid-life for dementia.¹¹ In the same line, Moore et al,⁵² using data from the UK Biobank study, observed that cognitive abilities decreased as SRTn increased; thus, HL could be a prodromal factor in the development of Alzheimer's disease, since people who develop dementia have accelerated deteriorations in cognitive performance up to 6 years earlier.⁵³ Regarding the

association between SRTn and Parkinson's disease, Leme et al,¹² in a systematic review, observed that sensorineural HL and cochlear impairment are more severe in participants with Parkinson's disease, which is consistent with our findings. Hearing function is susceptible to neurochemical changes, which can be produced by neurodegenerative diseases that alter the integrity of the synaptic pathway and the neurotransmitters involved; thus, HL may be an early marker of the disease.⁵⁴ With respect to the association between SRTn and stroke, our findings concur with those found by Fang et al,¹³ who found that HL was linked to hemorrhagic or ischemic stroke at speech and high frequencies. A plausible mechanism is microvascular damage at first instances, which would subsequently affect larger arteries. Indeed, Lee et al reported that there could be auditory manifestations up to 2 months before a stroke.⁵⁵

Hearing function was not associated with cancer; however, we observed a higher prevalence of cancer in the insufficient and poor SRTn categories with respect to normal hearing function, as has been observed in several studies with cancer survivors who underwent platinum-based treatments.⁵⁶ By contrast, we observed a strong association between insufficient and poor SRTn and depression; our findings are in line with those of a meta-analysis¹⁴ that reported an association between HL defined by audiometry, SRTn, or self-reported hearing impairment and depression, this could be explained by the psychosocial and functional difficulties that people with hearing disorders may suffer. Besides, we observed an association between poor SRTn and osteoarthritis, consistent with the results found by Bikbov et al,¹⁵ using self-reported HL in the middle-aged and older adult population.

We did not observe an association between SRTn and coronary heart disease in the models adjusted for the

other chronic diseases. Similar results were obtained by Sterling et al,⁵⁷ with NHANES data. Finally, we observed a strong association between insufficient and poor SRTn and diabetes, as in the meta-analysis of cross-sectional studies carried out by Horikawa et al.¹⁶ The presence of cochlear microangiopathy and degeneration of the stria vascularis and cochlear outer hair cells have been demonstrated in patients with diabetes when analyzing their temporal bones.⁵⁸

Currently, the causal relationship between hearing function and the chronic diseases described is uncertain, except for the relationship between HL and dementia. Hearing impairment is estimated to be responsible for approximately 8% of dementia cases.¹¹ Furthermore, it has been observed that speech-in-noise hearing impairment is independently associated with the risk of dementia, which adds evidence of a potentially modifiable risk factor.⁵⁹

Strengths of this study include the large sample size and the use of a speech-in-noise test, a tool that focuses on human communication, which is of clinical relevance. Also, we used multiple sources of information to obtain the chronic disease diagnoses included in the definition of multimorbidity. Moreover, these analyses were adjusted for major confounders, including socio-demographic, lifestyle, and auditory variables. We used a definition of multimorbidity that includes 9 chronic diseases; other definitions of multimorbidity are also plausible. Lastly, this study has a cross-sectional design, with no intention to attribute directionality to the observed association.

In conclusion, insufficient and poor SRTn were associated with multimorbidity. These findings, if confirmed in further well-designed longitudinal studies with long follow-ups, may provide evidence to support the association between hearing function and multimorbidity.

