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Age-related hearing loss and mild cognitive impairment: a meta-analysis and systematic review of population-based studies

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Review Article

Dr K Lau takes responsibility for the integrity of the content of the paper

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Abstract

Background. The aim of this study was to identify any relationship between hearing loss and mild cognitive impairment.

Method. This was a systematic review and meta-analysis of randomised controlled trials conducted using Medline and the Cochrane Library up to 24 June 2020. Prospective, cohort and cross-sectional, and observational studies that reported on the relationship between mild cognitive impairment and hearing loss were included.

Results. A total of 34 studies reporting data on 48 017 participants were included. Twenty-three studies observed a significant association between hearing loss and mild cognitive impairment. The pooled risk ratio across all studies of prevalence of mild cognitive impairment in people with hearing loss was 1.44 (random-effects; 95 per cent CI = 1.27–1.64; $p < 0.00001$; $I^2 = 0$ per cent). Significantly more people with mild cognitive impairment had peripheral hearing loss compared with those without (risk ratio, 1.40 random-effects; 95 per cent CI = 1.10–1.77; $p = 0.005$; $I^2 = 0$ per cent). When the incidence was studied, significantly more people with peripheral hearing loss had mild cognitive impairment compared with those without (risk ratio = 2.06 random-effects; 95 per cent CI = 1.35–3.15; $p = 0.0008$; $I^2 = 97$ per cent); however; a high level of statistical heterogeneity was evident.

Conclusion. Most of the studies included in this systematic review observed a significant association between hearing loss and mild cognitive impairment.

Introduction

Age-related hearing loss is a decrease in hearing ability that happens with age and is a common sensory abnormality of the elderly. According to the World Health Organisation, 466 million adults globally live with disabling hearing loss, including nearly one in three people aged over 65 years.[1] Hearing impairment not only affects interpersonal communication but also health, independence, wellbeing, quality of life and daily function and can lead to social isolation, depression and early mortality.[2–5] In recent years, there has been a growing speculation about the association between cognitive decline and age-related hearing loss.[6] Uhlmann *et al.* (1989) were amongst the first to find that hearing loss was a strong, independent risk factor for cognitive decline.[7] However, other studies have contested this association.[8,9]

A recent commission document by the *Lancet* postulated that hearing loss in mid- and later life is associated with increased risk of dementia.[10] Dementia is the loss of cognitive functioning and behavioural abilities to such an extent that it interferes with a person's daily life and activities. The aim of the present study was to identify any relationship between hearing loss and a prodromal state of dementia or mild cognitive impairment. Establishing such an association would strengthen the case for a relationship between hearing impairment and dementia and focus intervention development to an earlier stage. Mild cognitive impairment is an intermediate state between normal cognitive functioning and development of dementia.[11,12] Individuals with mild cognitive impairment have slight impairment in cognitive function with otherwise normal function in the performance of activities of daily living.[13] They are at a significantly elevated risk of developing dementia during their lifetime, which is estimated to be around 80 per cent.[14]

Hearing impairment can be either peripheral or central.[3] The peripheral hearing system consists of the peripheral components of hearing (including the cochlea), whereas the central hearing system encompasses the central auditory pathways and influences the way incoming auditory stimuli are perceived and understood (central auditory processing). The key symptom of central hearing loss is an inability of the individual to understand speech in a noisy environment,[15] particularly if peripheral hearing (the ability to hear in quiet) remains relatively normal. In the present review article, we include studies that have assessed the link between both types of hearing loss with early dementia.

Table 1. Inclusion and exclusion criteria for the population of interest, outcomes and study design

Parameter	Inclusion criteria	Exclusion criteria
Population	Cohort studies: adults with early dementia who were cognitively intact at baseline and were followed up for any period of time. Hearing and cognition assessment were available at baseline and end-point. Cross-sectional studies: adults who had hearing loss or mild cognitive impairment at the point of assessment	Paediatric populations and participants with a diagnosis of established dementia (instead of early dementia or mild cognitive impairment)
Outcomes	The proportion of patients with the condition (peripheral or central hearing loss, cognitive impairment) in the case group compared with the control group	None
Study Design	Prospective cohort, case-control and cross-sectional. Full-text was available. Published in English language	Book chapters, reviews, editorials and commentaries. Interventional studies

Table 2. Articles excluded at full-text

Reason for exclusion	Studies excluded
Outcomes were reported for patients with both visual and hearing impairments (could not distinguish results from patients with just hearing impairment)	Davidson and Guthrie, 2019,[38] Maharani *et al*., 2018[39]
Absence of control group	Ray *et al*., 2018,[36] Murphy *et al*., 2018,[37] Villeneuve *et al*., 2017,[18] Wong *et al*., 2014,[22] Daggett *et al*., 2014,[33] Pronk *et al*., 2013,[24] Gurina *et al*., 2011,[27] Srinivasan *et al*., 2010,[28] Munshi *et al*., 2006,[29] Riello *et al*., 2004,[30] Allen *et al*., 2003,[31] Uhlmann *et al*., 1986[32]
Relevant outcomes on cognition or hearing not available	Yu *et al*., 2017,[35] Schnitker *et al*., 2016,[19] Moradi *et al*., 2014,[23] Lin and Albert, 2014,[6] No authors listed, 2013,[25] Helvik *et al*., 2012[26]
No report on association between mild cognitive hearing impairment and hearing loss	Dotchin *et al*., 2015[21]
Article replaced by Fischer *et al*.[47] (2016) that reported outcomes of interest on the same population, after communication with senior author	Schubert *et al*., 2017[20]

Materials and methods

The systematic review was undertaken in accordance with the general principles recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[16] A systematic computer-based literature search was performed on the biomedical bibliographical databases Medline and Cochrane library. The search was done on the 24 June 2020 and run from database inception. A copy of the search strategy is presented in Appendix 1. The protocol for this systematic review has been deposited in the Prospero international prospective register of systematic reviews (identification number: CRD42017076183) and can be accessed at https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=76183.

The inclusion and exclusion criteria for the population of interest, outcomes and study design are presented in Table 1.

Data analysis

Three authors (KL, PAD and CM) independently selected studies, extracted data and assessed the quality of included studies. Data were extracted from each study and included information on the article identification, year of publication, population (continent), matching for covariates between groups, evaluation period (for longitudinal studies), number of patients per group, hearing and cognition assessment methods, number of male patients, and mean age of patients. Where data were missing, the corresponding authors of the articles were approached by email.

The quality assessment of the cohort studies included in the meta-analysis was done using the Newcastle–Ottawa Scale.[17]

Statistical analyses

The meta-analysis was undertaken using Cochrane RevMan review software (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014, Copenhagen, version 5.3). Outcomes reported as dichotomous were estimated as risk ratios with associated 95 per cent confidence interval (CI). Where studies did not report participant numbers but gave an effect size with 95 per cent CI, these were pooled in RevMan using the generic inverse variance method. Random-effects models were applied. Effect estimates (estimated in RevMan as *Z*-scores) were considered significant at $p < 0.05$. Statistical heterogeneity was assessed using the I-squared statistic. Where data were not suitable for pooling in a meta-analysis, a narrative synthesis using tables and text was reported.

Results

The electronic searches identified 521 unique citations. One additional citation was provided by a clinical expert. Of these, 465 were excluded based on their title and abstract. Of 56 citations obtained as full-text, 22 were excluded.[18–39] Details of the studies excluded at full-text are presented in Table 2.

