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FEATURED ARTICLE

Speech-in-noise hearing impairment is associated with an increased risk of incident dementia in 82,039 UK Biobank participants

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Abstract

Introduction: Little is known about the association between speech-in-noise (SiN) hearing impairment and dementia.

Methods: In 82,039 dementia-free participants aged ≥60 years were selected from the UK Biobank. Cox proportional-hazards models were used to investigate whether SiN hearing impairment is associated with an increased risk of incident dementia.

Results: Over 11 years of follow-up (median = 10.1), 1285 participants developed dementia. Insufficient and poor SiN hearing were associated with a 61% (hazard ratio [HR] = 1.61, 95% confidence [CI] 1.41–1.84) and 91% (HR = 1.91, 95% CI 1.55–2.36) increased risk of developing dementia, respectively, compared to normal SiN hearing. The association remained similar when restricting to follow-up intervals of ≤3, >3 to <6, >6 to <9, and >9 years. There was limited evidence for mediation through depressive symptoms and social isolation.

Discussion: SiN hearing impairment is independently associated with incident dementia, providing further evidence for hearing impairment as a potential modifiable dementia risk factor.

KEYWORDS
dementia, depression, hearing aid, hearing impairment, longitudinal, social isolation, speech-in-noise, UK Biobank

1 | NARRATIVE

Hearing impairment is common and increases with age, with approximately two thirds of adults aged 75 years or older estimated to have a hearing problem that adversely impacts communication.[1,2] The high prevalence of hearing impairment is particular cause for concern as there is growing evidence that it could increase the risk of dementia. In a 2020 Lancet Commission report on dementia prevention, hearing loss was identified as 1 of 12 major, modifiable risk factors for dementia.[3] The authors of the report estimated that, if causal, hearing impairment could be responsible for ≈8% of dementia cases, the highest burden out of the 12 factors presented.[3] Hearing impairment is a particularly promising target for dementia prevention due the widespread availability of cost-effective interventions.[4] However, treatment varies depending on the cause of hearing impairment and it is important to understand which forms of impairment are associated with dementia risk.

Meta-analyses of longitudinal studies have consistently reported that hearing impairment is associated with an increased risk of incident dementia and Alzheimer's disease (AD).[5–8] Aside from self-report, the most common instrument used to assess hearing in previous studies is pure tone audiometry, which measures hearing sensitivity to

HIGHLIGHTS

- Speech-in-noise hearing impairment is associated with increased risk of dementia.
- Association remains robust after excluding cases within 9 years of follow-up.
- ≤6.5% of excess risk is mediated by low mood and social isolation.

RESEARCH IN CONTEXT

1. **Systematic Review**: A PubMed search identified 23 cohort studies and four meta-analyses that have evaluated the association between hearing impairment and dementia; however, only two small studies have evaluated speech-in-noise (SiN) hearing. There has also been limited evaluation of factors hypothesized to influence the association between hearing impairment and dementia, such as reverse causation and mediation via social isolation or depression.
2. **Interpretation**: SiN hearing impairment is associated with an increased risk of incident all-cause dementia. There is no demonstrable evidence of reverse causation after excluding dementia cases in the first few years of follow-up or with poor/fair self-reported health at baseline. The percentage of excess risk mediated by low mood and social isolation is small.
3. **Future Directions**: Evaluation of the association between SiN hearing impairment and dementia is warranted in large prospective studies with concurrent measurement of SiN and pure tone hearing impairment.

pure tones in a controlled, quiet environment.[9,10] However, in addition to reduced hearing sensitivity, age-related hearing impairment is also characterized by reduced speech understanding in noisy environments. This occurs as a result of attenuation and distortion of sensory stimuli in the peripheral auditory system and may also be influenced by altered central auditory processing in the brain.[9,11,12] Hearing impairment measured using pure tone audiometry may not reflect the functional impact of the distortion of auditory stimuli and the subsequent speech-in-noise (SiN) impairment that occurs in age-related hearing impairment.[13] In contrast, a SiN hearing assessment specifically evaluates the listener's ability to detect and recognize speech in background noise, which may more closely approximate hearing in real-world settings.[9,14,15] Simple amplification of auditory stimuli with a hearing aid might not adequately address SiN impairment, with more complex technology and aural rehabilitation often required.[11,15] Consequently, if SiN is associated with an increased risk of dementia, this could have important implications for how interventions to treat age-related hearing impairment in the context of dementia prevention are implemented.

To our knowledge, only two studies have evaluated the association between SiN hearing and incident dementia. One reported that SiN hearing impairment was significantly associated with a higher risk of incident AD (hazard ratio [HR] = 23.3, 95% confidence interval [CI] 6.6–82.7)[16] and the second reported a non-statistically significant increased risk of dementia (HR = 2.5, 95% CI 0.9–7.5).[17] However, both studies were small (n = 740[16]; n = 274[17]); and had low numbers of AD and dementia cases (n = 40 [16]; n = 23[17]), which means that the findings in each study could have been due to chance.

To address the limited research on the role of SiN, we investigated the association between SiN-measured hearing impairment and incident dementia in 82,039 women and men selected from the population-based United Kingdom (UK) Biobank cohort.[18] We also investigated the role of reverse causation (i.e., whether any observed associations could be driven by pre-clinical dementia), mediation through social isolation and depressive symptoms, and effect modification through hearing aid use.

