Hearing loss and the risk of dementia in later life

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ABSTRACT

Dementia is a major source of disability worldwide and there are currently no available disease-modifying treatments. Hearing loss may be associated with increased risk of dementia in later life and therefore could be a modifiable risk factor, given the availability of efficacious interventions. We investigated the association of hearing loss and dementia through two complementary approaches: a prospective, cohort study of 37,898 older men (mean age 72.5 ± 4.6 years) with a mean follow-up of 11.1 years, and a systematic review and meta-analysis of prospective studies. In our cohort, men with hearing loss were more likely to develop dementia (n = 6948, 18.3%) than men free of significant hearing impairment – adjusted hazard ratio 1.69, 95% CI = 1.54–1.85. In our review, the aggregated hazard of dementia was 1.49 (95% CI 1.30–1.67) in those with hearing impairment (14 included studies). Study quality, duration and dementia type did not alter the results considerably. We found an increased risk of incident dementia with hearing impairment in both our novel data and the meta-analysis. This is an important finding, particularly in light of recent suggestions that mid-life hearing loss may account for up to 9.1% of dementia cases worldwide, and efforts to reduce its impact should continue to be explored.

1. Introduction

Dementia is a leading cause of disability worldwide and affects approximately 6.5% of the population over the age of 65 [1,2]. There are, unfortunately, no current disease-modifying treatments available for people with dementia and a focus on risk factor reduction, particularly modifiable ones, is justified [3]. In fact, evidence is emerging of declining dementia incidence thought to be secondary to societal changes and improvements in living conditions and management of vascular risk [2]. This is encouraging, but as the world's population continues to age the number of people living with dementia is expected to increase and will put increasing demands on health services across the world [4].

Hearing impairment is a significant health issue with the World Health Organisation estimating that 5.3% of the global population suffers from disabling hearing loss [5]. The risk of hearing loss increases with age (age-related hearing loss – ARHL) and is estimated to affect up to 40% of those over the age of 65 [6] and in as many as 75% in those older than 80 years [7]. Age-related hearing loss is usually progressive, bilateral and leads to a reduction in one's ability to communicate. The aetiology is often multifactorial with a variety of environmental, medical and genetic determinants [8]. Untreated hearing loss can undermine a person's lifestyle and contribute to social isolation, loss of self-esteem, reduced quality of life and increased risk of psychiatric illness [9,10]. Management of ARHL is relatively straight-forward but hearing aids are expensive and only around a third of those who may benefit from hearing aids actually purchase them, but a significant proportion of these do not utilise them correctly [11].

Hearing loss has fairly recently been proposed as a risk factor for dementia [12] but the mechanisms linking hearing loss to dementia have not been established. Hearing loss may accelerate existing but subtle cognitive impairment by increasing cognitive burden and

exhausting existing cognitive compensatory strategies [13]. Hearing loss could contribute to increase social isolation leading to poorer lifestyle practices (e.g. smoking, obesity, alcohol abuse) and increasing depressive symptoms [14]. It could also lead to volume loss in the auditory cortex and other areas of the brain and disrupt the integrity of central auditory white matter tracts and cortical reorganisation [15,16]. Further, hearing impairment appears to accelerate brain atrophy in the superior, middle and inferior temporal gyri and para-hippocampus, areas of the brain commonly implicated in Alzheimer's disease [15]. Lastly, histopathological changes (degeneration, plaques and tangles) of the auditory system have been described in the brains of people with Alzheimer's disease [17].

It is important to clarify if hearing loss contributes to cause dementia, as efficacious management is widely available and could lead to a decline in the incidence of dementia among those at risk. Data from cross-sectional and case-control studies generally support the association between ARHL and cognitive impairment but the direction of causality is difficult to establish from these studies. For example, does hearing loss increase the risk of cognitive impairment or is cognitive impairment over-diagnosed in those with hearing impairment? Could they simply be two common overlapping conditions associated with increasing age [18]? The best way to establish a causal relationship between ARHL and dementia would be through sufficiently powered randomized controlled trials, but clearly this is not feasible or practical in this population. Therefore, the next best approach is to examine the association of ARHL with incident dementia through large prospective cohort studies in populations free of dementia at baseline.

