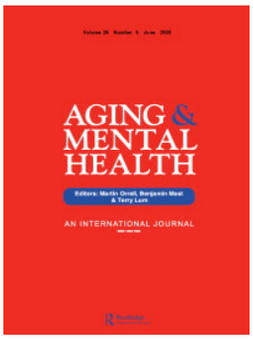

Aging & Mental Health

ISSN: 1360-7863 (Print) 1364-6915 (Online) Journal homepage: www.tandfonline.com/journals/camh20

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To cite this article: Megan Rose Readman, Jenna Littlejohn, Imogen Dodd, Sarah Rhodes, Lettie Wareing, Megan Polden, Christopher J. Plack & Clarissa Giebel (13 Jun 2025): Hearing loss as a risk factor for dementia: a systematic review and meta-analysis from a global perspective, Aging & Mental Health, DOI: 10.1080/13607863.2025.2515180

To link to this article: https://doi.org/10.1080/13607863.2025.2515180

AGING & MENTAL HEALTH
https://doi.org/10.1080/13607863.2025.2515180

Hearing loss as a risk factor for dementia: a systematic review and meta-analysis from a global perspective

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ABSTRACT

Objectives: Hearing loss is a risk factor for dementia with estimated hazard ratios (HRs) of 1.28–2.39. However, whether intercontinental variability exists in this relationship remains unexplored.

Method: MEDLINE, PsychInfo, Academic Search Ultimate, Web of Science, and EMBASE were searched, from inception to 2024, for cohort studies of dementia-free individuals with baseline hearing assessments ≥2-year follow-up, and incident dementia outcomes. Random-effect and multilevel models with subgroup difference tests were conducted.

Results: Forty-nine studies analysed cohorts from North America ($n = 20$), Europe ($n = 20$), Asia ($n = 7$), and Oceania ($n = 2$). Binary hearing loss was associated with increased dementia risk (HR = 1.32 [95% CI: 1.23–1.41]) with HRs being largest for Oceania and smallest for Asia ($p < 0.001$). In a sensitivity analysis excluding Oceania, HRs did not differ significantly by continent. Imprecise estimates create uncertainty around whether mild (HR = 1.35 [95% CI: 0.86–2.11]), moderate (HR = 1.39 [95% CI: 0.57–3.35]) or severe (HR = 1.66 [95% CI: 0.59–4.64]) hearing loss are associated with increased dementia risk, with little evidence that HRs by severity differ by continent ($p = 0.059$).

Conclusion: Findings indicate that the association between hearing loss and dementia is consistent globally, though HRs may vary slightly by continent.

Registration: This review was pre-registered on PROSPERO (CRD42024545209) and the OSF (https://osf.io/kew29/).

ARTICLE HISTORY
Received 23 January 2025
Accepted 27 May 2025

KEYWORDS
Dementia; hearing loss; risk factors; brain health

Background

Across the globe, dementia prevalence is increasing. Over 55 million people worldwide currently live with dementia, and this number is projected to increase threefold by 2050 (Nichols et al., 2022). While ageing is unequivocally the largest risk factor for the incidence of dementia (Riedel et al., 2016), identifying additional risk factors which may cause or hasten the onset of dementia is a global health priority (World Health Organization, 2019).

It has long been established that dementia and hearing loss often co-occur. For example, Nirmalasari et al. (Nirmalasari et al., 2017) observed that 60% of people seen in tertiary memory clinics had at least mild hearing impairment in their better ear, and Weinstein and Amsel (Weinstein & Amsel, 1986) observed that 55% of 30 people living with dementia in a care home setting had moderate to severe hearing loss. More recently, hearing loss has been implicated as a potentially modifiable risk factor for dementia incidence. Specifically, Lin et al. (Lin et al., 2011) observed in a sample of 639 community dwelling older adults that having mild hearing loss, 25–40 dB hearing loss, almost doubles dementia risk (hazard ratio (HR) = 1.89 [95% Confidence Interval (CI), 1.00–3.58]), moderate hearing loss, 41–70 dB HL, almost triples dementia risk (HR = 3.00 [95% CI, 1.43–6.30]), and profound hearing loss, >70 dB HL, increases dementia risk almost five times (HR = 4.94 [95% CI, 1.09–22.40]).

Since the work of Lin et al. (Lin et al., 2011), a multitude of cohort studies have investigated whether hearing loss is a substantial risk factor for dementia incidence (Lin & Albert, 2014; Livingston et al., 2020). Moreover, building on this growing body of literature, the 2024 iteration of the Lancet commissioned report on dementia prevention and care (Livingston et al., 2024) identified mid-life hearing loss as a potentially modifiable factor for dementia incidence with a relative risk (RR) of 1.37 [95% CI 1.00–1.87] and population attributable risk factor (PAF) of 7%. A PAF is an epidemiological measure which assesses the proportion of cases for an outcome (dementia), that can be attributed to a certain exposure (hearing loss), in a given population, assuming the relationship between these variables is causal (Mansournia & Altman, 2018). Thus, this estimate suggests that if hearing loss is causal for dementia, for which there is currently no clear evidence, up to 7% of dementia cases could potentially be prevented if it were possible to completely eliminate hearing loss from the population.

Previous meta-analyses of cohort studies on this topic have concluded that hearing loss is a substantial risk factor for dementia, with pooled estimates ranging from HR = 1.35–1.59 (Ford et al., 2018; Liang et al., 2021; Yu et al., 2024), odds ratio

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Supplemental data for this article can be accessed online at https://doi.org/10.1080/13607863.2025.2515180.

(OR) = 1.22 (Loughrey et al., 2018), RR = 1.94–4.87 (Lin & Albert, 2014; Wei et al., 2017; Zheng et al., 2017). Prospective cohort studies considering the degree to which hearing loss is a risk factor for dementia come from across the globe, including, but not limited to, cohorts from the US (e.g.Lin et al., 2011), UK (e.g.Stevenson et al., 2022), Korea (e.g. Byeon et al., 2021), and Australia (e.g.Ford et al., 2018). A recent analysis of geographical variation in dementia prevalence and risk factors found that risk of dementia incidence attributed to hearing impairment was greater in the North than in the South of China (Liu et al., 2024). Thus, highlighting the importance for the need to consider the influence of the geography of cohort analysed. Yet, prior meta-analyses have pooled together resulting indicators of the degree to which hearing loss is a risk factor for dementia (i.e. RR, OR and HR) irrespective of the country of the cohort analysed. As such, it remains unknown whether hearing loss is a substantial, potentially modifiable, risk factor for dementia across all populations or whether the magnitude of risk is dependent upon the cohort of interest.

The World Health Organisation's (WHO) 2022 'blueprint for dementia research' highlighted a move towards considering population-level risk reduction approaches. Under this approach, measures are applied to entire populations with the aim of making the environment less conducive to the incidence and maintenance of dementia and its associated risk factors (Walsh et al., 2022). If the magnitude to which hearing loss is a risk factor for dementia varies across populations, this must be considered during the development of population-level risk reduction messaging.

To this end, this systematic review and meta-analysis aimed to synthesise the literature considering hearing loss as a risk factor for incident dementia from a global perspective and, through a meta-analysis, ascertain the relation between hearing loss and dementia incidence at a continent-specific level. Specifically, we aim to answer the following question: 'Is the degree to which hearing loss is a risk factor for the incidence of dementia contingent upon the continent of the population in question?'