Participants included in the current study were aged 60 or older and free from dementia at baseline. SiN hearing was measured at baseline between 2009/2010 and 2012/2013 using a Digit Triplets Test with participants categorized as "normal" (speech reception threshold in noise [SRT_n] <-5.5 decibels [dB]; n = 67,645), "insufficient" (SRT_n ≥ −5.5–<−3.5 dB; n = 11,329), and "poor" (SRT_n ≥−3.5 dB; n = 3065).[14,19,20] Baseline characteristics by SiN hearing status are provided in Table 1. Over 11 years of follow-up (median = 10.1 years), 1285 participants developed dementia captured through linkage to electronic hospital inpatient and death registry records (see Figure 1 for Kaplan-Meier plot by SiN hearing status).

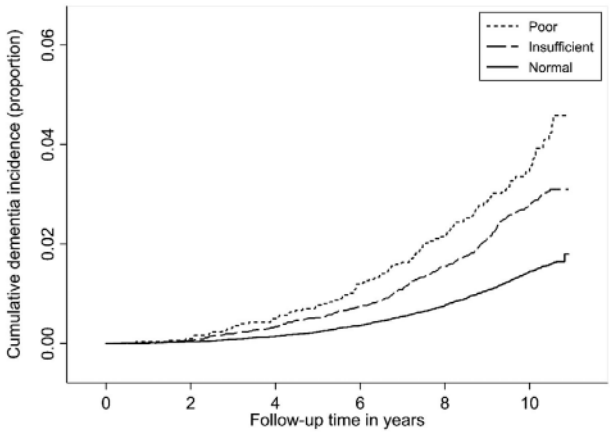

FIGURE 1 Cumulative unadjusted dementia incidence by speech-in-noise (SiN) hearing status

In Cox proportional-hazards regression models adjusted for sociodemographic, lifestyle, and health-related factors, insufficient and poor SiN hearing were associated with a 61% (HR = 1.61, 95% CI 1.41–1.84) and 91% (HR = 1.91, 95% CI 1.55–2.36) higher risk of developing dementia, respectively, compared to normal SiN hearing (Figure 2). These findings are consistent with the wider literature evaluating the association between hearing impairment and dementia.

TABLE 1 Baseline characteristics for 82,039 participants by SiN hearing status

Characteristics, n (%)	Total sample (n = 82,039)	SiN hearing status		
		Normal (n = 67,645)	Insufficient (n = 11,329)	Poor (n = 3065)
Age in years, median (IQR)	64 (62-67)	64 (62-66)	65 (63-67)	65 (63-68)
Men	39,267 (47.9)	32,117 (47.5)	5457 (48.2)	1693 (55.2)
White ethnic background	78,815 (96.1)	65,742 (97.2)	10,411 (91.9)	2662 (86.9)
Country				
England	80,718 (98.4)	66,904 (98.9)	10,887 (96.1)	2927 (95.5)
Wales	1321 (1.6)	741 (1.1)	442 (3.9)	138 (4.5)
Education				
Higher	37,996 (46.3)	32,292 (47.7)	4657 (41.1)	1047 (34.2)
Upper secondary	4872 (5.9)	4111 (6.1)	631 (5.6)	130 (4.2)
Lower secondary	15,719 (19.2)	13,151 (19.4)	2063 (18.2)	505 (16.5)
Vocational	5292 (6.5)	4281 (6.3)	776 (6.8)	235 (7.7)
No secondary education	18,160 (22.1)	13,810 (20.4)	3202 (28.3)	1148 (37.5)
Socioeconomic status (quartiles)				
1, least deprived	20,642 (25.2)	17,568 (26.0)	2511 (22.2)	563 (18.4)
2	20,595 (25.1)	17,229 (25.5)	2692 (23.8)	674 (22.0)
3	20,510 (25.0)	16,968 (25.1)	2773 (24.5)	769 (25.1)
4, most deprived	20,292 (24.7)	15,880 (23.5)	3353 (29.6)	1059 (34.6)
Smoking status				
Never	41,849 (51.0)	34,600 (51.1)	5735 (50.6)	1514 (49.4)
Previous	34,204 (41.7)	28,293 (41.8)	4634 (40.9)	1277 (41.7)
Current	5986 (7.3)	4752 (7.0)	960 (8.5)	274 (8.9)
Alcohol intake				
Daily or almost daily	19,448 (23.7)	16,514 (24.4)	2355 (20.8)	579 (18.9)
3–4 times/wk	18,443 (22.5)	15,627 (23.1)	2283 (20.2)	533 (17.4)
1–2 times/wk	19,181 (23.4)	15,830 (23.4)	2645 (23.3)	706 (23.0)
1–3 times/month	8268 (10.1)	6843 (10.1)	1133 (10.0)	292 (9.5)
Special occasions only	9891 (12.1)	7722 (11.4)	1651 (14.6)	518 (16.9)
Never	6808 (8.3)	5109 (7.6)	1262 (11.1)	437 (14.3)
BMI (kg/m^2)				
<24	25,475 (31.1)	21,141 (31.3)	3462 (30.6)	872 (28.5)
25–29	36,498 (44.5)	30,290 (44.8)	4881 (43.1)	1327 (43.3)
≥30	20,066 (24.5)	16,214 (24.0)	2986 (26.4)	866 (28.3)
Hypertension	31,836 (38.8)	25,693 (38.0)	4756 (42.0)	1387 (45.3)
Diabetes	5989 (7.3)	4582 (6.8)	1065 (9.4)	342 (11.2)
Stroke/TIA	1924 (2.3)	1467 (2.2)	322 (2.8)	135 (4.4)
Self-reported health				
Excellent	11,167 (13.6)	9525 (14.1)	1334 (11.8)	308 (10.1)
Good	49,251 (60.2)	41,253 (61.1)	6405 (56.7)	1593 (52.2)
Fair	18,118 (22.1)	14,328 (21.2)	2903 (25.7)	887 (29.1)
Poor	3308 (4.0)	2398 (3.6)	649 (5.7)	261 (8.6)
Depressive symptoms				
Not at all	65,060 (82.4)	54,068 (82.8)	8746 (80.7)	2246 (78.2)
Several days	11,391 (14.4)	9380 (14.4)	1568 (14.5)	443 (15.4)