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Authors Contributions

Humberto Yévenes-Briones, designed the research, performed the statistical analyses, contributed to the interpretation of the results, drafted the manuscript, had primary responsibility for final content and reviewed the manuscript for important intellectual content, and read and approved the final manuscript; **Francisco Félix Caballero**, designed the research, contributed to interpretation of the results, drafted the manuscript and reviewed the manuscript for important intellectual content, and read and approved the final manuscript; **Ellen A. Struijk**, contributed to interpretation of the results and reviewed the manuscript for important intellectual content, and read and approved the final manuscript; **Lucía Arias-Fernández**, contributed to interpretation of the results and reviewed the manuscript for

important intellectual content, and read and approved the final manuscript; **Alberto Lana**, contributed to the interpretation of the results and reviewed the manuscript for important intellectual content, and read and approved the final manuscript; **Jorge Rey-Martínez**, contributed to the interpretation of the results and reviewed the manuscript for important intellectual content, and read and approved the final manuscript; **Fernando Rodríguez-Artalejo**, contributed to the interpretation of the results and reviewed the manuscript for important intellectual content, and read and approved the final manuscript; **Esther Lopez-García**, designed the research, contributed to the interpretation of the results, drafted the manuscript, supervised the conduct of research, had primary responsibility for final content and reviewed the manuscript for important intellectual content, and read and approved the final manuscript.

Disclosures

Competing interests: None.


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Supplemental Material


Additional supporting information is available in the online version of the article.


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References

1. World Health Organization. *GHE: life expectancy and healthy life expectancy*; 2019. Accessed September 21, 2022. <https://www.who.int/data/gho/data/themes/mortality-and-global>