The aim of the present study was to investigate the association between hearing loss and incident dementia in the older age demographic that is at highest risk for both of these conditions. In order to examine our hypothesis that hearing impairment increases the risk of developing dementia in later life, we used two complementary approaches. First, we undertook a prospective, longitudinal study in a large cohort of older, community-dwelling men recruited as part of the Health in Men Study (HIMS) [19]. Second, we performed a systematic review and meta-analysis of relevant prospective studies investigating the association between hearing loss and incident dementia.

2. Methods

2.1. The health in men study

2.1.1. Study population

The HIMS recruited a community-representative sample of older Australian men living in the metropolitan region of Perth, Western Australia, between April 1996 and November 1998 [19]. The follow-up of participants for the current study closed on 31 December 2013.

We used the electoral roll (voting is compulsory in Australia) to retrieve the contact details of 49,801 men aged 65–85 years in the mid 1990s (1996–1998–wave 1). Of these, 1839 had died by the time the study started and another 9482 were not selected because they were living outside the Perth metropolitan region. Of the remaining 38,480 men, 307 were excluded because they were younger than 65 years (these men were invited in error), and a further 275 because they had a recorded diagnosis of dementia (see below), leaving a total study sample of 37,898 older men without dementia.

The Ethics Committees of the University of Western Australia and of the Department of Health of Western Australia approved the study procedures. Similarly, the Legal Data Custodian of Western Australia approved the conduction of the study – the Data Custodian is responsible for ensuring that all data are de-identified and used for the purposes of the approved medical research only. In addition, the Legal Data Custodian is responsible for ensuring that named investigators alone have access to the data.

Table 1

Clinical characteristics of a community-representative sample of older men without cognitive impairment and with hearing loss (data retrieved between 1996 and 1998).

		Population N = 37,898 n (%)	Hearing loss N = 1420 n (%)	Odds Ratio (95% CI)
Age (years)	65–69	13,359 (35.2)	297 (20.9)	1 (Reference)
	70–74	13,048 (34.4)	463 (32.6)	1.61 (1.40, 1.88)
	75–79	8604 (22.7)	441 (31.1)	2.38 (2.05, 2.76)
	≥80	2887 (7.6)	219 (15.4)	3.61 (3.02, 4.32)
Cardiovascular diseases		16,688 (44.0)	829 (58.4)	1.82 (1.64, 2.03)
Cancer (except of the skin)		6774 (17.9)	322 (22.7)	1.36 (1.20, 1.55)
Chronic respiratory diseases		8096 (21.4)	414 (29.1)	1.54 (1.37, 1.73)
Gastrointestinal diseases		18,535 (48.9)	846 (59.6)	1.57 (1.41, 1.74)
Renal diseases		774 (2.0)	48 (3.4)	1.72 (1.28, 2.32)

95% CI: 95% confidence interval of the odds ratio.
Cardiovascular diseases: included recorded medical history of myocardial infarction, angina or stroke.

2.1.2. Outcome measure: dementia

Dementia was the primary outcome of interest of the study. We used the Western Australian Data Linkage System (WADLS) to retrieve relevant clinical information about participants. Briefly, WADLS links health service data from inpatient and outpatient mental health services, hospital morbidity data, community aged care services, as well as cancer and death registries [20]. WADLS uses the International Classification of Diseases (ICD) system for the coding of clinical diagnoses and procedures: ICD-8 from 1st January 1966 to 31st December 1969, ICD-9 from 1st January 1970 to 30th June 1999, and ICD-10 from the 1st July 1999. WADLS records also show the date when the occasion of service started and finished.

We used the following codes to establish the diagnosis of dementia among participants: ICD-8 code 290; ICD-9 codes 290, 294.1, 294.2, 331.0, 331.1, 331.2, 331.82; ICD-10 codes F00-F03, G30, G31.0, G31.1, G31.83. As indicated before, men with a diagnosis of dementia prior to the date of enrolment (1996–1998) were excluded from this study.

2.1.3. Exposure: hearing loss

We used WADLS to retrieve information about diseases of the ear leading to hearing loss among participants according to the following codes: ICD-8 and ICD-9 codes 388.12 (hearing loss induced by noise), 388.2 (unspecified sudden hearing loss), 389 (hearing loss, conductive or sensorineural); ICD-10 codes H90 (conductive and sensorineural hearing loss) and H91 (hearing loss due to other causes).