(Continues)

TABLE 1 (Continued)

Characteristics, n (%)	Total sample (n = 82,039)	SiN hearing status		
		Normal (n = 67,645)	Insufficient (n = 11,329)	Poor (n = 3065)
More than half	1611 (2.0)	1143 (1.8)	347 (3.2)	121 (4.2)
Nearly every day	916 (1.2)	682 (1.0)	173 (1.6)	61 (2.1)
Social isolation	7161 (8.8)	5663 (8.5)	1164 (10.5)	334 (11.2)
Hearing aid use	4002 (4.9)	2158 (3.2)	1081 (9.6)	763 (25.0)
Self-reported hearing impairment	26,894 (34.7)	19,955 (31.2)	4996 (46.6)	1943 (66.2)

Abbreviations: BMI, body mass index; dB, Decibels; SiN, speech-in-noise; TIA, transient ischemic attack.

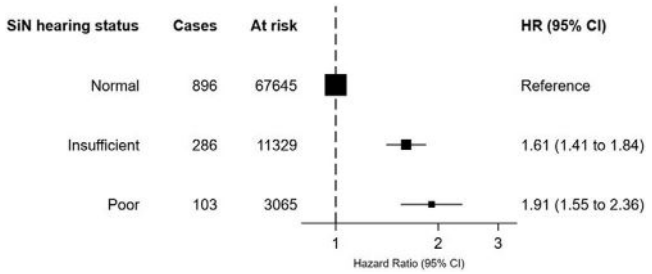

FIGURE 2 Cox proportional hazards model for the association between SiN hearing status and incident dementia. Models adjusted for age, sex, ethnicity, country, education, socioeconomic status, alcohol, smoking, body mass index, hypertension, diabetes, and stroke/transient ischemic attack. CI, confidence interval; HR, hazard ratio; SiN, speech-in-noise

A meta-analysis published in 2018 pooled results from 14 cohort studies with a total of 72,831 participants and reported that hearing impairment was associated with an almost 50% increased risk of dementia (HR = 1.49, 95% CI 1.30–1.67).[6] The included studies used a diversity of methods to assess hearing impairment, such as self-report and hearing loss documented in medical records. In a separate meta-analysis of three cohort studies with a total of 3439 participants, hearing impairment measured using pure tone audiometry was associated with 1.3 times the odds of incident dementia (odds ratio = 1.28, 95% CI 1.02–1.59).[5] Hearing impairment is therefore consistently associated with an increased risk of dementia regardless of the method of assessment.

However, a key concern in studies that investigate risk factors for dementia is reverse causation bias. Dementia pathology progresses several years prior to a formal dementia diagnosis, and this progression can affect other behavioral and physical measures.[21] It is also well established that neurodegeneration caused by the pathophysiological progression of AD, including cortical regions involved in sensory processing, occurs several years prior to clinical manifestation of the disease.[21,22] In the context of the current study, pre-clinical dementia could adversely affect performance on a hearing test or sensory processing, which in turn would be associated with a future diagnosis of dementia. To address this, we investigated whether associations differed by length of follow-up period or after exclusion of participants with poor or fair self-reported health at baseline. If reverse causation was a major source of bias then we hypothesized that any observed associations would become weaker over longer periods of follow-up or when restricting to a sample of "healthy" participants.

We found that the associations were slightly stronger when restricting to dementia cases that occurred within 3 years of follow-up, but remained similar to the main findings when restricting to cases that occurred over longer follow-up periods such as >3 to <6 years, >6 to <9 years, and >9 years (Table 2). Furthermore, compared to normal SiN hearing, insufficient and poor SiN hearing were associated with a 64% (HR = 1.64, 95% CI 1.39–1.97) and 118% (HR = 2.18, 95% CI 1.65–2.88) increased risk of dementia, respectively, when excluding participants with poor or fair self-reported health. Our findings are comparable to those of two previous studies that concluded that there was no evidence of reverse causation in participants with pure tone hearing impairment after excluding up to 6 years of follow-up.[10,23]