- health-estimates/ghe-life-expectancy-and-healthy-life-expectancy#:~:text=Globally,%20life%20expectancy%20has%20increased,reduced%20years%20lived%20with%20disability
- World Health Organization. *Non communicable diseases*; 2022. Accessed September 21, 2022. <https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases#:~:text=Key%20facts,-%20and%20middle-income%20countries>
 - Johnston MC, Crilly M, Black C, Prescott GJ, Mercer SW. Defining and measuring multimorbidity: a systematic review of systematic reviews. *Eur J Pub Health*. 2019;29(1):182-189. doi:10.1093/eurpub/cky098
 - Sheridan PE, Mair CA, Quiñones AR. Associations between prevalent multimorbidity combinations and prospective disability and self-rated health among older adults in Europe. *BMC Geriatr*. 2019;19(1):198. doi:10.1186/s12877-019-1214-z
 - Makovski TT, Schmitz S, Zeegers MP, Stranges S, van den Akker M. Multimorbidity and quality of life: systematic literature review and meta-analysis. *Ageing Res Rev*. 2019;53:100903. doi:10.1016/j.arr.2019.04.005
 - Read JR, Sharpe L, Modini M, Dear BF. Multimorbidity and depression: a systematic review and meta-analysis. *J Affect Disord*. 2017;221:36-46. doi:10.1016/j.jad.2017.06.009
 - Mavaddat N, Valderas JM, van der Linde R, Khaw KT, Kinmonth AL. Association of self-rated health with multimorbidity, chronic disease and psychosocial factors in a large middle-aged and older cohort from general practice: a cross-sectional study. *BMC Fam Pract*. 2014;15:185. doi:10.1186/s12875-014-0185-6
 - Palladino R, Tayu Lee J, Ashworth M, Triassi M, Millett C. Associations between multimorbidity, healthcare utilisation and health status: evidence from 16 European countries. *Age Ageing*. 2016;45(3):431-435. doi:10.1093/ageing/afw044
 - Agrawal Y. 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*. 2008;168(14):1522-1530. doi:10.1001/archinte.168.14.1522
 - Sharma RK, Chern A, Begasse de Dhaem O, Golub JS, Lalwani AK. Chronic obstructive pulmonary disease is a risk factor for sensorineural hearing loss: a US population study. *Otol Neurotol*. 2021;42(10):1467-1475. doi:10.1097/MAO.0000000000003317
 - Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *Lancet*. 2020;396(10248):413-446. doi:10.1016/S0140-6736(20)30367-6
 - Leme MS, Sanches SGG, Carvalho RMM. Peripheral hearing in Parkinson's disease: a systematic review. *Int J Audiol*. Published online August 18, 2022; 1-9. doi:10.1080/14992027.2022.2109073
 - Fang Q, Lai X, Yang L, et al. Hearing loss is associated with increased stroke risk in the Dongfeng-Tongji Cohort. *Atherosclerosis*. 2019;285:10-16. doi:10.1016/j.atherosclerosis.2019.03.012
 - Lawrence BJ, Jayakody DMP, Bennett RJ, Eikelboom RH, Gasson N, Friedland PL. Hearing loss and depression in older adults: a systematic review and meta-analysis. *Gerontologist*. 2020;60(3):e137-e154. doi:10.1093/geront/gnz009
 - Bikbov MM, Kazakbaeva GM, Gilmanshin TR, et al. Prevalence and associated factors of osteoarthritis in the Ural Eye and Medical Study and the Ural Very Old Study. *Sci Rep*. 2022;12(1):12607. doi:10.1038/s41598-022-16925-6
 - Horikawa C, Kodama S, Tanaka S, et al. Diabetes and risk of hearing impairment in adults: a meta-analysis. *J Clin Endocrinol Metab*. 2013;98(1):51-58. doi:10.1210/jc.2012-2119
 - Yévenes-Briones H, Caballero FF, Struijk EA, et al. Association between hearing loss and impaired physical function, frailty, and disability in older adults: a cross-sectional study. *JAMA Otolaryngol Head Neck Surg*. 2021;147(11):951-958. doi:10.1001/jamaoto.2021.2399
 - Brenowitz WD, Wallhagen MI. Does hearing impairment affect physical function? Current evidence, potential mechanisms, and future research directions for healthy aging. *JAMA Netw Open*. 2021;4(6):e2114782. doi:10.1001/jamanetworkopen.2021.14782
 - Martinez-Amezcuca P, Kuo PL, Reed NS, et al. Association of hearing impairment with higher level physical functioning and walking endurance: results from the Baltimore Longitudinal Study of Aging (BLSA). *J Gerontol A Biol Sci Med Sci*. 2021;76:e290-e298. doi:10.1093/gerona/Glab144
 - Sardone R, Castellana F, Bortone I, et al. Association between central and peripheral age-related hearing loss and different frailty phenotypes in an older population in Southern Italy. *JAMA Otolaryngol Head Neck Surg*. 2021;147(6):561-571. doi:10.1001/jamaoto.2020.5334
 - Lin TC, Yen M, Liao YC. Hearing loss is a risk factor of disability in older adults: a systematic review. *Arch Gerontol Geriatr*. 2019;85:103907. doi:10.1016/j.archger.2019.103907
 - Fabbri E, An Y, Zoli M, et al. Aging and the burden of multimorbidity: associations with inflammatory and anabolic hormonal biomarkers. *J Gerontol A Biol Sci Med Sci*. 2015;70(1):63-70. doi:10.1093/gerona/glu127
 - Friedman EM, Christ SL, Mroczek DK. Inflammation partially mediates the association of multimorbidity and functional limitations in a national sample of middle-aged and older adults: the MIDUS study. *J Aging Health*. 2015;27(5):843-863. doi:10.1177/0898264315569453
 - Ferrucci L, Gonzalez-Freire M, Fabbri E, et al. Measuring biological aging in humans: a quest. *Aging cell*. 2020;19(2):e13080. doi:10.1111/acel.13080
 - Collins R. What makes UK Biobank special? *Lancet*. 2012;379(9822):1173-1174.
 - UK Biobank. *Protocol for a large-scale prospective epidemiological resource*; 2007. Accessed July 7, 2023. <https://www.ukbiobank.ac.uk/media/gnkeyh2q/study-rationale.pdf>
 - Smits C, Kapteyn TS, Houtgast T. Development and validation of an automatic speech-in-noise screening test by telephone. *Int J Audiol*. 2004;43(1):15-28. doi:10.1080/14992020400050004
 - Dugravot A, Fayosse A, Dumurgier J, et al. Social inequalities in multimorbidity, frailty, disability, and transitions to mortality: a 24-year follow-up of the Whitehall II