2.1.4. Other study measures

We also retrieved from WADLS data on cardiovascular events, cancers (except skin cancer), chronic respiratory diseases, gastrointestinal and renal diseases using the following codes:

– cardiovascular diseases ICD-8 and 9 codes 390–398, 401, 402, 403, 404, 410–429, 430–434, 436–438, 440–448, and ICD-10 codes I00-09, I10, I11, I12, I13, I20-51, I60-69, I70-78;
– cancers ICD-8 and ICD-9 codes 140–209, and ICD-10 codes C00-C97;
– respiratory diseases ICD-8 and ICD-9 codes 490–496 and 507–519, and ICD-10 codes J00-09, J20-39, J40-47 and J60-99;
– gastrointestinal diseases ICD-8 and ICD-9 codes 520–537, 540–543, 5550-553, 555–589, and ICD-10 codes K00-K99;
– renal diseases ICD-8 and ICD-9 codes 580–589, and ICD-10 codes N00-07, N17-19 and N25-27.

We calculated the age of participants (in years) by subtracting the date of birth from the date of enrolment into the study.
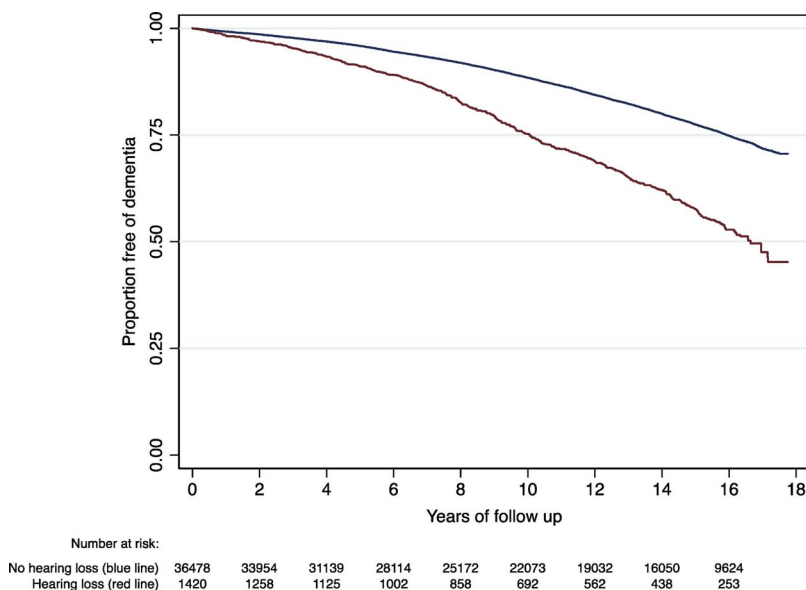
Fig. 1. The figure shows the proportion of participants who remained free of dementia during follow up according to the presence of a recorded diagnosis of hearing loss. The sub-hazard ratio of dementia associated with hearing loss was 1.69 (95% CI = 1.54, 1.85). These results were statistically adjusted for the effects of age and prevalent recorded history of cardiovascular diseases, chronic respiratory diseases, diseases of the digestive system and kidneys, as well as cancer. Men who received a diagnosis of hearing loss during follow up acted as controls until that point and as cases thereafter. The models included death as a competing risk.

Table 2
Hazard of dementia according to chronicity of hearing loss.

Time from diagnosis of hearing loss to dementia	Hazard Ratio (95% CI)
> 5 years	1.84 (1.41–2.41)
5–10 years	1.34 (1.02–1.76)
10–15 years	1.62 (1.30–2.01)
15–20 years	1.60 (1.31–1.94)
20–25 years	1.69 (1.42–2.02)
> 25 years	1.92 (1.42–2.59)

95% CI – 95% confidence interval of the hazard ratio.
All analyses adjusted for effects of age and prevalent recorded history of cardiovascular diseases, chronic respiratory diseases, diseases of the digestive system and kidneys, as well as cancer.

2.2. Systematic review and meta-analysis

2.2.1. Study selection

We conducted a comprehensive literature search of the PubMed, PsychINFO and Embase databases from inception to 31 August 2017. We searched only published material, although study authors were contacted where clarification of published data was required for the purposes of the meta-analysis. Additional studies were sought from article reference lists, review articles and conference abstracts.