A proposed explanation for the observed associations between hearing impairment and dementia is that they are mediated by other factors, such as social isolation and depression, although there is limited evidence to support this hypothesis.[24,25] We found that the percentage of excess risk mediated by depressive symptoms and social isolation combined was only 2.5% for insufficient SiN hearing and 6.5% for poor SiN hearing, suggesting that these two factors do not substantially mediate the association between SiN-measured hearing impairment and dementia (Figure 3). Previous findings have reported conflicting results. One study reported complete mediation of the association between self-reported hearing impairment and cognitive decline by "psychosocial factors" including social isolation and low mood.[26] However, another study suggested depression did not significantly mediate the association between hearing impairment and dementia.[27]

If the association between hearing impairment and dementia is causal, then it is plausible that hearing aid use may attenuate this association. Longitudinal studies investigating whether hearing aid use influences dementia risk in those with hearing impairment have yielded inconsistent findings.[10,28,29] We found that the association between hearing impairment and dementia risk was largely attenuated in those who wore hearing aids (Figure 4). However, statistical power to detect an effect was limited due to the small size of the

TABLE 2 Cox proportional hazards models for the association between SiN hearing status and incident dementia by follow-up period

	SiN hearing status					
	Normal		Insufficient		Poor	
Follow-up period	Cases/at risk	HR (95% CI)	Cases/at risk	HR (95% CI)	Cases/at risk	HR (95% CI)
≤3 years	57/67,645	1 (Reference)	22/11,329	1.91 (1.16–3.15)	10/3055	2.80 (1.40–5.57)
>3–<6 years	184/66,807	1 (Reference)	60/11,138	1.66 (1.24–2.23)	25/2987	2.26 (1.47–3.47)
>6–<9 years	412/64,551	1 (Reference)	131/10,366	1.59 (1.30–1.94)	42/2726	1.67 (1.21–2.31)
>9 years	243/54,645	1 (Reference)	73/8946	1.54 (1.18–2.00)	26/2323	1.85 (1.23–2.80)

Abbreviations: CI, confidence interval; HR, hazard ratio; SiN, speech-in-noise.
Notes: Models adjusted for age, sex, ethnicity, country, education, socioeconomic status, alcohol, smoking, body mass index, hypertension, diabetes, and stroke/transient ischemic attack.

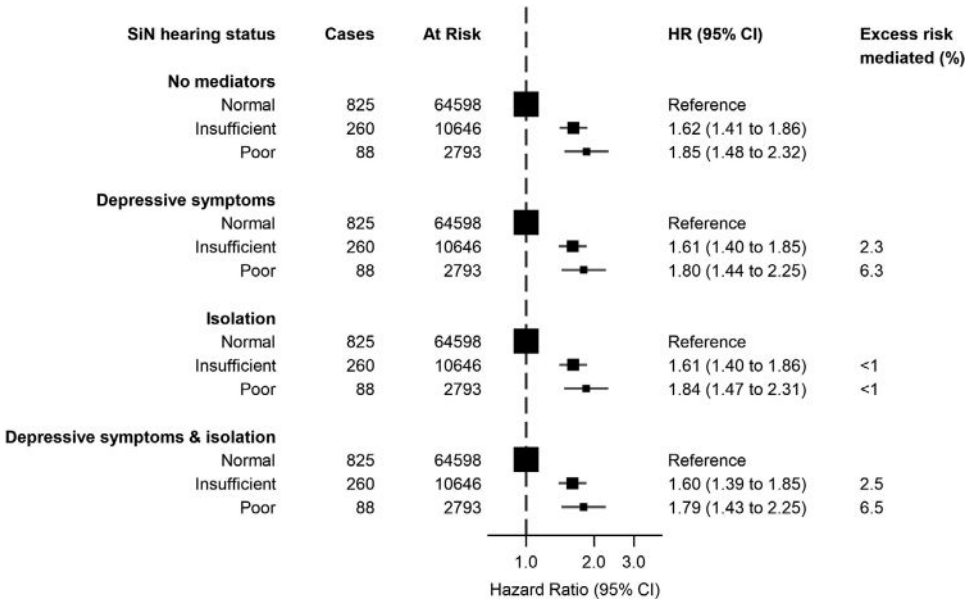

FIGURE 3 Cox proportional hazards models for the association between SiN hearing status and incident dementia with excess risk mediated by depressive symptoms and social isolation. Box area proportional to number of participants. Models adjusted for age, sex, ethnicity, country, education, socioeconomic status, alcohol, smoking, body mass index, hypertension, diabetes, and stroke/transient ischemic attack. CI, confidence interval; HR, hazard ratio; SiN, speech-in-noise

hearing aid subgroups in our study and the test for interaction was not significant ($P = .18$). Exploring the effect of hearing aid use on dementia incidence in observational studies is challenging, because hearing aid users may have a more severe hearing impairment than non–hearing aid users; use is often inconsistent; and even when used correctly, hearing impairment (particularly SiN hearing impairment) may not be entirely corrected.[12,30,31] Hearing aid uptake among those with a hearing impairment is low, and various sociodemographic, lifestyle, and behavioral characteristics are associated with uptake.[32,33] A cross-sectional study using the UK Biobank cohort found that hearing aid use was associated with higher cognitive functioning.[34] While hearing aid use might improve cognitive performance, it is possible that cognitively healthy individuals are more likely to seek out treatment for hearing impairment, or the associations are confounded by other factors. Due to the biases inherent in observational studies, in particular the lack of control for adherence and length of use, randomized controlled trials are required to address whether hearing aids could reduce the risk of dementia. Furthermore, treatments other than hearing aids might be necessary to address impaired SiN and this warrants further consideration when considering which types of hearing impairment are associated with dementia risk.