Thirty-four studies, reporting on 48 017 participants, fulfilled the inclusion criteria and were included in the systematic review. Eighteen of these studies were eligible for and were included in the meta-analysis. A Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of the study selection process is shown in Figure 1. The characteristics of the included studies are shown in Table 3.

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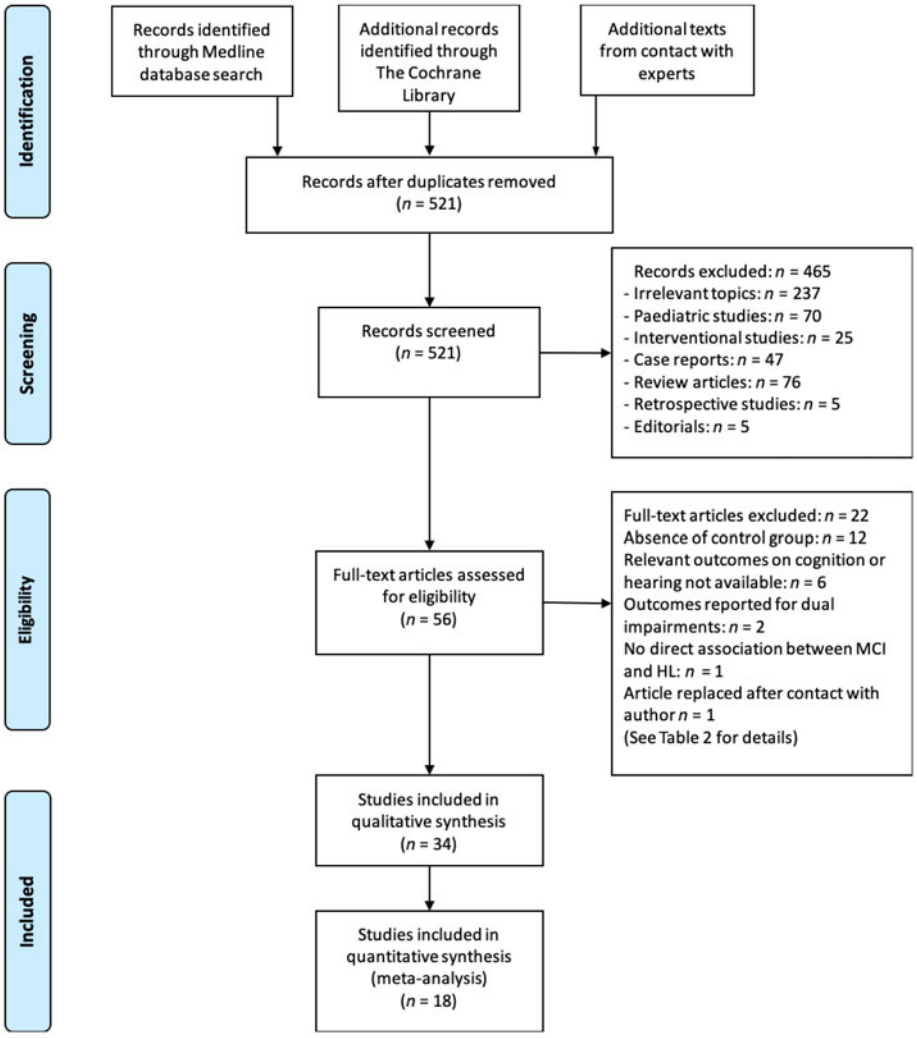

Fig. 1. A Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of the study selection process. MCI = mild cognitive impairment; HL = hearing loss

These studies were published between 1986 and 2019 and conducted in America, Asia, Australia, Africa and Europe. Ten of the studies were cohort,[40–49] 23 were cross-sectional,[7,50–71] and 1 study was both a cross-sectional and cohort study.[72] Recruited participant numbers ranged from 20[70] to 13 731.[46] The results of the quality assessment are presented in Table 4. All of the cohort studies scored more than six stars (out of a total of nine stars).

Hearing assessment

Most of the studies used pure tone audiometry as the main auditory assessment method, and this measures hearing sensitivity. Self-reported or assessor-reported hearing loss was used by 10 studies,[41–44,46,48,51,64,71,72] and in 1 paper the assessment method was not reported.[50] Some studies used central auditory function tests, such as dichotic digits test, speech audiometry, synthetic sentence identification with ipsilateral competing message and so on.[7,49,56,59,61–63,65,68,70] The definition of hearing loss from the World Health Organization[73] was used by most studies, but the frequencies tested ranged from: 500 to 4000 Hz,[45,47,54,55,57,60,66] 1000 to 4000 Hz,[67] 250 to 2000 Hz[58] and 500 to 3000 Hz.[7] One study used the hearing threshold at 4 kHz only to separate the different groups of hearing loss.[68]

Cognitive assessment

The cognitive assessment tool that was used by most researchers was the Mini Mental State Examination[7,40,42,46,47,49,50,53,54,58,59,60,62,64,66,71,72] or its modified version, the Modified Mini Mental State tool.[45,48,70] A score below 24 on the Mini Mental State Examination[74] was considered abnormal by most studies.[7,40,46,47,53,58,66] The cut-off score was 27 in two studies.[71,72] In another study, Mini Mental State examination score thresholds were adjusted for education level.[50] Other cognitive assessment tests used included the Montreal Cognitive Assessment,[53,56] Cognitive Drug Research Computerised Assessment System,[55] verbal fluency,[42,55,57,64] National Adult Reading Test,[55] Delayed Word Recall Test,[57] Digit Symbol Substitution Test,[57] Wechsler Adult Intelligence Test,[58] Clinical Dementia Rating Scale,[44,59,72] Frontal Assessment Battery,[59] Free and Cued Selective Reminding Test,[60] Trail Making Test (parts A and B),[40,42,60,63,64] Rey–Osterrieth Complex Figure Recall Test,[42] Stroop Letter and Category Fluency,[60,63] the American version of the Nelson Adult Reading Test,[60] Abbreviated Memory Inventory for the Chinese,[41] Cambridge Cognitive Examination,[61] Clock Drawing Test,[42,63] Cognitive Abilities Screening Instrument,[63,65] Letter-Digit Symbol Test,[67] Auditory Verbal Learning Test,[67] Clinical Dementia Rating Scale[69] and Storandt Battery.[70]

Results of quantitative analysis

Prevalence of mild cognitive impairment

Across four cross-sectional studies comparing mild cognitive impairment between people with peripheral hearing loss ($n = 1292$) and without peripheral hearing loss ($n = 1041$), the risk ratio was 1.39 (random-effects, 95 per cent CI = 1.18

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Table 3. Characteristics of included studies