We used the following search terms and strategy: (Alzheimer OR dementia OR "cognitive impairment") AND ("hearing loss" OR "hearing impairment" OR "hearing dysfunction" OR "hearing disorder" OR deaf OR deafness) AND (prospective OR longitudinal OR incident OR incidence OR cohort).

We limited our search to English peer-reviewed publications. Only studies reporting a prospective association of hearing loss with dementia (i.e. free of dementia at baseline) were included and those that had a valid outcome measure of risk e.g. risk ratio (RR), odds ratio (OR) or hazard ratio (HR). Potentially eligible studies were rated for quality in six areas: (1) the assessment of exposure (hearing) was objective i.e. through direct testing (yes/no), (2) the diagnosis of dementia was made through direct clinical contact (yes/no), (3) confounding was taken into account (yes/no/uncertain), (4) the statistical analysis was appropriate (yes/no/uncertain) and (5) other sources of bias were considered in the analysis of the data; e.g. selection bias, unacceptable loss to follow-up (yes/no/uncertain).

2.3. Statistical analyses

We used the statistical software Stata 15.0 (StataCorp LLC, 2017) to manage and analyze the data. Descriptive statistics summarized categorical variables as counts and proportions (%), and continuous variables as mean, range, and standard deviation of the mean (SD). We employed t-tests to compare the age of participants with and without hearing loss, and reported the t-statistic, the number of degrees of freedom (df) and p-value. We used logistic regression to investigate the odds of dementia in men with compared with those without hearing loss, and Cox regression to investigate the HR of dementia during follow up. As both hearing loss and dementia increase the risk of death, we used competing risk regression (with death as the competing outcome) to investigate the longitudinal association between hearing loss and dementia [21]. In these models, we split and joined time-span sets according to the diagnosis of hearing loss, so that men without hearing loss contributed data as controls until the time of diagnosis and as cases thereafter. We used age as the time scale in the Cox regression models in order to control as accurately as possible the effect of age on dementia and mortality [22]. In addition, we investigated and modelled the potential contribution of other measured factors on the risk estimates of dementia associated with hearing loss (i.e., prevalent cardiovascular diseases, cancer, chronic respiratory diseases, digestive and renal diseases). Alpha was set at 5% and all risk estimates were reported alongside their respective 95% confidence interval (95% CI).

We used the 'metan' command and random effects option of Stata for the meta-analysis. We included the individual study's measure of dementia risk (RR, OR or HR) and the 95% confidence interval (95% CI) of this effect. The outcome of dementia was binary in all studies apart from one study that included mild cognitive impairment (MCI) and dementia in one category due to low numbers of dementia [23]. Hearing loss was generally reported in a dichotomous manner (present/absent) but a number of studies reported this in terms of severity (normal, mild, moderate/severe). In the primary meta-analysis, we compared the risk of dementia for those with hearing loss compared to no hearing loss. If hearing loss was not reported in a binary manner, we used data comparing the risk of dementia in the most severely impaired category of hearing loss to normal hearing.