A key research question we were unable to address is whether SiN hearing impairment and pure tone hearing impairment are independently associated with dementia. If age-related hearing impairment represents a modifiable risk factor for dementia, then establishing the roles of both SiN hearing impairment and pure tone hearing impairment in the causal pathway may have significant implications for how interventions to prevent dementia are designed and implemented. Further research integrating testing of both components of age-related hearing impairment concurrently is required to comprehensively

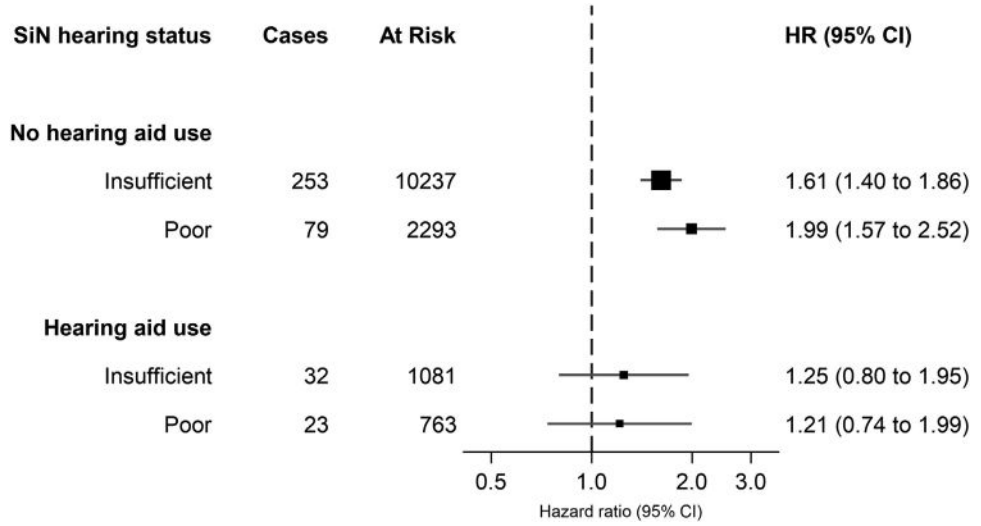

FIGURE 4 Cox proportional hazards models for the association between SiN hearing status and incident dementia stratified by hearing aid use. Box area proportional to number of participants. Models adjusted for age, sex, ethnicity, country, education, socioeconomic status, alcohol, smoking, body mass index, hypertension, diabetes, and stroke/transient ischemic attack. CI, confidence interval; HR, hazard ratio; SiN, speech-in-noise

evaluate the overall association between age-related hearing impairment and dementia.

The current study has a number of strengths. The large study population, diversity of data, and the long duration of follow-up improves the precision of the study findings and facilitates exploration of reverse causation, mediation though depressive symptoms and social isolation and effect modification by hearing aid use. The current study also has several limitations. The use of hospital in-patient and death records to capture dementia could introduce misclassification bias, although this method has been found to have a high level of accuracy compared to a reference standard of expert clinical adjudication.[35] Given the long pre-clinical phase of dementia, it is also possible that our study follow-up was of insufficient duration to exclude the possibility of reverse causation.[21] Pre-clinical AD causes neurodegeneration, which could in turn affect SiN processing.[22] Studies with longer follow-up or with repeat neuroimaging outcomes (to investigate pre-clinical neurodegeneration over time) could elucidate whether SiN impairment precedes the pathophysiological processes associated with dementia. Furthermore, due to the observational design, confounding by other factors remains and causality cannot be inferred.

In conclusion, SiN hearing impairment is associated with an increased risk of incident dementia with a lack of evidence for reverse causation and limited evidence of mediation by social isolation and depressive symptoms. If SiN hearing impairment is a modifiable risk factor for dementia, then this may have important implications for the design and implementation of interventions to treat age-related hearing impairment and prevent dementia. Further evaluation of the association between SiN hearing impairment and dementia is warranted in large prospective studies with concurrent measurement of SiN and pure tone hearing impairment.

2 | DETAILED METHODS AND RESULTS

2.1 | Methods

2.1.1 | Population

UK Biobank is a population-based prospective cohort study of ≈500,000 women and men aged 40 to 69 years recruited between 2006 and 2010.[18] All participants attended one of 22 assessment centers located in England, Scotland, or Wales. After providing informed consent, participants completed a touchscreen questionnaire, verbal interview, and physical examination and provided biological samples. Approximately 20,000 participants underwent a repeat assessment during 2012 to 2013. Ethics Committee approval for UK Biobank was obtained from the North West Multi-Centre Research Ethics Committee (Research Ethics Committee reference: 16/NW/0274).