Reference	Design	Matching*	Population	Cognition assessment	Auditory assessment	Patients (*n*)	Control (*n*)	Follow up (years)
Schubert *et al.*, 2019[40]	Cohort	1, 2, visual impairment	America	Mini Mental State Examination, Trail Making Tests A & B	Pure tone audiometry	331	2126	10
Yu and Woo, 2019[41]	Cohort	1, 2, 3, 4, marital status, diabetes, baseline cognitive status	Asia	Abbreviated Memory Inventory for the Chinese	Self-reported	858	1089	1
Vaccaro *et al.*, 2019[42]	Cohort	1	Europe	Mini Mental State Examination, Semantic Verbal Fluency Test, Rey–Osterrieth Complex Figure Recall Test, Clock Drawing Test, Trail Making Test part A	Self-reported, Whispered Voice Test	159	1012	5
Curhan *et al.*, 2019[43]	Cohort	1, 4, race, occupation, body mass index, smoking, cholesterol, diabetes	America	Subjective Cognitive Decline	Self-reported	1181	1208	8
Han *et al.*, 2019[50]	Cross-sectional	None	Asia	Mini Mental State Examination	Not reported	274	1743	NA
Gallagher *et al.*, 2018[44]	Cohort	None	America	Clinical Dementia Rating Scale	Observed by assessor	505	2150	3.5
Heward *et al.*, 2018[51]	Cross-sectional	3	Africa	Intervention for Dementia in Elderly Africans cognitive screen	Self-reported	50	255	NA
MacDonald *et al.*, 2018[52]	Cross-sectional	1	America	Word recall task, Letter Series Test, Wechsler Adult Intelligence Scale-Revised Digit Symbol Substitution Task, Controlled Associations Test, Recognition Vocabulary Test	Pure tone audiometry	211	197	NA
Iliadou *et al.*, 2017[53]	Cross-sectional	1, 2, pure tone thresholds	Europe	Mini Mental State Examination, Montreal Cognitive Assessment, Clinical Dementia Rating Scale, Geriatric Depression Scale	Pure tone audiometry, speech in quiet, central auditory processing test (Random Gap Detection Test, speech in bubble, gaps-in-noise)	18	11	NA
Heywood *et al.*, 2017[72]	Cross-sectional; cohort	1, 2, 3, 4, ethnicity, central obesity, diabetes, dyslipidaemia, smoking, alcohol, leisure time activity, cardiac diseases, depressive symptoms	Asia	Mini Mental State Examination, Clinical Dementia Rating Scale	Whispered Voice Test	Cross-sectional: 507; cohort: 144	Cross-sectional: 2052; cohort: 1360	Cross-sectional: NA; cohort: 3.8
Deal *et al.*, 2017[45]	Cohort	1, 2, 3	America	Modified Mini Mental State	Pure tone audiometry	1103	786	9

Bruckmann and Pinheiro, 2016[54]	Cross-sectional	3	America	Mini Mental State Examination	Pure tone audiometry	17	13	NA
Yang and Gu, 2016[46]	Cohort	1, 2, 3, occupation, wealth	Asia	Mini Mental State Examination	Self-reported	4820	8911	3
Fischer *et al.*, 2016[47]	Cohort	1, 2, 3, 4, smoking, exercise, alcohol consumption, hypertension, diabetes, non-high-density lipoprotein cholesterol, frailty score, intima media thickness	America	Mini Mental State Examination	Pure tone audiometry	1209	1209	17
Bucks *et al.*, 2016[55]	Cross-sectional	1, 2, 3, depression, cognitive reserve (premorbid intelligence quotient)	Australia	Cognitive Drug Research System, verbal fluency, National Adult Reading Test	Pure tone audiometry	112	1857	NA
Lister *et al.*, 2016[56]	Cross-sectional	1, 3, race, pure tone audiometry	America	Montreal Cognitive Assessment	Cortical auditory evoked potential, pure tone audiometry, tympanometry, Speech Reception Threshold, speech in noise	13	17	NA
Deal *et al.*, 2015[57]	Cross-sectional	1, 2, 3, 4	America	Delayed Word Recall Test, word fluency test, Digit Symbol Substitution Test	Pure tone audiometry	180	73	23
Zhang *et al.*, 2015[58]	Cross-sectional	1, 3	Asia	Mini Mental State Examination, Wechsler Adult Intelligence Test	Pure tone audiometry	21	11	NA
Gurgel *et al.*, 2014[48]	Cohort	1, 2, 3, 4, apolipoprotein E-ϵ4 allele, diabetes, smoking, high cholesterol	America	Modified Mini Mental State-Revised, interview, neuropsychological testing	Observed by assessor, self-reported	836	3627	Mean follow-up: 4.32 (hearing loss group), 6.08 (control group)
Quaranta *et al.*, 2014[59]	Cross-sectional	1, 2, 3	Europe	Mini Mental State Examination, Clinical Dementia Rating Scale, Frontal Assessment Battery	Pure tone audiometry, speech audiometry, synthetic sentence identification with ipsilateral competing message, Hearing Handicap Inventory for the Elderly Screening version questionnaire	207	245	NA
Lin *et al.*, 2011[60]	Cross-sectional	1, 2, 3, 5, race, depression, smoking	America	Mini Mental State Examination, Free and Cued Selective Reminding Test, Trail Making A & B, Stroop, Letter & Category Fluency, American version of the Nelson Adult Reading Test	Pure tone audiometry	142	205	NA

(*Continued*)

Table 3. (*Continued.*)

Reference	Design	Matching*	Population	Cognition assessment	Auditory assessment	Patients (*n*)	Control (*n*)	Follow up (years)
Rahman *et al.*, 2011[61]	Cross-sectional	1, 2, 3, 5, pure tone audiometry	Africa	Cambridge Cognitive Examination	Speech audiometry, CAP, pure tone audiometry, tympanometry	150	150	NA
Idrizbegovic *et al.*, 2011[62]	Cross-sectional	1	Europe	Mini Mental State Examination	Pure tone audiometry, speech audiometry, Dichotic Digits Test	59	34	NA
Gates *et al.*, 2010[63]	Cross-sectional	1, 3, pure tone audiometry	America	Trail Making Test; Clock Drawing, Stroop Color and Word and subtests from the Cognitive Abilities Screening Instrument	Pure tone audiometry, distortion product otoacoustic emissions, synthetic sentence identification with ipsilateral competing message, Dichotic Sentence Identification, Dichotic Digits Test	60	232	NA
Benito-León *et al.*, 2010[64]	Cross-sectional	1, 2, 3, premorbid intelligence, cognition altering medications, depression	Europe	Expanded version of Mini Mental State Examination, Trail Making Test A, verbal fluency, memory, premorbid intelligence	Self-reported	1073	1073	NA
Gates *et al.*, 2008[65]	Cross-sectional	1, 2, hearing threshold, word recognitions score, frequency of exercise, depressive symptoms	America	Cognitive Ability Screening Instrument	Identification Test, Dichotic Digits Test, Pitch Pattern Sequence	64	232	NA
Tay *et al.*, 2006[66]	Cross-sectional	1, 2 cerebrovascular disease	Australia	Mini Mental State Examination	Pure tone audiometry	89	75	NA
Van Boxtel *et al.*, 2000[67]	Cross-sectional	1, 2, 3, information processing speed	Europe	Letter-Digit Symbol Test, Auditory Verbal Learning Test	Pure tone audiometry	56	397	NA
Frisina and Frisina, 1997[68]	Cross-sectional	5, cardiovascular disorders	America	Extent of benefit gained from supportive context during speech audiometry	Pure tone audiometry, speech audiometry	30	20	NA
Gates *et al.*, 1996[49]	Cohort	Stroke	America	Mini Mental State Examination	Pure tone audiometry, speech audiometry, synthetic sentence identification with ipsilateral competing message, staggered spondaic word, Performance Intensity function of Phonetically Balanced Words	452	364	6
Gates *et al.*, 1995[69]	Cross-sectional	1, 2, 3	America	Clinical Dementia Rating Scale	Pure tone audiometry, speech audiometry, synthetic sentence identification with	40	42	NA

					ipsilateral competing message, distortion product otoacoustic emissions, auditory brainstem response			
Strouse *et al.*, 1995[70]	Cross-sectional	1, 2, hearing loss	America	Modified Mini Mental State, Storandt Battery	Pure tone audiometry, speech and immittance audiometry, synthetic sentence identification with ipsilateral competing message, otoacoustic emissions, dichotic digits, dichotic sentence identification, pitch and duration patterns	10	10	NA
DeVore, 1992[71]	Cross-sectional	None	America	Mini Mental State Examination	Self-reported	5	45	NA
Uhlmann *et al.*, 1989[7]	Cross-sectional	1, 2, 3	America	Mini Mental State Examination	Pure tone audiometry, speech audiometry	100	100	NA