Methods

This systematic review and meta-analysis is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (See Supplementary Materials Tables S1 and S2 for PRISMA checklist), and was pre-registered, both on the Open Science Framework (OSF) (OSF, 2024) and PROSPERO (CRD42024545209), prior to completion. The OSF pre-registration contains documentation of the search strategy, planned statistical analyses, and the data analysis code book (OSF, 2024). Implementation adhered to the pre-registered protocol. We summarise the implementation below.

Search strategy

To address the multidisciplinary nature of the research question, a comprehensive literature search using MEDLINE, PsychInfo, Academic Search Ultimate, Web of Science and EMBASE, was conducted on 6th July 2024. EMBASE and PsychInfo were selected as they include pre-print databases such as BioArXiv and MedArXiv, and theses, thereby ensuring grey literature capture. All databases were searched for papers from their inception up to 6th July 2024.

Three independent search strings, one pertaining to the outcome of interest (incident 'all-cause' dementia), one pertaining to the exposure of interest (hearing loss), and one pertaining to study methodology (prospective cohort studies), were applied. These three independent search strings were then combined using Boolean operators ('AND'). Each search string comprised of dictionary terms specific to the database in question and free-text search terms. Therefore, the search strings applied to each database differed only in terms of the database-specific dictionary terms applied (see Supplementary Material, Table S3, for the final applied search strings applied to each database).

The sensitivity of the applied search strategy was checked by assessing whether seven highly relevant papers (Amieva et al., 2018; Deal et al., 2017; Ford et al., 2018; Gallacher et al., 2012; Lin et al., 2011; Mukadam et al., 2019; Osler et al., 2019), which were identified *a priori* during scoping searches, were returned by the search strings. The initially developed search strings proved to be sensitive for all databases, and so were not updated.

To further ensure that all relevant records were captured, forward and backward citation tracking of all included papers and two particularly relevant prior reviews (Liang et al., 2021; Yu et al., 2024) was conducted using Google Scholar. In circumstances in which we could not access the relevant record, The University of Liverpool Library requested access to these records.

Inclusion criteria

Screening was conducted in two phases: (1) title and abstract screening, and (2) full text screening. The inclusion criteria differed depending on the phase of screening (see Table 1 for screening criteria).

Screening

Four reviewers (MRR, JL, LW and ID) were involved in the screening process with each paper being screened by two independent reviewers in parallel, blinded to each other's decisions. Any discrepancies that arose between the two independent reviewers were resolved by a third reviewer. Prior to screening all relevant records, 10% of papers were screened to check inter-rater consistency. The full text of all title/abstracts that were deemed

Table 1. Inclusion criteria applied at the level of title and abstract and full text screening.

Title and Abstract inclusion criteria:
(1) The title/abstract was written in the English Language
(2) An original quantitative study with a prospective/longitudinal/cohort design (i.e. no case-control, cross-sectional, case, qualitative studies, or reviews)
(3) The study involved human adult cohorts
(4) There was mention of hearing loss (hearing impairment) as the exposure measure
(5) There was mention of dementia as the outcome measure(5)
Full text inclusion criteria:
(1) Prospective/longitudinal/cohort study design was employed
(2) Hearing loss (hearing impairment, clinically diagnosed, audiometrically derived and self-reported) was included as an exposure measure
(3) Dementia was included as the outcome measure
(4) Minimum of 2 years follow up
(5) Statistical models have been adjusted for ages as a minimum
(6) Adjusted Hazard/Risk Ratio or Relative Risk (HR, OR, RR) present with standard error or 95% CI
(7) The country(s) of the cohort was defined

potentially relevant were then screened by two independent reviewers, again blinded to each other's decisions. As with title and abstract level screening, any discrepancies were resolved by a third reviewer.

Of 6575 screened papers, 6525 did not meet the inclusion criteria. All studies that did meet inclusion criteria and passed full text screening were checked for retraction using the Retraction Watch Database (http://retractiondatabase.org/RetractionSearch). One paper was retracted (Jiang et al., 2023) and so was removed prior to analysis.

Data extraction

Data were extracted by two reviewers (MRR and ID) independently, and if a discrepancy did arise, the inconsistency was resolved through review by a third author (LW). The following data were extracted into an excel spreadsheet: study authors; year of study; sample size (*n*); country of sample; mean sample age (standard deviation); proportion of male participants; number of patients with hearing impairment (*n*); method of hearing loss diagnosis (e.g. clinically diagnosed, audiometrically derived and self-report); mean years of follow-up (standard deviation); number of incident dementia cases; outcome measures (e.g. incident 'all-cause' dementia, Alzheimer's disease dementia); method of outcome measure diagnosis (e.g. clinically diagnosed and self-report); variables adjusted for/covariates; all reported adjusted HRs, ORs, or RRs and associated 95% CIs; and any relevant conclusions made by the authors (see Supplementary Material Table S4).

Quality assessment

The methodological quality of all studies that passed through full-text screening were assessed using the Newcastle-Ottawa quality assessment scale (NOS) (Wells et al., 2014). This scale evaluates three methodological quality parameters (selection, comparability, and outcome) divided across eight specific items. Each item on the scale is scored either 0 or 1, except for comparability which is scored from 0 to 2, in which 0 indicates the presence of potential bias. Thus, the maximum for each study is 9. Publication bias was assessed visually using funnel plots, in which visually asymmetrical funnel plots imply potential publication bias (Egger et al., 1997).

Statistical analysis

Prior to any formal analysis, we produced a table detailing the cohort analysed (and accompanying demographics), continent of the cohort analysed, outcomes (all-cause dementia, Alzheimer's disease and vascular dementia), covariates controlled for, and main results (OR, HR, RR, and associated 95% CI) (See Supplementary Materials Table S4).

We chose to use hazard ratios as our summary statistic because this is what was reported in the majority of cases. For the small number of studies that reported odds ratios (ORs) we elected to transform the OR to a HR using Grant's formula (Grant, 2014) to maximise the number of studies included in out analysis. Full documentation of the transformation of ORs can be found in the analysis script. All analyses were conducted used R software (version 4.3.1), using the meta and metafor packages (Viechtbauer, 2010).

Primary analyses

Within the literature hearing loss has been defined in several ways. Some studies classify the degree of hearing loss categorically (e.g. mild, moderate and profound) in accordance with standardised criteria (e.g. the British Society of Audiology criteria, WHO criteria, or the Global Burden of Disease Expert Group on Hearing Loss criteria (World Health Organization, 2007)). Some studies treat hearing loss as a binary variable (Yes v No), and others consider hearing loss as a continuous variable (e.g. pure-tone audiometry (PTA) average threshold). As such, the current body of literature contains measures of risk for several different exposure formats. The resulting statistics are different in definition, computation and interpretation (George et al., 2020). Therefore, we computed separate pooled estimates for each form of exposure variable. Specifically, in accordance with the pre-registered protocol, we: (1) conducted a random effects meta-analysis including statistics relating to a binary exposure variable, which was assumed *a priori* to be the most common exposure format, and (2) conducted a multilevel meta-analysis, that accounts for the within-study correlations (Mavridis & Salanti, 2013; Riley, 2009), including studies which have classified hearing loss categorically in terms of severity based on PTA measures. We elected to only include studies which have categorised hearing loss based on PTA measures as all studies that have done so used the same cut off values for categorisation, therefore making the outcomes easier to interpret. Due to fundamental differences in the categorisation systems and the data drawn upon to categorise hearing loss severity, all other studies employing a categorised hearing loss exposure variable were synthesised qualitatively. For all analyses, a test for subgroup differences was employed to ascertain whether there is evidence that effect sizes vary by continent. Heterogeneity of included studies was assessed using the I^2 statistic (Lin, 2020).