2.1.2 | Speech-in-noise hearing

SiN hearing was incorporated into the baseline assessment at centers in England and Wales during 2009 to 2010, and was measured at repeat assessment during 2012 to 2013.[19] SiN hearing was quantified using the SRT_n measured by the Digit Triplets Test.[20] Fifteen sets of three monosyllabic digits were presented against background noise via circumaural headphones. The background noise level varied adaptively after each triplet. The SRT_n was defined as the signal-to-noise ratio at which correct recognition occurred for 50% of the presented speech.[19]

2.1.3 | Dementia

Dementia diagnoses were ascertained using hospital inpatient records from the Hospital Episode Statistics for England and Patient Episode Database for Wales and death register data from NHS Digital. Participants with dementia were identified using International Classification of Diseases (ICD)-10 codes specified by the UK Biobank all-cause dementia algorithm (see Table A.1 for ICD codes used to ascertain dementia).[36]

2.1.4 | Covariates

Townsend deprivation score was used as a measure of socioeconomic status and was assigned to participants based on their residential postcode at recruitment.[37] Information on ethnicity, education, smoking, alcohol consumption, overall health status, depressive symptoms, social isolation, hearing aid use, and hearing impairment was collected from the touchscreen questionnaire. Social isolation was quantified using a composite score previously derived in UK Biobank.[38] Information on prevalent hypertension, diabetes, and stroke or transient ischemic attack (TIA) was collected from both the touchscreen questionnaire and verbal interview. Body mass index (BMI; kg/m^2) was derived from weight (kg) using scales and standing height (meters) measured during the physical examination. For more detail on covariate collection and definitions see Table A.2.

2.1.5 | Statistical analysis

Multivariable Cox proportional hazards regression was used to investigate the association between baseline SiN hearing and incident dementia. Follow-up was calculated in person-years from date of recruitment until date of first incident dementia diagnosis, date of death, date of loss to follow-up, or last date of hospital admission data available for England (March 31, 2020) and Wales (February 29, 2016), whichever came first. SiN hearing was categorized using unaided thresholds in the better hearing ear of "normal" (SRT_n <-5.5 dB), "insufficient" (–5.5 dB ≤SRT_n <–3.5 dB), or "poor" (SRT_n ≥–3.5 dB).[14] The model was adjusted for age in years, sex, ethnicity (White, non-White), country (England, Wales), education (higher, upper secondary, lower secondary, vocational, no secondary education), Townsend deprivation score (quartiles), smoking (current, previous, never), alcohol consumption (daily or almost daily, 3 or 4 times a week, once or twice a week, 1 to 3 times a month, special occasions only, never), BMI (<25, 25-29, ≥30 kg/m^2), hypertension (no, yes), diabetes (no, yes), stroke or TIA (no, yes). Normal SiN hearing was defined as the reference category and results were presented as HR with 95% CIs. The proportional hazards assumption was evaluated using tests of Schoenfeld residuals and Kaplan-Meier plots of the log of the cumulative hazard function plotted against time for each covariate.[39]

Two sensitivity analyses were performed to explore the potential impact of reverse causation as a consequence of dementia influencing health-related factors during the preclinical phase. First, the main model evaluating the association between SiN hearing and incident dementia was repeated using four separate follow-up periods of ≤3, 3.1 to 6, 6.1 to 9, and >9 years. Second, the main analysis was repeated after excluding participants who self-reported their overall health as either poor or fair. In a further sensitivity analysis to investigate the impact of missingness, the main model was repeated using multiple imputation by chained equations with 10 imputed datasets.

In secondary analyses we investigated the role of depressive symptoms and social isolation as potential mediators in the association between SiN hearing and dementia by calculating the percentage of excess risk mediated (PERM):

$$\text{PERM} = \frac{\text{HR}_{\text{confounder adjusted}} - \text{HR}_{\text{confounder \&mediator adjusted}}}{\text{HR}_{\text{confounder }\mathbf{adjusted}} - 1} \times 100$$

To investigate potential effect modification through hearing aid use, a test for interaction between SiN hearing and hearing aid use was performed using a likelihood ratio test. Finally, a secondary analysis was performed using self-reported hearing impairment as the main exposure without the inclusion of SiN hearing.

Stata 16.1 (StataCorp) was used to perform analyses and generate figures.

2.2 | Results

Of 502,506 participants, 180,925 had SiN assessed (see Figure A1 for flowchart). After excluding participants < 60 years old (n = 96,345), with prevalent dementia or cognitive impairment (n = 58) and missing data on confounders used in the main analysis (n = 2483), the final sample size was 82,039. Of these, 1285 participants developed incident dementia over 777,416 person-years of follow-up (median individual follow-up = 10.1 years). There were 67,645 (82.5%) participants with normal SiN hearing, 11,329 (13.8%) with insufficient SiN hearing, and 3065 (3.7%) with poor SiN hearing (Table 1). Insufficient or poor SiN hearing was associated with older age, male sex, non-White ethnicity, residence in Wales, lower education, lower socioeconomic status, smoking, lower alcohol intake, hypertension, diabetes, higher BMI, previous stroke/TIA, depressive symptoms, social isolation, and hearing aid use.

The proportion of participants self-reporting hearing impairment increased with worsening SiN hearing (Table 1). However, 53.4% and 43.8% of participants with insufficient and poor SiN hearing, respectively, did not self-report hearing impairment.