*Matching: 1 = age; 2 = gender; 3 = education; 4 = hypertension. CAP = selective auditory attention test, dichotic digits test, auditory fusion test, pitch pattern sequences test and auditory memory battery of Goldman–Fristoe–Woodcock; NA = not available

to 1.64; $p = 0.0001$; $I^2 = 0$ per cent); significantly more people with peripheral hearing loss had mild cognitive impairment compared with those without peripheral hearing loss.

The risk ratio for one study comparing mild cognitive impairment between people with central hearing loss ($n = 113$) and without central hearing loss ($n = 86$) was 1.54 (random-effects, 95 per cent CI = 1.24 to 1.90; $p < 0.0001$; I^2 not applicable); significantly more people with central hearing loss had mild cognitive impairment compared with those without central hearing loss.

The pooled risk ratio across all studies was 1.44 (random-effects, 95 per cent CI = 1.27 to 1.64; $p < 0.00001$; $I^2 = 0$ per cent) (Figure 2).

Prevalence of hearing impairment

Across three cross-sectional studies comparing peripheral hearing loss between people with mild cognitive impairment ($n = 82$) and without mild cognitive impairment ($n = 108$), the risk ratio (risk ratio) was 1.40 (random-effects, 95 per cent CI = 1.10 to 1.77; $p = 0.005$; $I^2 = 0$ per cent); significantly more people with mild cognitive impairment had peripheral hearing loss compared with those without (Figure 3).

Across two cross-sectional studies reporting the between-group difference as an odds ratio (i.e., no raw data were available) comparing peripheral hearing loss between people with mild cognitive impairment and without mild cognitive impairment, the odds ratio was 1.41 (random-effects, 95 per cent CI = 1.02 to 1.96; $p = 0.04$; $I^2 = 59$ per cent); statistical heterogeneity was evident and the between-group difference was not statistically significant (Figure 4).

Hearing loss in people with mild cognitive impairment

Peripheral hearing loss

Across six cohort studies comparing mild cognitive impairment between people with peripheral hearing loss ($n = 8235$) and without peripheral hearing loss ($n = 17\ 891$), the risk ratio was 2.06 (random-effects, 95 per cent CI = 1.35 to 3.15; $p = 0.0008$; $I^2 = 97$ per cent); significantly more people with peripheral hearing loss had mild cognitive impairment compared with those without, although a high level of statistical heterogeneity was evident (Figure 5).

Across two cohort studies reporting the between-group difference as a hazard ratio (i.e. no raw data were available) comparing mild cognitive impairment between people with and without peripheral hearing loss, the hazard ratio was 1.40 (random-effects, 95 per cent CI = 1.64 to 1.95; $p < 0.00001$; $I^2 = 0$ per cent); significantly more people with peripheral hearing loss had mild cognitive impairment compared with those without peripheral hearing loss (Figure 6).

The between-group difference for one cohort study reporting the outcome as an odds ratio (i.e. no raw data were available) comparing mild cognitive impairment between people with and without peripheral hearing loss was 1.70 (random-effects, 95 per cent CI = 1.30 to 2.22; $p = 0.0001$); significantly more people with peripheral hearing loss had mild cognitive impairment compared with those without peripheral hearing loss (Figure 7).

The between-group differences for one cohort study reporting the outcome as risk ratio (i.e. no raw data were available) comparing mild cognitive impairment between people with and without mild, moderate or severe peripheral hearing loss were: mild 1.26 (random-effects, 95 per cent CI = 1.15 to 1.38; $p < 0.0001$), moderate 1.29 (random-effects, 95 per cent

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Table 4. Quality assessment of the included cohort studies using the Newcastle–Ottawa Scale

	Selection				Comparability	Outcome		
Reference	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Of cohorts on the basis of the design or analysis	Assessment	Follow up long enough	Adequacy of follow up of cohorts
Schubert *et al.*, 2019[40]	★	★	★	★	★★	★	★	★
Yu and Woo, 2019[41]	★	★	★	★	★★	★		★
Vaccaro *et al.*, 2019[42]	★	★	★	★	★★	★	★	★
Curhan *et al.*, 2019[43]		★	★	★	★★	★	★	★
Gallagher *et al.*, 2018[44]	★	★	★	★	★★	★		★
Heywood *et al.*, 2017[72]	★	★	★	★	★★	★	★	★
Deal *et al.*, 2017[45]	★	★	★	★	★★	★	★	★
Yang and Gu, 2016[46]	★	★	★	★	★★		★	
Fischer *et al.*, 2016[47]	★	★	★	★	★★	★	★	★
Gurgel *et al.*, 2014[48]	★	★	★	★	★★		★	★
Gates *et al.*, 1996[49]	★	★	★	★		★	★	★

One star is attributed per item if achieved, except for 'comparability' which can achieve up to two stars. All of the cohort studies scored more than six stars (out of a maximum of nine).

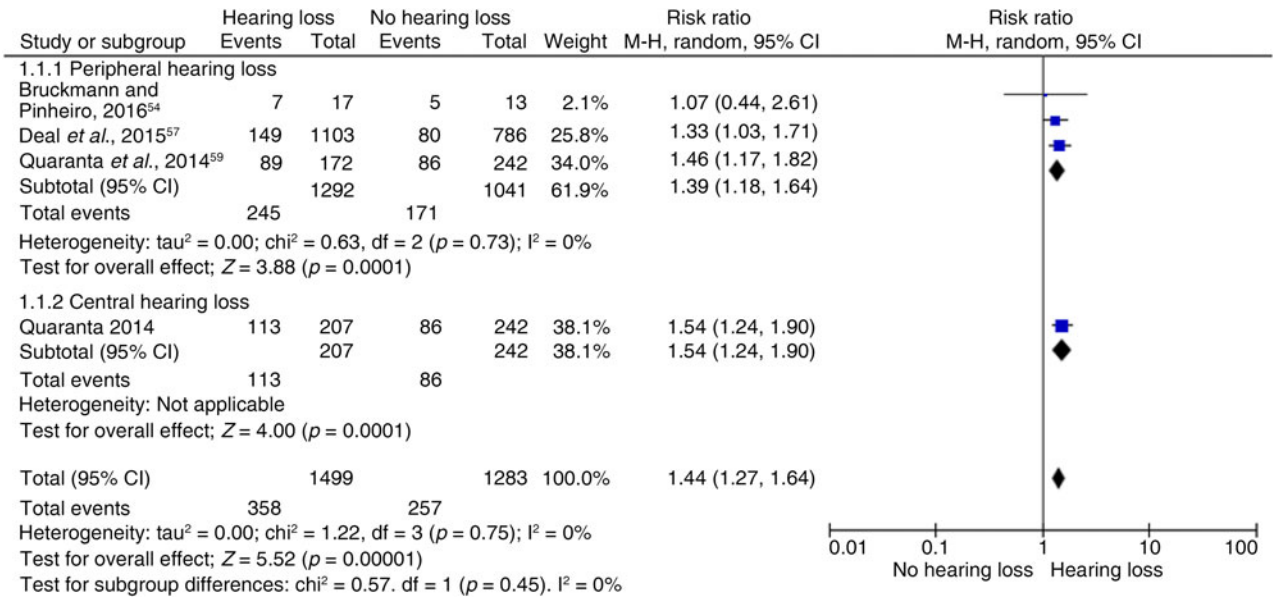

Fig. 2. Prevalence of mild cognitive impairment amongst hearing impaired patients. M-H = Mantel-Haenszel; CI = confidence interval