We subsequently performed a series of post-hoc analyses: studies that assessed hearing and dementia in an objective manner (i.e. 'good quality studies'), outcome of Alzheimer's dementia and analyses according to length of follow up (≥5 years and < 5 years). Summary data were presented as HR's and 95% CI. Heterogeneity between studies was
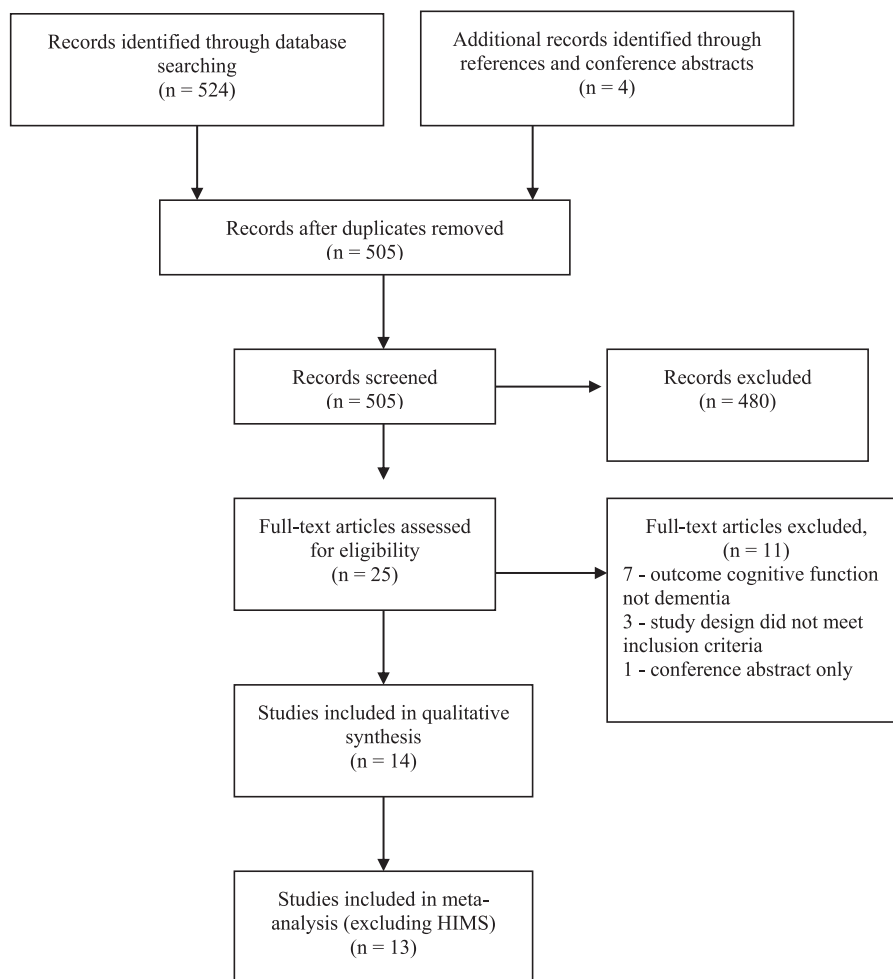
Fig. 2. Flow chart showing results of the literature search.

determined with the I-squared statistic. We used funnel plots to examine the risk of population bias.

3. Results

3.1. Health in men study

The mean age of the 37898 men included in the study was 72.5 years (SD = 4.6; range 65.0–85.7 years) with a mean follow up period of 11.1 (SD 5.4) years. Men with hearing loss were older than those without (74.4 ± 4.8 vs 72.4 ± 4.5; t = 16.17, df = 37896, p < 0.001). Table 1 summarizes the clinical features of the study sample and of men with recorded history of hearing loss (n = 1420, 3.7%). The prevalence of cardiovascular and respiratory diseases, cancer, as well as digestive and renal diseases was greater among men with than without hearing loss.

Men with hearing loss were more likely to develop dementia (n = 6948, 18.3%) over the follow-up period than men who were free of significant hearing impairment – adjusted HR 1.69, 95% CI = 1.54–1.85 (Fig. 1). We examined the effect of chronicity of hearing loss on dementia risk and, although the risk of dementia was consistently elevated, there was no consistent trend with increased length of exposure to hearing impairment (Table 2).

3.2. Systematic review

We identified 524 manuscripts from our search strategy. We added a further four manuscripts from manual searches and were left with 505

manuscripts after removal of duplicates. Fourteen papers met our inclusion criteria and 13 of these were suitable for meta-analysis (Fritze et al. [24] were excluded, as authors did not report 95% CI's for their data). This resulted in 14 separate data sets being available for the meta-analysis when our data from HIMS was included (Fig. 2).

Table 3 summarizes the characteristics of the 15 included studies involving 227,614 individuals of which 72,831 were included in the meta-analysis. The quality rating of the studies appears in Table 4.

3.2.1. Meta-analysis of primary outcome

The overall hazard of all-cause dementia for previously published studies was 1.38 (95% CI 1.23–1.53) in those with hearing loss compared to no reported/observed hearing loss (Fig. 3). The I^2 statistic was 18% (p = 0.262) indicating acceptable heterogeneity between the various studies. The hazard of dementia increased to 1.49 (95% CI 1.30–1.67) when we included data from HIMS (Fig. 4) but this also increased the statistical heterogeneity of the analysis (I^2 = 53%, p = 0.010).