A Kaplan-Meier plot of cumulative dementia incidence demonstrates clear differences in risk by SiN hearing status after 2 to 3 years of follow-up (Figure 1). After adjusting for sociodemographic, lifestyle, and health-related factors, the risk of dementia increased monotonically by SiN hearing status (Figure 2). Compared to those with normal

SiN hearing, the HRs for insufficient and poor SiN hearing were 1.61 (95% CI 1.41–1.84) and 1.91 (1.55–2.36), respectively.

In sensitivity analyses addressing possible reverse causation, the observed associations were slightly stronger when restricting to the first few years of follow-up, but remained similar to the main analyses when restricting to longer follow-up periods (Table 2). Compared to normal SiN hearing, the HRs for insufficient and poor hearing were 1.91 (95% CI 1.16–3.15) and 2.80 (95% CI 1.40–5.57) when restricting to ≤3 years follow-up, and 1.54 (95% CI 1.18–2.00) and 1.85 (95% CI 1.23–2.80) when restricting to ≥9 years follow-up, respectively. Furthermore, compared to normal SiN hearing, insufficient (HR 1.64, 95% CI 1.39–1.97) and poor (HR 2.18, 95% CI 1.65–2.88) SiN hearing demonstrated similar patterns of association with incident dementia after excluding participants with poor or fair self-reported health. Multiple imputation of missing data resulted in no qualitative change in the association between insufficient (HR 1.58; 95% CI 1.38–1.80) or poor (HR 1.82, 95% CI 1.49–2.24) SiN hearing and incident dementia.

In secondary analyses exploring the role of potential mediators, the PERM by depressive symptoms was 2.3% and 6.3% for insufficient and poor SiN hearing, respectively (Figure 3). The PERM by social isolation was <1% for both insufficient and poor SiN hearing. Depressive symptoms and isolation combined were estimated to account for only 2.5% and 6.5% of the excess risk of dementia associated with insufficient and poor SiN hearing, respectively.

When stratifying by hearing aid use, the pattern of associations remained similar to the main findings in those who reported hearing aid use, but were substantially attenuated and became statistically non-significant in those who reported hearing aid use (Figure 4). However, the test for interaction between SiN hearing status and hearing aid use was not statistically significant ($P = .18$). Self-reported hearing impairment was associated with an increased risk of dementia (HR 1.14, 95% CI 1.01–1.28), compared to no self-reported hearing impairment.

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CONFLICTS OF INTEREST

The authors report no conflicts of interest.