Within the studies analysed, confounding factors were adjusted for to a varying degree, with several studies reporting more than one HR for multiple models with varying covariate structures. To reduce the degree of variability for studies that report multiple HRs, with multiple covariate structures, the simplest structure was included in the primary analysis.

Exploratory analyses

The pre-specified analysis plan included: (1) a random effects meta-analysis including studies which employed a binary hearing loss variable, and (2) a multilevel meta-analysis including studies that categorised multiple levels of hearing loss. During data extraction it was observed that some studies also analysed hearing loss as a continuous variable (i.e. per 10 dB increase in hearing loss). Therefore, we conducted an additional random-effects meta-analysis including only studies that included continuous PTA data.

Within the studies that met the inclusion criteria, the dementia outcome was determined in several ways. Specifically, some studies employed an incident all-cause dementia outcome, whilst others employed more specific dementia subtype outcome variables, namely Alzheimer's disease dementia and vascular dementia. In the main primary analyses, we included all studies, regardless of their outcome variable. Therefore, to ascertain whether the observed trends are true for all types of dementia, or whether they are unique to specific subtypes of dementia, as an exploratory analysis we re-conducted analyses sub-grouped by dementia outcome variable.

Finally, the covariate adjustment sets of the included studies were largely heterogeneous, with some studies adjusting only for age and other adjusting for age, sex, socioeconomic status and comorbid health conditions. To explore whether the observed HR varies by the adjustment set applied, as an exploratory analysis we re-conducted the primary analysis subgrouped by adjustment set.

Sensitivity analyses

To assess the robustness of the primary findings, several sensitivity analyses were conducted. Several studies included in this review analysed data from the same datasets. To ensure that potentially double-counting participants did not bias the results we conducted sensitivity analyses in which only one study per database was included. Furthermore, to ensure that the transformation of ORs to a HRs did not influence the results of the primary analysis including binary hearing loss, we re-conducted the analysis with transformed variables. Moreover, self-reported hearing capabilities correlate poorly with audiometrically derived measures of hearing (Tsimpida et al., 2020). Therefore, we re-conducted analyses with self-reported hearing outcomes removed. Finally, as only one study included in the primary analysis analysed data obtained from a cohort in Oceania (Ford et al., 2018), we re-conducted the primary analysis with this study removed.

Results

A total of 49 studies, comprising 9,727,195 (average $n = 198,514$, $SD = 748,938.69$, range 280-4,724,646 participants) participants, were identified (see Figure 1 for PRISMA diagram) (Amieva et al., 2018; Brenowitz et al., 2019; Brewster et al., 2021; Byeon et al., 2021; Cantuaria et al., 2024; Chan et al., 2020; Chern et al., 2022;

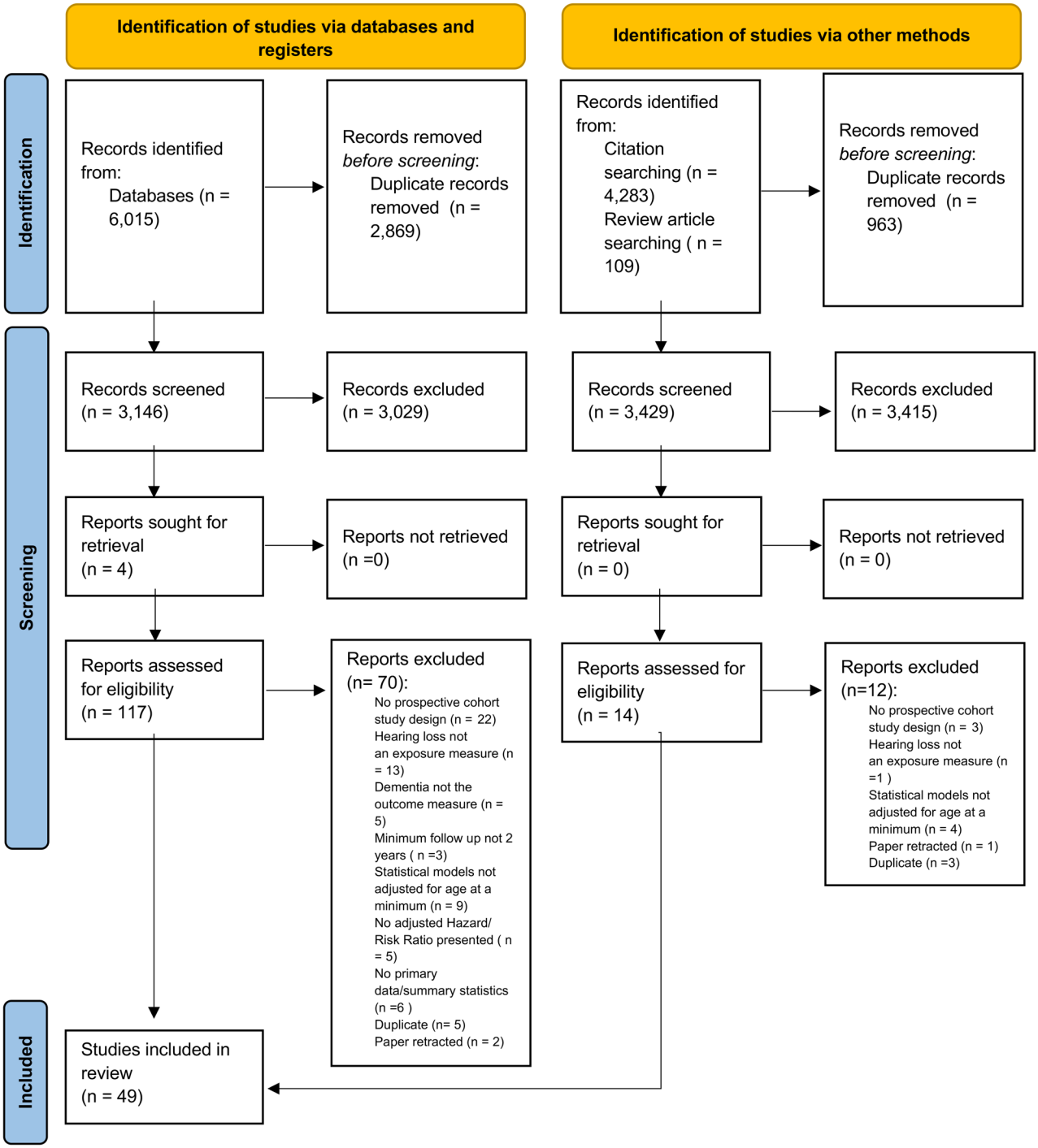

Figure 1. PRISMA flowchart outlining number of papers excluded at each stage of screening. Only the first reason for exclusion is reported.