- cohort study. *Lancet Public Health*. 2020;5(1):e42-e50. doi:10.1016/S2468-2667(19)30226-9
29. World Health Organization. *Multimorbidity: Technical Series on Safer Primary Care*. Licence: CC BY-NC-SA 3.0 IGO. World Health Organization; 2016.
 30. UK Biobank. *Algorithmically defined outcomes*. January 3, 2022. Accessed June 14, 2022. https://biobank.ndph.ox.ac.uk/showcase/ukb/docs/alg_outcome_main.pdf
 31. Zhang YB, Chen C, Pan XF, et al. Associations of healthy lifestyle and socioeconomic status with mortality and incident cardiovascular disease: two prospective cohort studies. *BMJ*. 2021;373:n604. doi:10.1136/bmj.n604
 32. Townsend P. Deprivation. *J Soc Policy*. 1987;16(2):125-146. doi:10.1017/S0047279400020341
 33. Craig CL, Marshall AL, Sjöström M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc*. 2003;35(8):1381-1395. doi:10.1249/01.MSS.0000078924.61453.FB
 34. Chudasama YV, Khunti K, Gillies CL, et al. Healthy lifestyle and life expectancy in people with multimorbidity in the UK Biobank: a longitudinal cohort study. *PLoS Med*. 2020;17(9):e1003332. doi:10.1371/journal.pmed.1003332
 35. Fawns-Ritchie C, Deary IJ. Reliability and validity of the UK Biobank cognitive tests. *PLoS One*. 2020;15(4):e0231627. doi:10.1371/journal.pone.0231627
 36. Galante J, Adamska L, Young A, et al. The acceptability of repeat Internet-based hybrid diet assessment of previous 24-h dietary intake: administration of the Oxford WebQ in UK Biobank. *Br J Nutr*. 2016;115(4):681-686. doi:10.1017/S0007114515004821
 37. Food Standards Agency. *McCance and Widdowson's the Composition of Foods*. 6th ed. Royal Society of Chemistry; 2002.
 38. Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. *N Engl J Med*. 2001;344(1):3-10. doi:10.1056/NEJM200101043440101
 39. World Health Organization. *Diet, nutrition, and the prevention of chronic diseases: report of a joint WHO/FAO expert consultation*; 2002. Accessed July 7, 2023. <https://apps.who.int/iris/handle/10665/42665?locale-attribute=es&>
 40. Curhan SG, Halpin C, Wang M, Eavey RD, Curhan GC. Prospective study of dietary patterns and hearing threshold elevation. *Am J Epidemiol*. 2020;189(3):204-214. doi:10.1093/aje/kwz223
 41. Yévenes-Briones H, Caballero FF, Struijk EA, Lana A, Rodríguez-Artalejo F, Lopez-García E. Dietary fat intake and risk of disabling hearing impairment: a prospective population-based cohort study. *Eur J Nutr*. 2022;61(1):231-242. doi:10.1007/s00394-021-02644-7
 42. Cunningham LL, Tucci DL. Hearing Loss in Adults. *N Engl J Med*. 2017;377(25):2465-2473. doi:10.1056/NEJMra1616601
 43. Eisenhut M. Evidence supporting the hypothesis that inflammation-induced vasospasm is involved in the pathogenesis of acquired sensorineural hearing loss. *Int J Otolaryngol*. 2019;2019:4367240. doi:10.1155/2019/4367240
 44. Kamogashira T, Fujimoto C, Yamasoba T. Reactive oxygen species, apoptosis, and mitochondrial dysfunction in hearing loss. *BioMed Res Int*. 2015;2015:617207. doi:10.1155/2015/617207
 45. Friedman E, Shorey C. Inflammation in multimorbidity and disability: an integrative review. *Health Psychol*. 2019;38(9):791-801. doi:10.1037/hea0000749