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APPENDIX

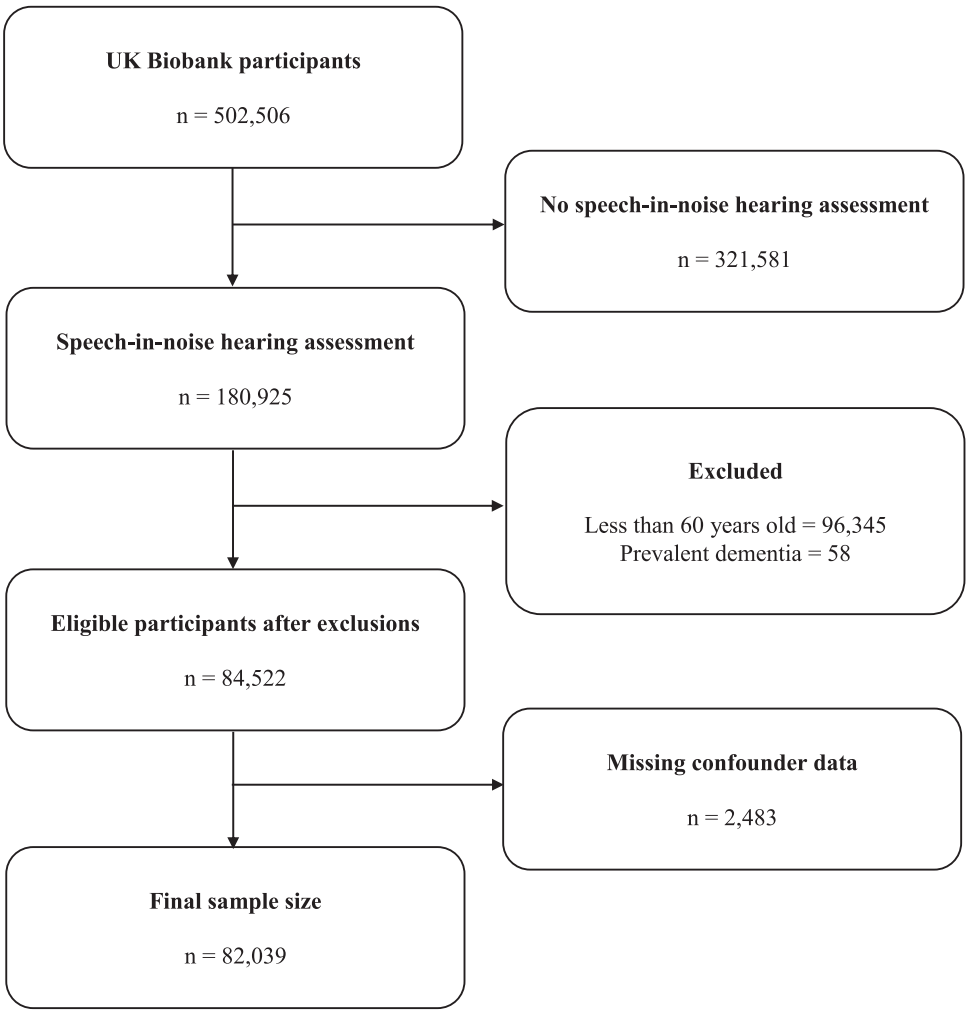

FIGURE A1 Flow diagram of study participant selection

TABLE A.1 ICD-10 codes used to ascertain dementia

ICD-10 Code	Description
F00	Dementia in Alzheimer's disease
F00.0	Dementia in Alzheimer's disease with early onset
F00.1	Dementia in Alzheimer's disease with late onset
F00.2	Dementia in Alzheimer's disease, atypical or mixed type
F00.9	Dementia in Alzheimer's disease, unspecified
F01	Vascular dementia
F01.0	Vascular dementia of acute onset
F01.1	Multi-infarct dementia
F01.2	Subcortical vascular dementia
F01.3	Mixed cortical and sub-cortical vascular dementia
F01.8	Other vascular dementia
F01.9	Vascular dementia, unspecified
F02	Dementia in other diseases classified elsewhere
F02.0	Dementia in Picks disease
F02.1	Dementia in Creutzfeldt-Jacob disease
F02.2	Dementia in Huntington's disease
F02.3	Dementia in Parkinson's disease
F02.4	Dementia in HIV disease
F02.8	Dementia in other specified diseases classified elsewhere
F03	Unspecified dementia
F05.1	Delirium superimposed on dementia
F10.6	Mental and behavioral disorders due to use of alcohol—amnesic syndrome
G30.0	Alzheimer's disease with early onset
G30.1	Alzheimer's disease with late onset
G30.8	Other Alzheimer's disease
G30.9	Alzheimer's disease unspecified
G31.0	Circumscribed brain atrophy
G31.1	Senile degeneration of brain
G31.8	Other specified degenerative diseases of nervous system
I67.3	Binswanger's disease
A81.0	Sporadic Creutzfeldt-Jakob disease

Abbreviations: HIV, human immunodeficiency virus; ICD, International Classification of Diseases.

TABLE A.2 Covariate definitions and method of assessment

Covariate	Description	Assessment	UK Biobank Code
Age (years)	Age in years	Date attended baseline assessment minus date of birth	21003
Sex	Male, female	NHS derived and/or touchscreen questionnaire	31
Ethnicity	White, non-White (Mixed, Asian, Black, Chinese, Other)	Touchscreen questionnaire: "What is your ethnic group?"	21000
Country	England, Wales	Location of baseline assessment center attended	54
Education	Higher (college or university degree, other professional qualifications), upper secondary (A levels, AS levels or equivalent), lower secondary (O levels/GCSEs or equivalent, CSEs or equivalent), vocational (NVQ or HND or HNC or equivalent); no secondary education (none of the above)	Touchscreen questionnaire: "Which of the following qualifications do you have?"	6138
Socioeconomic status	Quartiles	Townsend deprivation index calculated prior to participant joining UK Biobank. Based on the preceding national census output areas. Each participant is assigned a score corresponding to the output area in which their postcode is located	189
Smoking status	Never, previous, current	Touchscreen questionnaire:	20116
Alcohol intake	Daily or almost daily, 3–4 times/wk, 1–2 times/wk, 1–3 times/month, special occasions only, never	Touchscreen questionnaire: "About how often do you drink alcohol?"	1558
BMI (kg/m^2)	Underweight or normal (<25), overweight (25–29) or obese (≥30)	Physical examination: body mass index	21001
Hypertension	No, yes	Touchscreen questionnaire and verbal interview: self-reported hypertension or anti-hypertensive medication use	6150, 20002, 6177
Diabetes	No, yes	Touchscreen questionnaire and verbal interview: self-reported diabetes (diabetes, type 1 diabetes or type 2 diabetes) or insulin use	2443, 20002, 6177
Prior stroke/TIA	No, yes	Touchscreen questionnaire and verbal interview: self-reported previous stroke or TIA	6150, 20002
Self-reported health	Excellent, good, fair or poor	Touchscreen questionnaire: "In general how would you rate your overall health"	2178
Low mood	Nearly every day, more than half the days, several days or not at all	Touchscreen questionnaire: "Over the past two weeks, how often have you felt down, depressed or hopeless?"	2050
Social isolation	No (composite score <2), yes (composite score ≥2)	Touchscreen questionnaire: (i) "Including yourself, how many people are living together in your household?" (1 point if living alone); (ii) "How often do you visit friends or family or have them visit you?" (1 point if friends/family visits less than once a month); (iii) "Which of the following [leisure/social activities] do you engage in once a week or more often?" (1 point if no activities selected).	709, 1031, 6160
Hearing aid use	No, yes	Touchscreen questionnaire: "Do you use a hearing aid most of the time?"	3393
Self-reported hearing impairment	No, yes	Touchscreen questionnaire: "Do you have any difficulty with your hearing."	2247

Abbreviations: BMI, body mass index; TIA, transient ischemic attack.