Davies et al., 2017; Deal et al., 2017; Dintica et al., 2023; Fitzhugh & Pa, 2023; Ford et al., 2018; Gallacher et al., 2012; Gates et al., 1996; Golub et al., 2017; Gurgel et al., 2014; Han Oh et al., 2023; Hendriks et al., 2024; Heywood et al., 2017; Hu et al., 2022; Hwang et al., 2020; 2022; Kim et al., 2024; Kojima et al., 2022; Kuo et al., 2021; Lad et al., 2024; Lim et al., 2023; Lin et al., 2011; Luck et al., 2020; Marinelli et al., 2022; Maruta et al., 2020; Mohammed et al., 2022; Möller et al., 2024; Myrstad et al., 2023; Osler et al., 2019; Pabst et al., 2021; Powell et al., 2022; Riedel-Heller et al., 2019; Rolandi et al., 2019; Santabárbara et al., 2021; Maharani et al., 2020; Stevenson et al., 2022; Stevenson-Hoare et al., 2024; Strutt et al., 2022; Tomata et al., 2020; Tonelli et al., 2023; Tremblay et al., 2019; Vassilaki et al., 2019; Vo et al., 2022). As some studies drew on the same databases, it is likely that this is not 9,727,195 unique participants. Full study details can be found in Supplementary Materials Table S4.

Regarding the determination of hearing loss, 18 (37%) studies used self-report identification methods, 11 (23%) studies used PTA, six (12%) studies drew upon clinical diagnostic criteria (ICD or DSM criteria), seven (14%) studies used clinical interview, four (8%) studies used speech-reception-thresholds, one (2%) study used a hearing loss screening check, one (2%) used an informant identification method only, and one (2%) study used self-report combined with PTA. A total of 681,947 cases of hearing loss at baseline were identified. The number of cases of hearing loss was not reported in six studies (Byeon et al., 2021; Chan et al., 2020; Gallacher et al., 2012; Gates et al., 1996; Rolandi et al., 2019; Tremblay et al., 2019).

With a mean follow-up duration between 2 and 44.4 years (median range of follow-up across studies = 4.4-14.4), 366,170 incidences of dementia occurred. Two studies did not report the number of incident cases. When considering the outcome variable, incident 'all cause' dementia was reported in 45 (92%) studies, Alzheimer's disease in 10 (22%) studies, vascular dementia in four (10%) studies, non-Alzheimer's dementia in one (2%) study, and young onset dementia in one (2%) study. Several studies reported more than one outcome. Diagnosis of dementia was based on clinical evaluation, which included medication use, hospital records, and neurocognitive test scores in 33 studies, by ICD codes in 12 studies, through self-report in two studies, and the method of diagnosis was not disclosed in the remaining two studies.

Regarding the main variable of interest, the included studies analysed cohorts from four continents, namely: North America ($n = 20$), Europe ($n = 20$), Asia ($n = 7$), and Oceania ($n = 2$) (See Table 2 for breakdown of studies by Country).

Table 2. Breakdown of studies by country.

	Papers
North America	
US ($n = 17$)	6, 24, 40–41, 43–48, 50–56
Canada ($n = 2$)	42, 49
Not specified ($n = 1$)	39
Europe	
United Kingdom ($n = 6$)	17, 58, 59 61,65, 66
Germany ($n = 4$)	63, 67, 69, 71
Sweden ($n = 2$)	62, 64
Denmark ($n = 2$)	25,57
France ($n = 1$)	26
Ireland ($n = 1$)	23
Italy ($n = 1$)	68
Norway ($n = 1$)	70
Spain ($n = 1$)	60
Multiple European countries: Denmark, Sweden, Austria, Germany, the Netherlands, France, Switzerland, Belgium, and Luxembourg, Spain, Italy, Greece, Portugal, Czech Republic, Poland, Hungary, Slovenia, Estonia, and Croatia.(n = 1).	72
Asia	
Korea ($n = 2$)	18,77
Singapore ($n = 1$)	78
South Korea ($n = 1$)	76
Oceania	
Australia ($n = 2$)	19,79

Primary analysis

Hearing loss as a binary exposure variable

Across all studies, the presence of hearing loss (any degree of hearing loss vs. none) was associated with an increased HR of incident dementia (HR = 1.32 [95% CI: 1.23–1.41], based on $k = 39$ studies, $p < 0.001$). A test of subgroup differences indicated that the HR differed depending on the continent from which the cohort was obtained ($Q = 34.88(3)$, $p < 0.001$). The HR was largest for Oceania (HR = 1.69 [95% CI: 1.54–1.85], based on $k = 1$ study), followed by North America (HR = 1.40 [95%CI: 1.23–1.60], based on $k = 15$ studies), Europe (HR = 1.326 [95% CI: 1.17–1.37], based on $k = 16$ studies) and finally the smallest in Asia (HR = 1.18 [95% CI: 1.08–1.29], based on $k = 7$ studies) (see Figure 2). Studies employing a binary hearing loss variable showed a substantial degree of between-study heterogeneity, explained in part by variation by continent ($I^2 = 99.0\%$ [95% CI: 98.9%–99.1%]).

Categorical hearing loss

Of the nine studies that employed a categorical hearing loss exposure variable (Cantuaria et al., 2024; Davies et al., 2017; Deal et al., 2017; Fitzhugh & Pa, 2023; Lin et al., 2011; Mohammed et al., 2022; Powell et al., 2022; Strutt et al., 2022; Tremblay et al., 2019), five determined category membership based on PTA (Cantuaria et al., 2024; Deal et al., 2017; Lin et al., 2011; Mohammed et al., 2022; Powell et al., 2022), and so were included in the multilevel meta-analysis. Regarding the severity of hearing loss, all HRs were consistent with the positive relationship seen in our primary analysis, but estimates were imprecise leaving it uncertain whether or not mild (HR = 1.35 [95% CI: 0.86–2.11]), moderate (HR = 1.39 [95% CI: 0.57–3.35]) or severe (HR = 1.66 [95% CI: 0.59–4.64]) hearing loss are associated with increased HR of incident dementia ($p = 0.723$). The five studies included in this analysis drew on cohorts from Europe ($n = 1$) and North America ($n = 4$). A test of subgroup differences indicated that the HR, at all severities, did not significantly vary depending on the continent from which the cohort was obtained ($p = 0.059$) (see Figure 3). Studies employing a binary hearing loss variable were deemed to be largely heterogenous (QE= 3.52 (7), $p = 0.833$).

The remaining four studies determined hearing loss severity based on speech reception thresholds (SRT) (Fitzhugh & Pa, 2023; Tremblay et al., 2019), self-report (Strutt et al., 2022), and a screening tool (Davies et al., 2017). Critically, while both Tremblay et al. (2019) and Fitzhugh and Pa (2023) determined hearing loss severity based on SRT, the categories of severity employed were different. Therefore, it was not appropriate to meta analyse these two studies. Both Tremblay et al. (2019), who drew on SRT data, and Davies et al. (2017), who drew on hearing loss screening tool data, observed that hearing loss significantly increases the risk of dementia incidence with the degree of risk increasing with more severe hearing loss. However, Fitzhugh and Pa (2023), who also drew on SRT data, observed that insufficient but not poor hearing increased dementia incidence risk.