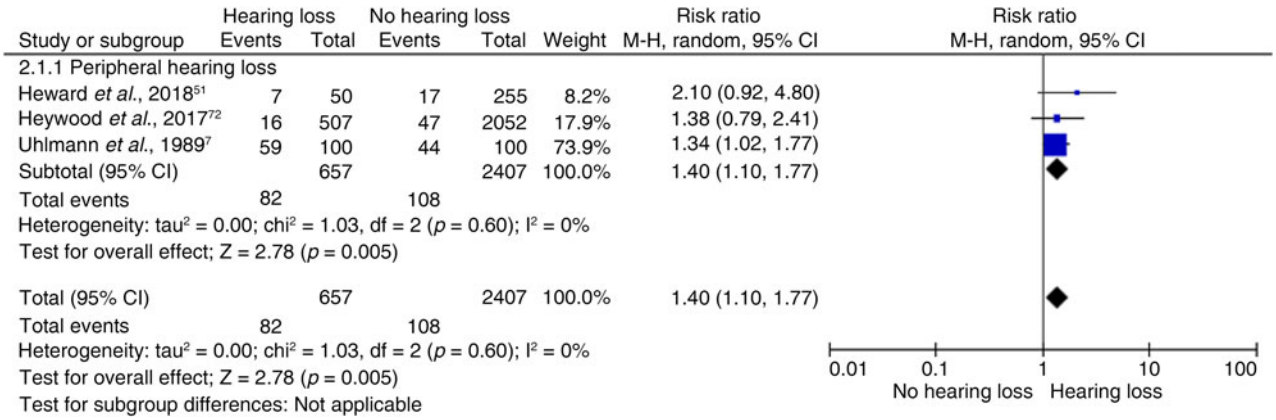

Fig. 3. Prevalence of hearing impairment amongst patients with mild cognitive impairment (risk ratio). M-H = Mantel-Haenszel; CI = confidence interval

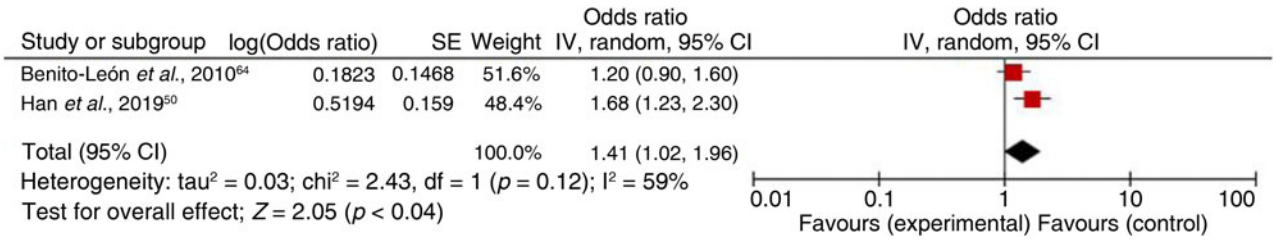

Fig. 4. Prevalence of hearing impairment amongst patients with mild cognitive impairment (odds ratio). SE = standard error; IV = Instrumental variable; CI = confidence interval

CI = 1.13 to 1.47; $p = 0.0002$) and severe 1.37 (random-effects, 95 per cent CI = 1.06 to 1.7; $p = 0.02$); significantly more people with peripheral hearing loss had mild cognitive impairment compared with those without peripheral hearing loss in all categories (Figure 8).

Results of narrative synthesis

Prevalence of early dementia

The outcomes from the studies on early dementia amongst hearing impaired patients are presented in Table 5. Out of nine studies included in this category, four[54,55,58,66] did not identify a significant association between hearing loss and early dementia. The demographic data of the participants (age, gender, race, comorbidities) and the outcome measures used differed between the studies, and a direct comparison of the results was not possible. The number of participants ranged from 21[58] to 1969.[55] Bucks *et al.* (2016) assessed the participants' premorbid intelligence quotient using the National Adult Reading Test as an index of cognitive reserve.[55] They concluded that hearing loss is not an important factor of contemporaneous attention, memory or executive function in middle-aged adults once several covariates, including cognitive reserve, education, age, sex and depression are accounted for.

During the 23-year follow up and after adjusting for demographic data and disease covariates, Deal *et al.* (2015) found

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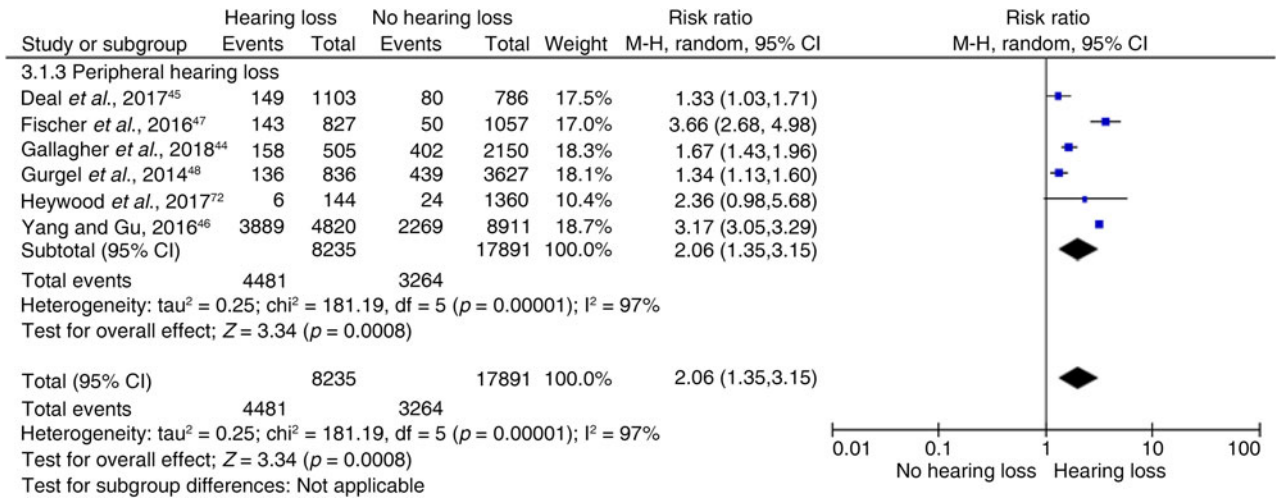

Fig. 5. Incidence of mild cognitive impairment with and without peripheral hearing loss (risk ratio). M-H = Mantel-Haenszel; CI = confidence interval