 46. Schubert CR, Fischer ME, Pinto AA, et al. Inflammation, metabolic dysregulation and environmental neurotoxins and risk of cognitive decline and impairment in midlife. *Neurol Sci*. 2023;44:149-157. doi:10.1007/s10072-022-06386-0
 47. Kinney JW, Bemiller SM, Murtishaw AS, Leisgang AM, Salazar AM, Lamb BT. Inflammation as a central mechanism in Alzheimer's disease. *Alzheimers Dement*. 2018;4:575-590. doi:10.1016/j.trci.2018.06.014
 48. Schöttker B, Saum KU, Jansen EHJM, Holleczeck B, Brenner H. Associations of metabolic, inflammatory and oxidative stress markers with total morbidity and multimorbidity in a large cohort of older German adults. *Age Ageing*. 2016;45(1):127-135. doi:10.1093/ageing/afv159
 49. Pandey KB, Rizvi SI. Markers of oxidative stress in erythrocytes and plasma during aging in humans. *Oxid Med Cell Longevity*. 2010;3(1):2-12. doi:10.4161/oxim.3.1.10476
 50. Koloverou E, Panagiotakos DB, Georgousopoulou EN, et al. Single and combined effects of inflammatory markers on 10 year diabetes incidence: the mediating role of adiposity—results from the ATTICA cohort study. *Diabetes Metab Res Rev*. 2018;34(1):e2939. doi:10.1002/dmrr.2939
 51. Olivetto E, Simoni E, Guaran V, Astolfi L, Martini A. Sensorineural hearing loss and ischemic injury: Development of animal models to assess vascular and oxidative effects. *Hear Res*. 2015;327:58-68. doi:10.1016/j.heares.2015.05.004
 52. Moore DR, Edmondson-Jones M, Dawes P, et al. Relation between speech-in-noise threshold, hearing loss and cognition from 40-69 years of age. *PLoS One*. 2014;9(9):e107720. doi:10.1371/journal.pone.0107720
 53. Wilson RS, Leurgans SE, Boyle PA, Bennett DA. Cognitive decline in prodromal Alzheimer disease and mild cognitive impairment. *Arch Neurol*. 2011;68(3):351-356. doi:10.1001/archneurol.2011.31
 54. Jafari Z, Kolb BE, Mohajerani MH. Auditory dysfunction in Parkinson's disease. *Mov Disorders*. 2020;35(4):537-550. doi:10.1002/mds.28000
 55. Lee H, Sohn SI, Jung DK, et al. Sudden deafness and anterior inferior cerebellar artery infarction. *Stroke*. 2002;33(12):2807-2812. doi:10.1161/01.str.0000038692.17290.24
 56. Dillard LK, Lopez-Perez L, Martinez RX, Fullerton AM, Chadha S, McMahon CM. Global burden of ototoxic hearing loss associated with platinum-based cancer treatment: a systematic review and meta-analysis. *Cancer Epidemiol*. 2022;79:102203. doi:10.1016/j.canep.2022.102203

57. Sterling MR, Lin FR, Jannat-Khah DP, Goman AM, Echeverria SE, Safford MM. Hearing loss among older adults with heart failure in the United States: data from the National Health and Nutrition Examination Survey. *JAMA Otolaryngol Head Neck Surg.* 2018;144(3):273-275. doi:10.1001/jamaoto.2017.2979
58. Fukushima H, Cureoglu S, Schachern PA, Paparella MM, Harada T, Oktay MF. Effects of type 2 diabetes mellitus on cochlear structure in humans. *Arch Otolaryngol Head Neck Surg.* 2006;132(9):934-938. doi:10.1001/archotol.132.9.934
59. Stevenson JS, Clifton L, Kuźma E, Littlejohns TJ. Speech-in-noise hearing impairment is associated with an increased risk of incident dementia in 82,039 UK Biobank participants. *Alzheimer's Dementia.* 2022;18(3):445-456. doi:10.1002/alz.12416