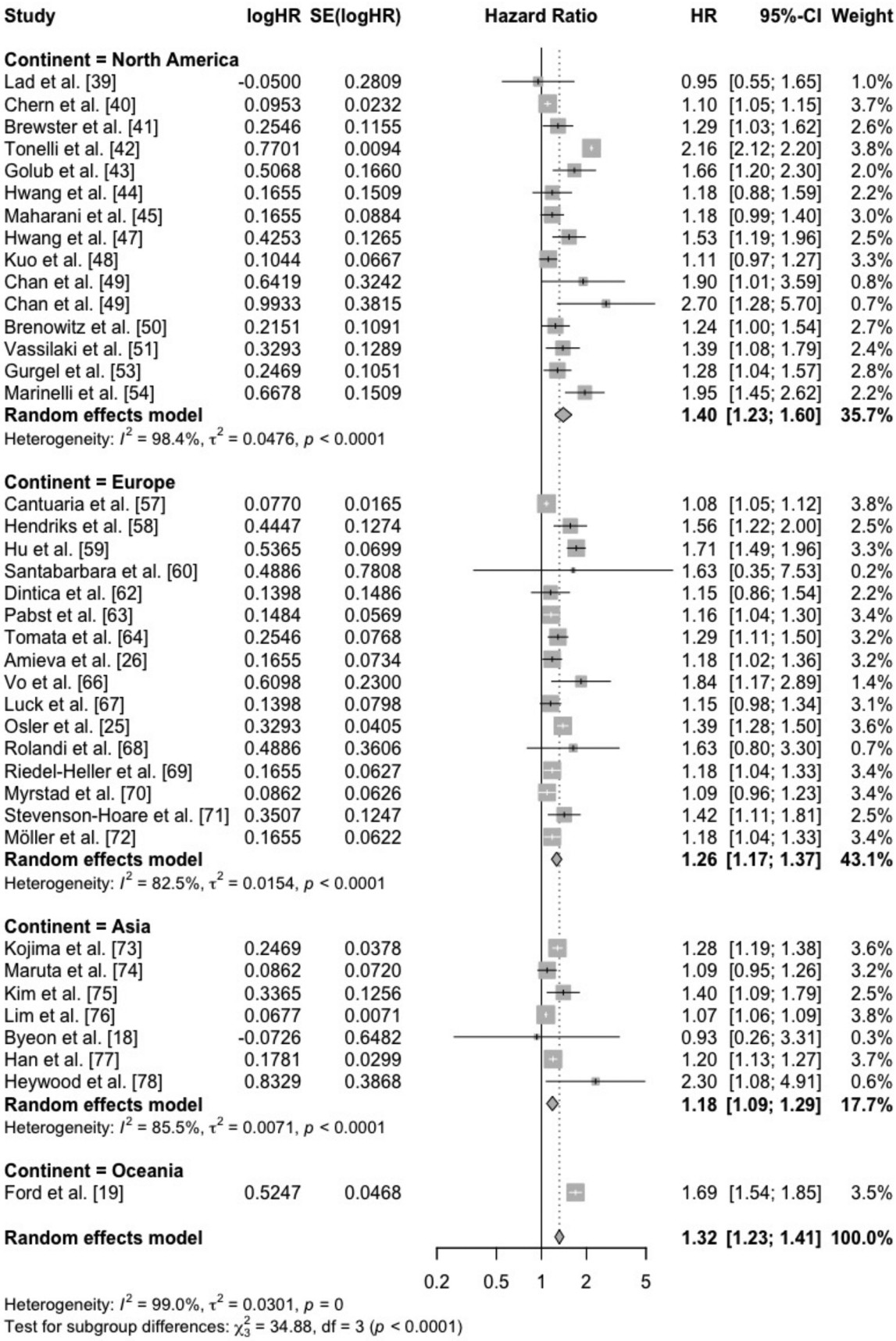

Figure 2. Meta-analysis of the association between binary hearing loss (any degree of hearing loss vs. non) and dementia.
Note. The solid line on the Forest plot is the point of no effect (HR = 1) and the dashed line represents the overall pooled estimate. The grey squares and horizontal lines represent the odds ratios of each study and their 95% confidence intervals. The size of the grey square represents the weight contributed by each study in the meta-analysis. The diamond represents the pooled odds ratio and its 95% confidence intervals.

Furthermore, Strutt et al. (2022), who drew on self-report measures, observed that neither mild nor moderate hearing loss increased dementia risk. As it was not possible to conduct formal analyses on these studies no reflections regarding continent are made (see Supplementary Materials Table S4 for a full summary of these studies).

Exploratory analyses

Hearing loss as a continuous measure

Six studies investigated how dementia risk changes with every 10 dB increase in hearing loss. The pooled HR was consistent in direction with our primary analysis but with considerable imprecision (HR = 1.26 [95% CI: 0.89; 1.78] based on $k = 6$ studies; $p = 0.20$). These papers drew on cohorts from Europe ($n = 2$) and North America ($n = 4$). A test of between-group differences did not suggest that HR per 10 dB increase in hearing loss differed depending on the continent of the cohort (Europe HR = 2.01 [95% CI: 0.54–7.44] based on $k = 2$ studies, North America HR = 1.10 [95% CI: 0.97–1.26] based on $k = 4$ studies, $p = 0.371$) (see Supplementary Materials Figure S1 for forest plot). Studies employing a continuous hearing loss exposure measure were heterogenous ($I^2 = 80.8\%$ [58.7%–91.1%]).

Given that we were not able to transform the OR reported by Gallacher et al. (2012) to a HR we conducted a sensitivity analysis in which this study was excluded. Once Gallacher et al. (2012) was excluded a 10 dB increase in hearing loss was associated with an increased HR for incident dementia (HR= 1.09 [95% CI: 1.01–1.18] based on $k = 5$ studies) ($p = 0.027$).

Dementia subtype outcomes

Alzheimer's disease dementia. Ten studies employed an Alzheimer's disease dementia outcome measure (Golub et al., 2017; Hwang et al., 2020; 2022; Kim et al., 2024; Lad et al., 2024; Lin et al., 2011; Mohammed et al., 2022; Myrstad et al., 2023; Santabárbara et al., 2021; Tremblay et al., 2019). Of these studies, seven employed a binary hearing loss exposure measure (Golub et al., 2017; Hwang et al., 2020; 2022; Kim et al., 2024; Lad et al., 2024; Myrstad et al., 2023; Vo et al., 2022), two studies employed a categorical hearing loss exposure measure (Mohammed et al., 2022; Tremblay et al., 2019), and two studies employed a continuous hearing loss exposure measure (Lin et al., 2011; Myrstad et al., 2023). As an exploratory analysis we reconducted the primary analysis drawing on binary hearing loss, with studies that report an Alzheimer's disease dementia outcome only.

The presence of hearing loss was associated with an increased HR of Alzheimer's disease (HR = 1.32 [1.11–1.58], based on $k = 7$ studies, $p = 0.002$). HR varied by continent with the highest in North America (HR = 1.44 [1.17–1.79], based on $k = 4$ studies), closely followed by Asia (HR = 1.40 [1.09–1.79], based on $k = 1$ study) and the smallest in Europe (HR = 1.07 [0.–1.27], based on $k = 2$ studies) ($p = 0.05$). Studies employing a binary hearing loss exposure variable and Alzheimer's disease dementia outcome variable were moderately heterogenous ($I^2 = 47.1\%$ [95% CI: 0.0%–77.7%]) (see Supplementary Materials Figure S2 for forest plot).