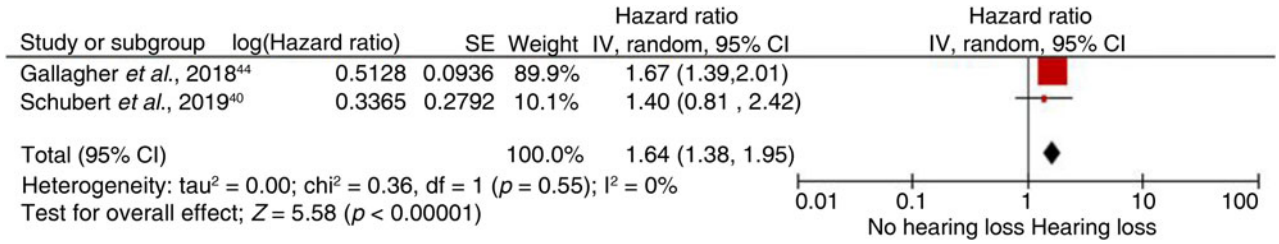

Fig. 6. Incidence of mild cognitive impairment with and without peripheral hearing loss (hazard ratio). SE = standard error; IV = Instrumental variable; CI = confidence interval

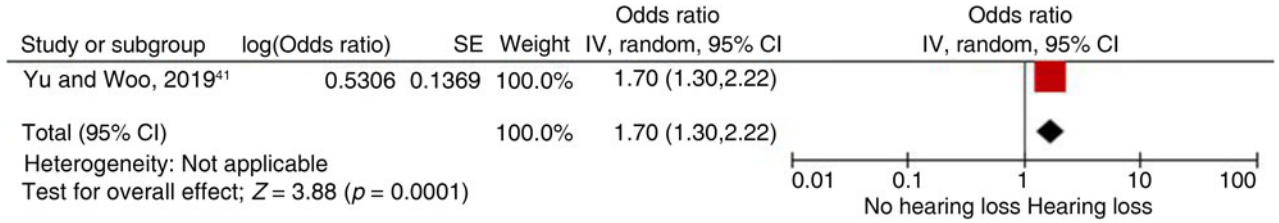

Fig. 7. Odds ratio outcomes in between-group difference (with and without peripheral hearing loss). SE = standard error; IV = Instrumental variable; CI = confidence interval

that patients with moderate or severe hearing loss had a 0.29 standard deviation (SD; 95 per cent CI = 0.05 to 0.54) decline for the global composite score (sum of the three neuropsychological tests administered: Word Fluency Test, Delayed Word Recall Test and Digit Symbol Substitution Test).[57] A hearing assessment was completed at baseline only. There was no strong association observed on the global composite score between patients with mild hearing loss and those with normal hearing at baseline ($p = 0.570$). Interestingly, it was observed that hearing aid users had a slower rate of cognitive decline compared with non-users. Lin *et al.* (2011) commented 'the magnitude of the reduction in cognitive performance associated with hearing loss is clinically significant with the reduction associated with a 25 dB hearing loss being equivalent to an age difference of 6.8 years on tests of executive function'.[60]

Hearing impairment and early dementia

The outcomes of the studies on hearing impairment and mild cognitive impairment are presented in Table 6.

Similar to the studies described above, the results in this category vary considerably. Four studies out of 15 failed to find any strong association between mild cognitive impairment and hearing loss.[51,52,64,72] Some studies found a strong association between mild cognitive impairment and central hearing loss.[50,56,61–63,65,69,70]

Peripheral hearing loss was found to be significantly associated with mild cognitive impairment in two studies,[32,71] but no such association was observed in two other studies.[62,69] There was considerable variance in the number of recruited participants per study from 20[70] to 2146.[64] There was no consistency in the outcome measures used (e.g. in DeVore's study (1992), the participants did not undergo any formal audiometry[71] whereas in the study by Gates *et al.* (1995) they underwent several tests including pure tone audiometry, speech audiometry, synthetic sentence identification with ipsilateral competing message, distortion product otoacoustic emissions, and auditory brainstem response.[69] Lister *et al.* (2016) sought to identify an association between cortical auditory evoked potentials and mild cognitive impairment by means of changes to the P1-N1-P2 complex.[56] Their findings might be

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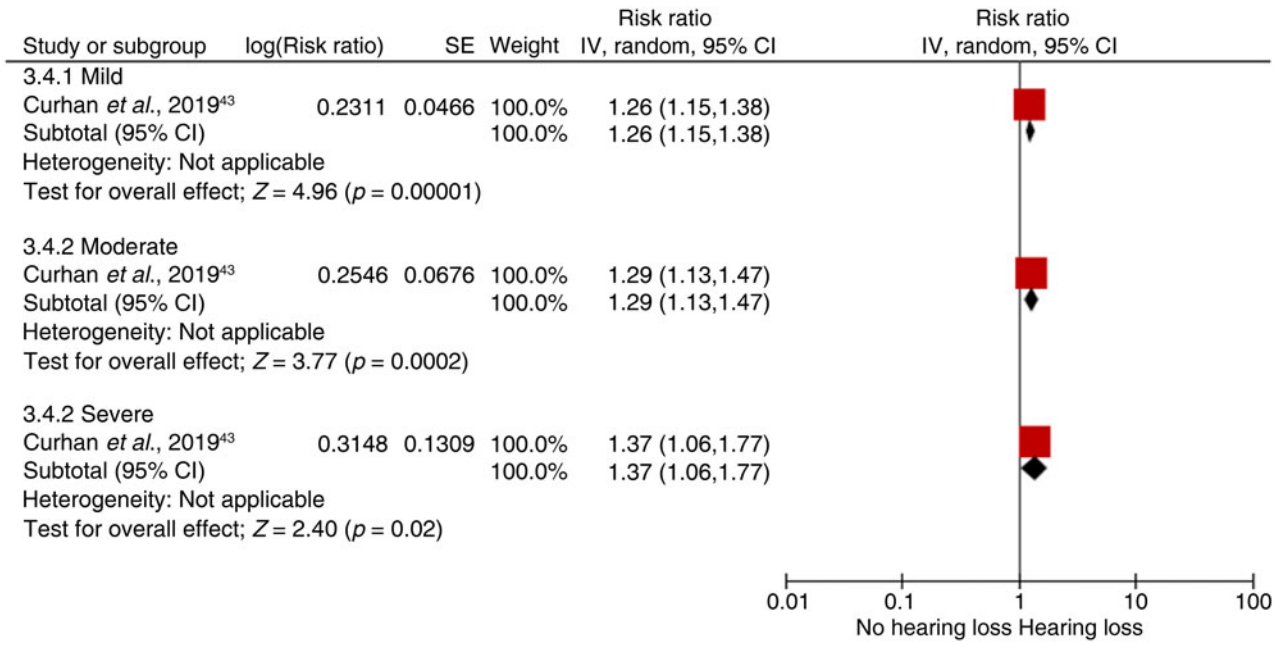

Fig. 8. Risk ratio outcomes in between-group difference (with and without peripheral hearing loss). SE = standard error; IV = Instrumental variable; CI = confidence interval

Table 5. Outcomes from the studies of prevalence of early dementia amongst hearing-impaired patients