Vascular dementia. Four studies employed a vascular dementia outcome measure (Gallacher et al., 2012; Golub et al., 2017; Hwang et al., 2020; 2022). Of these studies, three employed a binary hearing loss exposure measure (Golub et al., 2017; Hwang et al., 2020; 2022) and the remaining one employed a continuous hearing loss

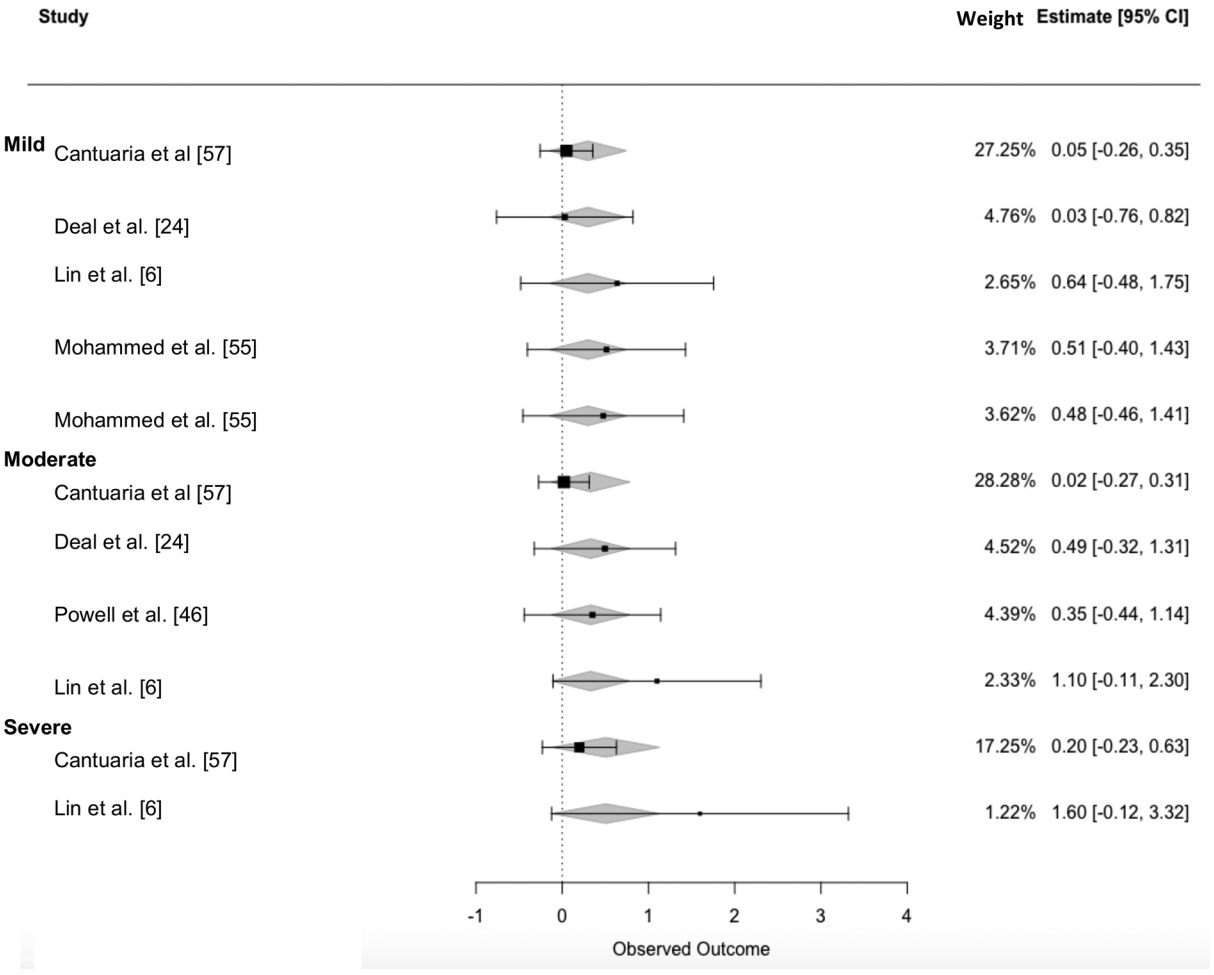

Figure 3. Meta-analysis of the association between categorical hearing loss (mild, moderate and sever) and dementia.

exposure measure (Gallacher et al., 2012). Therefore, as an exploratory analysis we reconducted the primary analysis drawing on binary hearing loss with studies that report a vascular dementia outcome only.

Hearing loss was associated increased HR for vascular dementia (HR = 1.23 [95% CI: 0.77–1.97]), but did not reach statistical significance ($p = 0.39$). All studies were conducted in North America; therefore, no subgroup analyses were conducted. Studies employing a binary hearing loss exposure variable and vascular dementia outcome variable were moderately heterogenous (I^2 = 60.5% [0.0%–88.8%]) (see Supplementary Materials Figure S3 for forest plot).

Adjustment sets

Adjustment sets were inconsistent with three studies adjusting for only age (Luck et al., 2020; Möller et al., 2024; Osler et al., 2019), seven studies adjusting for age and sex (Cantuaria et al., 2024; Chan et al., 2020; Hu et al., 2022; Kim et al., 2024; Kojima et al., 2022; Tomata et al., 2020; Tonelli et al., 2023), three study adjusting for age and comorbid health conditions (Ford et al., 2018; Rolandi et al., 2019; Vo et al., 2022), eight studies adjusting for age, sex, and socioeconomic status (Brenowitz et al., 2019; Byeon et al., 2021; Dintica et al., 2023; Golub et al., 2017; Kuo et al., 2021; Maharani et al., 2020; Stevenson-Hoare et al., 2024; Vassilaki et al., 2019), one study adjusting for age, sex and comorbid health conditions (Maruta et al., 2020) and 16 studies fully adjusting for age, sex, socioeconomic status and concurrent health conditions (Amieva et al., 2018; Brewster et al., 2021; Chern et al., 2022; Gurgel et al., 2014; Han Oh et al., 2023; Hendriks et al., 2024; Heywood et al., 2017; Hwang et al., 2020; 2022; Lad et al., 2024; Lim et al., 2023; Marinelli et al., 2022; Myrstad et al., 2023; Pabst et al., 2021; Riedel-Heller et al., 2019; Santabárbara et al., 2021) (See Supplementary Materials Table S4 for summary of adjustments factors for each study). HRs varied by covariate structure ($p < 0.001$) with the highest HR being observed in studies that controlled for age and comorbid health conditions (HR = 1.69 [95% CI: 1.55–1.85], based on $k = 3$ studies), and the lowest HR being observed in studies that controlled for age, sex and comorbid health conditions (HR = 1.09 [95% CI: 0.95–1.26], based on $k = 1$ study) (See Supplementary Materials Figure S4 for forest plot).

Sensitivity analyses

Hearing loss as a binary exposure variable

Sensitivity analyses which (1) excluded studies which employed the same database (Hu et al., 2022; Marinelli et al., 2022), (2) excluded Chan et al. (2020) due to transformation of statistics, and (3) excluded studies which relied upon a self-reported exposure measure (Amieva et al., 2018; Byeon et al., 2021; Golub et al., 2017; Gurgel et al., 2014; Hendriks et al., 2024; Heywood et al., 2017; Hwang et al., 2020; 2022; Kojima et al., 2022; Kuo et al., 2021; Lad et al., 2024; Luck et al., 2020; Maruta et al., 2020; Möller et al., 2024; Osler et al., 2019; Pabst et al., 2021; Riedel-Heller et al., 2019; Rolandi et al., 2019; Santabárbara et al., 2021; Maharani et al., 2020; Stevenson-Hoare et al., 2024; Tomata et al., 2020; Vo et al., 2022) produced virtually unchanged results. Specifically, across all three sensitivity analyses, the presence of hearing loss (any degree of hearing loss vs. none) was associated with an increased HR of incident dementia ((1) HR = 1.33 [95% CI: 1.23–1.44], based on $k = 34$ studies; (2) HR = 1.34 [95% CI: 1.24–1.45], based on $k = 35$ studies; (3) HR = 1.41 [95% CI: 1.22–1.63], based on $k = 13$ studies). Moreover, the tests for subgroup differences indicated that HR differed by the continent from which the cohort was obtained ((1) $Q = 33.39$ (3), $p < 0.001$; (2) $Q = 31.17$ (3), $p < 0.001$; (3) $Q = 26.65$ (3), $p < 0.001$). Critically, sensitivity analyses on (1) and (2) both revealed that the HR was the largest in Oceania and smallest in Asia. However, for sensitivity analysis (3), in which studies using self-report were excluded, the HR was the largest in North America and smallest in Asia.

Congruent with sensitivity analyses 1–3, the final sensitivity analysis (4) in which the one study which analysed data from Oceania (Ford et al., 2018) was removed, also observed that the presence of hearing loss (any degree of hearing loss vs. none) was associated with an increased HR of incident dementia (HR = 1.30[95% CI: 1.22–1.39], based on $k = 39$ studies). However, critically the test for subgroup differences revealed that the HR no longer differed significantly by the continent from which the cohort was obtained ($Q = 4.35$ (2), $p = 0.11$). Full details of all sensitivity analyses can be found in the Supplementary Materials (Supplementary Materials Table S5).

Publication bias

Visual exploration of publication bias, through funnel plots, revealed no evidence of systematic asymmetry on examination for both studies employing a binary hearing loss exposure variable and categorical hearing loss exposure variable (Supplementary Materials Figures S5 and S6).

Methodological quality

The methodological quality of the included studies was good, evidenced by NOS scores ranging from 6 to 9 ($M = 7.10$, SD = 0.82) (see Supplementary Materials Table S6 for all ratings).

Discussion

Prior estimates of the pooled HR for the relation between hearing loss and the incidence of dementia have disregarded the potential influence of the continent from which the cohorts analysed were derived. To explore whether the magnitude of risk varied by the continent from which the data was obtained we conducted a series of meta-analyses with tests of subgroup differences based on the continent of the cohort analysed. Across 49 included studies we observed that the presence of hearing loss (any hearing loss vs. none) was associated with an increased HR of incident dementia and that magnitude of the HR varied by the continent from which the cohort was obtained. Specifically, within the included studies the HR was the largest in studies analysing cohorts from Oceania followed by North America, Europe, and the smallest in Asia. However, a sensitivity analysis, in which the one study analysing data from Oceania was removed revealed, that HRs no longer differed significantly by the continent from which the cohort was obtained.

These findings contribute to the literature regarding hearing loss as a risk factor for dementia. Specifically, the magnitudes of the increased risk for dementia in people with hearing loss defined as a binary (Ford et al., 2018; Liang et al., 2021; Loughrey et al., 2018; Wei et al., 2017; Yu et al., 2024; Zheng et al., 2017), categorical (Yu et al., 2024), or continuous (Yu et al., 2024)

variable are largely congruent with prior meta-analyses, which typically relied upon smaller samples of studies. Moreover, the observation that the HR varies by the continent from which the analysed cohort was obtained support emerging discussions within the field emphasising the need to exercise a certain degree of caution when (1) generalising the findings of cohort studies to alternative populations, and (2) interpreting the findings of cohort studies at the level of individual risk (British Society of Audiology et al., 2024) when considering hearing loss as a risk factor for dementia. It is, however, important to note that a sensitivity analysis in which the one study analysing data from Oceania was removed revealed that HRs did not substantially differ by continent. Thus, the present findings may only partially support such emerging discussions.

While the mechanism accounting for the relation between hearing loss and dementia incidence is yet to be elucidated, current hypotheses considering this relationship may shed light on the mechanism behind the observed findings. First, all pooled HRs were consistent with the presence of hearing loss increasing the risk of incident dementia. This degree of consistency, regardless of the variability in the continent from which the data were obtained, could suggest that a common factor present across all analysed populations contributes to the relation between hearing loss and dementia. This is perhaps consistent with the common cause hypothesis, which postulates that a common pathology gives rise to both hearing loss, by affecting the cochlea and ascending auditory pathways, and dementia, by affecting the cortex (Griffiths et al., 2020). Specifically, some evidence suggests that deficits in key neurobiological mechanisms implicated in the pathology of dementia, including amyloid-β accumulation, mitochondrial dysfunction, neuroinflammation, and oxidative stress (Zhang et al., 2024), are observed globally across populations (Nichols et al., 2023). As such a potential common factor may be a neurobiological mechanism. Alternatively, some propose that the impoverished auditory input, resulting from impaired auditory function, may indirectly lead to reduced socialisation and communication (Griffiths et al., 2020), which is asserted to be an independent risk factor for dementia (Wang et al., 2023), and thus may moderate the relationship between hearing loss and dementia. Interestingly, in a recent analysis of the National Health and Aging Trends Study, Tianxue et al. (2025) observed that social isolation increases dementia risk across all racial and ethnic groups assessed; thus, potentially implicating social isolation as a common factor leading to hearing loss increasing the risk of dementia incidence regardless of the continent from which the data were obtained.

However, the finding that the magnitude of the HR may slightly vary by the continent from which the data are obtained suggests that factors which differ across countries/continents may also influence this relationship. Returning to the common cause hypothesis, additional evidence suggests that the increased risk of AD incidence associated with $PM_{2.5}$, a particulate matter strongly implicated in triggering of neuroinflammation and oxidative stress states, is approximately two times greater in black women compared to white women (Younan et al., 2022). Thus, a common pathological cause may not only drive commonalities in the observed HR but may influence the degree of variability seen across HRs. Moreover, there are a multitude of potential social, economic, and cultural factors that differ across continents which may influence the relation between hearing loss and dementia. However, most studies included in this review did not consider factors that moderate this relationship, thus leaving it problematic for us to speculate on these factors and whether they vary across continent. Therefore, further research investigating factors that moderate the relation between hearing loss and dementia across different continents is required to appropriately inform the hypothesised mechanisms.

A test of subgroup differences can be used to explore sources of heterogeneity in the results of individual studies included in a meta-analysis, however, critically one cannot assume causality from such analyses (Cuijpers et al., 2021). In the context of the present study, the test of subgroup differences indicated that the HR may differ by continent. However, we cannot infer that the continent caused such differences. Rather, it is possible that the differences observed by continent are driven by alternative confounding variables not accounted for in this analysis, such as methodological differences in the way the relationship between hearing loss and dementia incidence was estimated or how samples were recruited. The adjustment factors applied to the included studies varied substantially with some studies adjusting only for age and other studies applying complex adjustments for multiple concurrent health conditions. While we did observe a difference in HR between studies that adjusted for comorbid conditions and those that didn't, the adjustment structures applied did not appear to differ at the level of continent, rather studies from all continents applied maximal adjustment factors. Therefore, it is unlikely that the observed difference at the level of continent are due to methodological differences in the adjustment sets. However, the subgroup difference between studies that adjusted for comorbidity and those that didn't suggests that comorbidity could be an important confounder in the relationship between hearing loss and dementia. Therefore, where epidemiological studies intend to infer causal conclusions about the relationship between hearing loss and dementia, we recommend that they consider adjustment sets carefully and distinguish between confounders and mediators (Textor et al., 2016).