Study	Participants (*n* (mean age; years)	Outcomes from cognitive assessment
Bruckmann and Pinheiro, 2016[54]	30 (68.5)	No difference in Mini Mental State Examination scores ($p = 0.880$)
Bucks *et al.*, 2016[55]	1969 (56.2)	No difference in contemporaneous attention, memory or executive function
Zhang *et al.*, 2015[58]	21 (51.7)	No difference in the neuropsychological tests between a group of patients with unilateral hearing loss and normal hearing
Deal *et al.*, 2015[57]	253 (76.9)	Participants with mild hearing loss showed poorer concurrent memory domain performance (−0.35 standard deviation; 95% confidence interval, −0.62 to −0.07; $p = 0.01$)
Quaranta *et al.*, 2014[59]	488 (72.8)	Strong association between mild cognitive impairment and hearing loss (odds ratio, 1.6; $p = 0.05$)
Lin *et al.*, 2011[60]	347 (71)	Significant deterioration on scores of Mini Mental State Examination ($p < 0.05$), Cued Selective Reminding Free recall ($p < 0.01$) and Stroop Mixed ($p < 0.05$) was observed with greater hearing loss. There was some association between hearing loss and Trail Making Test part A & B ($p < 0.10$), but no association between Stroop colours and words or verbal function and language tests
Tay *et al.*, 2006[66]	164 (not reported)	No significant differences in the cognitive function between people with none-to-mild and moderate-to-severe hearing loss ($p = 0.571$)
Van Boxtel *et al.*, 2000[67]	453 (not reported)	The predictive value of a 10 dB loss in hearing acuity was comparable in size to that of being up to 7.1 years cognitively older
Frisina and Frisina, 1997[68]	50 (43.2)	Patients with hearing loss took significantly better advantage of supportive context during speech audiometry than patients without hearing loss ($p < 0.05$)

consistent with further changes of inhibition, in the presence of mild cognitive impairment, with fewer overall resources being available to devote to the task. The cognitively normal older adults had significantly larger P2 amplitudes than those with probable mild cognitive impairment (3.7 (SD, 1.9) vs 1.8 (SD, 1.0)), but P1-N1-P2 latencies were similar in both groups. Gates *et al.* (2010) recruited 313 patients from the longitudinal Adult Changes in Thought study and grouped them according to their cognitive function as normal ($n = 232$), memory-impaired ($n = 60$) or demented ($n = 21$).[63] One SD poorer executive function was associated with a −9.2 per cent point difference in synthetic sentence identification with ipsilateral competing message, −15 per cent point difference in Dichotic Sentence Identification Test and −8.4 per cent point difference in Dichotic Digits Test. Finally, Uhlmann *et al.* (1989) postulated that the risk of dementia was increased for mild and moderate hearing loss and reached statistical significance for hearing loss of more than 40 dB ($p < 0.05$).[7]

Early dementia or cognitive decline and hearing impairment

The outcomes of studies of early dementia or cognitive decline amongst patients with hearing impairment are presented in Table 7. A significant correlation between hearing loss and incidence of early dementia or cognitive decline was reported in 7 out of 11 studies included in this category.[41–47] The number of recruited participants ranged from 1662[49] to 13 731.[46] The means of assessing hearing varied between the studies

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Table 6. Outcomes from the studies of prevalence of hearing loss amongst patients with mild cognitive impairment

Study	Participants (*n* (mean age; years)	Outcomes from hearing assessment
Han *et al.*, 2019[50]	2017 (73.2)	Significant association between hearing loss and mild cognitive impairment ($p = 0.001$)
Heward *et al.*, 2018[51]	305 (77.6)	No strong association between the two groups ($p = 0.109$)
MacDonald *et al.*, 2018[52]	408 (74.2)	No significant association between hearing loss and cognitive impairment ($p > 0.05$)
Iliadou *et al.*, 2017[53]	29 (66.1)	The mild cognitive impairment group had significantly poorer scores for speech in bubble and temporal resolution abilities of mild cognitive impairments versus normal controls for both ears
Heywood *et al.*, 2017[72]	2559 (not reported)	There was no significant association of hearing loss with prevalent mild cognitive impairment at baseline
Lister *et al.*, 2016[56]	30 (74.5)	Comparable P1 and N1 amplitudes of cortical auditory evoked potentials between the two groups, but significantly lower P2 amplitudes for patients with mild cognitive impairment ($p < 0.05$). The P1-N1-P2 latencies were similar in both groups
Rahman *et al.*, 2011[61]	300 (66.5)	The mild cognitive impairment group scored significantly lower than the control group in Selective Auditory Attention Test, Dichotic Digit Test left ear, pitch pattern sequence test, recognition memory, auditory memory for content and auditory memory for sequence. There were no significant differences between the two groups in the Dichotic Digits Test right ear and auditory fusion tests
Idrizbegovic *et al.*, 2011[62]	136 (64.3)	No significant differences in pure tone audiometry, speech in quiet or speech in noise. Mild cognitive impairment group performed worse at the Dichotic Digits Test
Gates *et al.*, 2010[63]	313 (not reported)	Strong association between executive function score and central auditory processing disorder, as measured by synthetic sentence identification with ipsilateral competing message
Benito-León *et al.*, 2010[64]	2146 (75.7)	No strong association between the two groups ($p = 0.114$)
Gates *et al.*, 2008[65]	313 (80)	Strong negative association between mild memory impairment and central auditory processing disorders
Gates *et al.*, 1995[69]	82 (not reported)	No significant difference in pure tone audiometry. However, a significant association was observed between central auditory dysfunction and mild cognitive impairment (synthetic sentence identification with ipsilateral competing message; $p < 0.001$)
Strouse *et al.*, 1995[70]	20 (71.2)	Significant association between central auditory dysfunction and cognitive impairment ($p < 0.05$)
DeVore, 1992[71]	50 (75.9)	Mild cognitive impairment present in 60% of those with hearing loss but only 24.4% of those with normal hearing
Uhlmann *et al.*, 1989[7]	200 (77)	Significant association between hearing loss and mild cognitive impairment ($p = 0.03$)

(pure tone audiometry[40,45] versus self-reported.[41–44,46] The majority of studies used the Mini Mental State Examination or Modified Mini Mental State to assess cognition, but in a few studies the Clinical Dementia Rating Scale,[44] abbreviated Memory Inventory for the Chinese[41] and subjective cognitive decline tests[43] were used.

In a study by Gurgel *et al.* (2014), all-cause dementia was observed in 16.3 per cent of patients with hearing loss (at baseline) but only in 12.1 per cent of those without hearing loss ($p < 0.001$).[48] Following multivariate analysis, hearing loss was found to be an independent factor for dementia. When evaluating the subgroup of patients who were cognitively intact at baseline and taking into account all covariates, hearing loss was not found to be a strong independent risk factor for developing dementia ($p = 0.09$). Gates *et al.* (1996) postulated that central hearing dysfunction precedes the emergence of cognitive decline and dementia and recommended that both peripheral and central hearing tests be obtained as part of the general health evaluation of the elderly.[49]

Discussion

We present a quantitative and qualitative analysis of cross-sectional and longitudinal, observational studies looking at the relationship between hearing impairment and mild cognitive impairment. Most of the included studies, except 11 studies[40,46,51,52,54,55,58,64,66,71,72], observed a significant association between hearing loss and early dementia or cognitive decline.

The pooled risk ratio across all studies of prevalence of mild cognitive impairment in people with hearing loss[54,57,59] was 1.44 (random-effects, 95 per cent CI = 1.27 to 1.64; $p < 0.00001$; $I^2 = 0$ per cent). When analysed separately, significantly more people with either peripheral or central hearing loss had mild cognitive impairment compared with those without. When analysing the prevalence of hearing loss amongst patients with mild cognitive impairment, the risk ratio was 1.40 (random-effects, 95 per cent CI = 1.10 to 1.77; $p = 0.005$; $I^2 = 0$ per cent), showing significantly more people with mild cognitive impairment had peripheral hearing loss compared with those without. However, on analysis of the papers that presented their data as an odds ratio, statistical heterogeneity was evident, and the between-group difference was not statistically significant.

The meta-analysis of incidence of hearing loss in patients with mild cognitive impairment showed that there was a correlation between hearing loss and incidence of early dementia or cognitive decline. Across 6 cohort studies where data was provided, the risk ratio was 2.06 (random-effects, 95 per cent

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Table 7. Studies of incidence of early dementia or cognitive decline amongst patients with hearing impairment

Study	Participants (*n*)	Outcomes from cognitive assessment
Schubert *et al.*, 2019[40]	2457	There was no association between hearing loss and cognition when visual impairment was included in the model
Yu and Woo, 2019[41]	2258	Poor hearing is significantly associated with an increased risk of subjective memory complaints. Odds ratio = 1.7 (95% CI = 1.3–2.1)
Curhan *et al.*, 2019[43]	2389	There is significant association with hearing loss and risk of cognitive impairment with risk ($p < 0.001$)
Vaccaro *et al.*, 2019[42]	1171	Significant relationship between hearing loss and cognitive impairment ($p = 0.001$)
Gallagher *et al.*, 2018[44]	2655	Hearing loss associated with increased risk of mild cognitive impairment ($p < 0.001$)
Heywood *et al.*, 2017[72]	1504	Hearing loss is not associated with an increase of mild cognitive impairment (HR = 1.85; 95% CI = 0.78–4.40; $p = 0.161$)
Deal *et al.*, 2017[45]	1889	Strong association between hearing loss and increased risk of developing dementia. Moderate or severe hearing loss to normal hearing: HR = 1.64 (95% CI = 1.16–2.30). Mild hearing loss to normal hearing: HR = 1.03 (95% CI = 0.75–1.42)
Yang and Gu, 2016[46]	13 731	Abnormal cognition was found in 96.7% of those with hearing loss but only in 36.8% of those with normal hearing
Fischer *et al.*, 2016[47]	1884	Significant relationship between hearing loss and cognitive impairment (HR = 2.09; 95% CI = 1.29–3.39)
Gurgel *et al.*, 2014[48]	4463	No significant association between hearing loss and risk for developing dementia ($p = 0.09$)
Gates *et al.*, 1996[49]	1662	No significant association between pure tone audiometry and cognitive decline. Significant association between central auditory disorder and incident dementia ($p < 0.05$)

CI = confidence interval; HR = hazard ratio

CI = 1.35 to 3.15; $p = 0.0008$; $I^2 = 97$ per cent); across 2 cohort studies, the hazard ratio was 1.40 (random-effects, 95 per cent CI = 1.64 to 1.95; $p < 0.00001$; $I^2 = 0$ per cent). Even in two separate cohort studies where the raw data was not available, the report outcomes that were reported as odds ratio and risk ratio did show that significantly more people with peripheral hearing loss had mild cognitive impairment compared with those without.

The included studies varied significantly in terms of the outcome measures used, the number of participants, the length of follow up and the use of covariates when analysing their results. Therefore, a direct comparison of the studies was not always possible. Most studies present cross-sectional data rather than data on longitudinal trajectories of cognitive function and hearing loss over time. Therefore, our estimates of the expected change in cognitive scores associated with hearing loss and age may be subject to bias by cohort effects or obscured by inter-individual heterogeneity in participant characteristics.

- This study looks at all cross-sectional and cohort studies evaluating the relationship between age-related hearing loss and mild cognitive impairment
- Most studies included in this review observed a significant association between hearing loss and incident mild cognitive impairment
- Further well-designed, large scale, prospective studies are needed to verify this association

Most studies included homogeneous populations (e.g. white people, well-educated, heath-aware[60]). Therefore, we should be cautious when generalising the outcomes of these studies. One key limitation across multiple studies is the variability in how hearing loss was measured and how audiometric data were analysed (e.g. choice of pure tone thresholds used to define hearing loss). The effect of biased or imprecise assessments of hearing thresholds would likely decrease sensitivity to detect associations because of increased variance. Some studies relied on subjective reporting of hearing loss.[41–43,46,48,51,64] This represents a crude method for identifying hard of hearing individuals, but studies have shown that subjective hearing assessments have been valid and reliable when compared against standard audiometry.[75,76] Similarly, the cognitive assessment tools used varied between the studies; therefore, making a direct comparison of the outcomes difficult. Finally, the use of covariates during regression analysis varied between the studies included in this meta-analysis, from none[71] to many.[64] Using the Newcastle–Ottawa Scale, all of the cohort studies scored seven or more stars out of nine, indicating generally good quality of the individual studies.

Strengths and limitations

This study was undertaken according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses; two electronic sources were searched and there was contact with experts. Study selection and data extraction were undertaken independently, and a quality assessment was undertaken and data were pooled in a meta-analysis. The limitations were that grey literature and conference abstracts were not searched. We also acknowledge the limitations of pooling data from observational studies in a meta-analysis and the potential for spurious results. Finally, a formal assessment of publication bias was not undertaken.

A recent commissioning document postulated that hearing loss is an independent risk factor for developing dementia.[10] This is consistent with our findings that there might be a link between hearing loss and mild cognitive impairment, a

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prodromal stage of dementia. Finally, hearing loss may be causally related to mild cognitive impairment and dementia, possibly through exhaustion of cognitive reserve, social isolation, environmental deafferentation or a combination of these pathways.[60] Studies have shown that in cases where auditory perception is difficult (i.e. hearing loss), greater cognitive resources are dedicated to auditory processing mechanisms rather than other cognitive processes, such as memory.[77,78] In a continually increasing aging population, this has obvious implications for health policy and social care services, aiming towards prevention, early diagnosis and treatment.

Brief cognitive assessments (such as Montreal Cognitive Assessment and Mini Mental State Examination) can successfully detect mild cognitive impairment in primary care, although their sensitivity is not as high as for established dementia.[79] There might be a role for routine cognitive assessment for people who present with hearing loss in an audiology clinic. Similarly, a referral for hearing assessment might be in the patient's best interest when they are diagnosed with mild cognitive impairment in primary care. Early intervention to address both issues might prove crucial in improving quality of life and reducing morbidity associated with hearing loss and dementia. Prospective cohort studies need to investigate whether early diagnosis of cognitive impairment improves important patient or caregiver outcomes.[79] Moreover, it is not yet known whether prompt hearing rehabilitation prevents cognitive decline. Future research should focus on identifying the underlying mechanisms linking hearing loss with dementia and developing rehabilitation strategies to delay or prevent its occurrence.

Conclusion

Most of the studies included in this systematic review observed a significant association between hearing loss and incident mild cognitive impairment. It is important for clinicians to be aware of this association and allow for early detection and intervention to try and delay onset of dementia. Further research investigating the mechanisms of this observed association and whether prompt hearing rehabilitation alters the natural course of this relationship should be the focus of future research.

Competing interests. None declared

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Appendix 1. Search Strategy, performed on 24 June 2020

Search Terms:
(Deafness OR Hearing Or Presbycusis) AND (Mild Cognitive Impairment OR MCI)

Filters:
Text Availability: Full Text
Species: Humans
Languages: English

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