The findings obtained here are only partially congruent with prior evidence. In an exploratory analysis, Jiang et al. (2024) also observed that the magnitude of the HR differed when studies were stratified by continent. However, whilst we observed the magnitude of the HR to be highest in Oceania and the smallest in Asia, Jiang et al. (2024) observed the HR to be the highest in Asia and the smallest in Europe. The discrepancies between these findings may in part be due to fundamental differences in the meta-analyses conducted. Whilst we conducted separate meta-analyses based on the exposure variable (i.e. binary hearing loss, categorised hearing loss and continuous hearing loss) Jiang et al. (2024) included all studies regardless of differences in the exposure in the same analysis. Moreover, Jiang et al. (2024) included fewer studies in their sensitivity analysis considering continent ($n = 21$) than we included in our study. Moreover, in a sensitivity analysis in which the one study analysing data from Oceania was removed, we observed that the HR did not differ by continent. The discrepancies between the present study and Wang et al. (2023) suggest the need for additional analyses that draw on alternative data, for example case-control studies, to further inform our understanding of whether HRs for the relationship between hearing impairment and dementia differ by continent and, if so, the pattern of differences.

Our findings provide important implications at the continent level. However, it remains unclear whether both country and ethnicity play a role in the relation between hearing loss and

dementia risk. Various risk factors for dementia, including hypertension, obesity, diabetes, and sleep disorders, interact differently with different ethnicities which may be due to a combination of genetic, environmental, and socio-cultural factors (Mukadam et al., 2023). Considering hearing loss, Brenowitz et al. (2019) observed that the association between risk of dementia and hearing impairment is lower in white women compared with black women and white and black men. Moreover, Möller et al. (2024) observed that the association between risk of dementia and hearing loss varied slightly across Europe with the risk being highest in Southern Europe, followed by Western then Eastern Europe. Similarly, Walsh et al. (2022) found that risk of dementia incidence attributed to hearing impairment was greater in the North than in the South of China. This suggests that the level of continent may be too broad and perhaps non-specific enough, and so additional studies that focus on variance at the level of country and ethnicity are required.

Studies included in this systematic review and meta-analysis employed multiple different outcome variables, namely incident all-cause dementia ($n = 45$), Alzheimer's disease dementia ($n = 7$) and vascular dementia ($n = 4$). Consistent with our primary findings, hearing loss was associated with an increased HR for Alzheimer's disease (HR = 1.32 [1.11–1.58]), and the magnitude of the HR varied by continent. However, the trend observed was different compared to our primary findings, with the HR magnitude being highest in North America and lowest in Europe. For vascular dementia, while all HRs were consistent with a positive relationship, estimates were imprecise leaving it uncertain whether hearing loss increases vascular dementia incidence risk ($p = 0.39$). These findings suggests that caution should be applied when generalising pooled HRs to specific dementia subtypes, and that further research exploring hearing loss as a risk factor for alternative dementia subtypes, such as Parkinson's disease dementia and dementia with Lewy bodies for example, are required.

These findings may have clinical and global public health messaging implications. While there may be a small degree of variability in the magnitude of the relationship between hearing loss and dementia incidence between continents, across all studies the presence of hearing loss (any hearing loss vs. none) was associated with an increased HR of incident dementia. This suggests that the relationship between hearing loss and dementia is important across the globe and should be considered in population-level dementia risk reduction strategies globally. These findings also further support current movements to consider hearing impairment in the clinical management of dementia. Moreover, the small degree of variability in the magnitude of the relationship between hearing loss and dementia between continents is unlikely to be clinically significant, thus potentially indicating that the consideration of hearing loss in the clinical management of dementia could be beneficial globally.

This review has several strengths. First, as this meta-analysis sought to synthesise evidence from across the globe, we did not restrict the analysis to articles in the English language. Thus, ensuring non-English language articles were not omitted. However, as we did not specifically search non-English language databases, such as Index Medicus for the Eastern Mediterranean Region, Index Medicus Afro and KoreaMed (Walpole, 2019), there may still have been non-English language studies that were not captured. Second, we only included studies which adjusted for the confound of age at a minimum in the meta-analysis. Given that age is one of the largest risk factors for dementia and hearing loss, by controlling for this, we can be reasonably confident that the pooled HR across the whole sample, and individual continents, is not confounded by the age of the cohort and hence that hearing loss is a risk factor independent of age.

The present study is not without limitations. First, due to data availability, studies were grouped at the level of the continent from which data were collected. However, substantial variability, in relation to health and lifestyle factors, occur across countries within a continent. This potentially reduces the ability to draw strong theoretical and mechanistic implications from the analysis. Therefore, future studies should consider grouping studies according to lifestyle, health status or genetic factors alongside methodological features, such as study design and measurement methods, to explore the mechanism by which measures of association vary. Furthermore, studies from only four of the seven continents, North America, Europe, Asia, and Oceania, were obtained in our search, with a higher number of studies from high income countries within each continent. This may indicate that more research is other continents. This may in part be due to only prospective/longitudinal studies by design being included in this review. Alternative study designs have been used to investigate the association between hearing impairment and dementia risk in other continents (e.g Cyrille et al., 2023), however there is a need for future cohort studies to be conducted with these populations. Second, whilst our systematic literature search identified many studies, the identified studies were methodologically heterogeneous. Heterogeneity was in part addressed by conducting separate meta-analyses by the exposure variable. However, moderate to substantial residual heterogeneity, beyond the variability accounted for by cohort continent, was still observed (see Figures S2 and S3, Supplementary Materials Figure S1 and Table S5). Prior meta-analyses have observed that the length of follow-up, adjustment for covariates, the severity of hearing loss, and age and gender proportion at baseline do not moderate the relationship between hearing loss and incident dementia (Yu et al., 2024). It is, however, possible that alternative methodological factors, such as the method of identification of hearing loss (e.g. self-report, PTA and digit triplet test), may be contributing to this residual heterogeneity. Consequently, future studies which aim to systematically investigate the influence of the method of hearing assessment, and other methodological facets, on the relationship between hearing loss and dementia incidence are required.

Conclusion

Findings indicate that the association between hearing loss and incidence of dementia is consistent globally. However, the magnitude of the relationship may vary slightly by continent. Thus, caution should be exercised when generalising cohort-level findings specifying this relationship to other populations and individuals.

Author contributions

MRR: Conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, visualization, writing—original draft. **JL:** Conceptualization, data curation, investigation, methodology, writing—original draft, review & editing. **ID:** Data curation, writing- review & editing. **SR:**

Conceptualization, formal analysis, investigation, methodology, software, writing—review &editing. **LW:** Data curation, writing- review & editing. **MP:** Funding acquisition, writing- review & editing. **CJP:** Conceptualization, investigation, methodology, software, supervision, writing—review & editing. **CG:** Conceptualization, funding acquisition, supervision, writing—review & editing.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This independent research is funded by the National Institute for Health and Care Research Applied Research Collaboration North West Coast (ARC NWC). The views expressed in this publication are those of the author(s) and not necessarily those of the National Institute for Health and Care Research or the Department of Health and Social Care. This research was also supported by an NIHR undergraduate internship scheme awarded to MR, MP, and CG as supervisors. MR and MP are funded by NIHR/Alzheimer Society DEMCOMM fellowships. LW is funded by the ESRC [Grant number ES/P000665/1] and JL and CJP are funded by the National Institute for Health and Care Research Manchester Biomedical Research Centre [Grant number NIHR203308].

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