3.2.2. Post-hoc analyses

Four studies assessed hearing via audiometry and had a clinical assessment of dementia (Fig. 5). The aggregated HR for dementia in these studies was 3.10 (95% CI 1.28–4.91) in those with hearing impairment compared to normal hearing. Five studies specifically reported the incidence of Alzheimer's type dementia with hearing loss (Fig. 6). Overall, the effect was essentially unchanged from that of all-cause dementia (HR 1.36, 95% CI 1.05–1.66).

Length of follow-up varied in the included studies (mean range

Table 3
Summary of included prospective cohort studies.

Study (country)	Participants	Auditory assessment	Diagnosis of dementia or cognitive impairment	Follow-up	Main results (all adjusted for relevant confounders)	Limitations
Davies et al. [31] (UK)	≥50 years, male and female, n = 8780. English Longitudinal Study of Ageing cohort.	Self-reported hearing impairment. Three groups of hearing impairment – normal, moderate and poor.	Dementia – physician diagnosis as reported by participants or informants. Taking medication.	Mean = 11 years	269 incident cases. HR 1.39 (95% CI 1.01–1.92) in moderate and HR 1.57 (95% CI 1.12–2.02) in poor compared to normal group. Adjusted for various lifestyle and clinical factors	Self-reported physician diagnosis of dementia and hearing impairment. Low incidence of dementia compared to population estimates. Attrition bias mentioned but numbers lost not stated.
Deal et al. [28] (USA)	Age 70–79, both male and female, n = 1889. Community-dwelling cohort of Medicare enrolees	Pure-tone air conduction audiometry. Normal, mild, moderate/severe.	Dementia – taking medication, hospital records, decline of > 1.5 SD on 3MS cognitive test.	9 years	229 incident cases. HR 1.02 (95% CI 0.75–1.40) for mild, HR 1.55 (95% CI 1.10–2.19) for moderate/severe compared to normal. Adjusted for age, sex, race, education, study site, smoking, hypertension, diabetes and stroke	Hearing assessment completed only once 4 years after study initiated. No data on loss to follow up.
Fischer [33] (2016) (USA)	Male and female, mean age 66.7, n = 1884. Population-based cohort, Epidemiology of Hearing Loss Study	Audiometry.	MMSE < 24 or self or proxy reported history of dementia or Alzheimer's.	10 years	187 incident cases. HR 2.11 (95% CI 1.3–3.4) of cognitive impairment for those with baseline hearing impairment (adjusted for age, sex and education). HR 2.09 (95% CI 1.29–3.39) fully adjusted.	Panel data – assessed every 5 years. 258 people died and 1470 (78%) participants available at 10-year follow up.
Fritze et al. [24] (Germany)	154,783 people from health insurance database. Age 65 plus at study entry	ICD coding consistent with hearing loss.	ICD codes consistent with dementia	4 years	14,602 incident cases of dementia. HR 1.43 (p < 0.001) for dementia adjusted for age, gender, tinnitus, comorbidities, care level, institutionalization and depression.	No face-to-face assessment. No indication of severity or use of hearing aids. Loss to follow up uncertain.
Gallacher et al. [30] (Wales)	1612 men from Caerphilly Prospective Study cohort born between 1920 and 1939. Mean age 56.1 years at baseline.	Audiometry on two occasions average 8.6 years apart.	Clinician diagnosis of dementia according to accepted criteria and cognitive battery. Also CIND. Those lost to follow up were followed via medical and death records.	Mean 16.8 (1.1) years	79 cases of dementia. 146 of CIND. OR 2.67 (1.38–5.18) for all-cause dementia per 10 dB rise in pure-tone average threshold.	Panel data. Uncertain definition of hearing impairment. Only men. 1300 (80.6%) available for follow up but only 1050 (65.1%) were cognitively screened (others followed through health records).
Gates [34] (1996) (USA)	1509 men and women from Framingham Heart Study Cohort.	Synthetic Sentence Identification with Ipsilateral Competing Message (SSI-ICM) test	Assessment by neurologist and neuropsychologist and subsequent panel consensus diagnosis.	6 years.	RR 2.74 (95% CI 0.72–10.03) of dementia in those with bilateral hearing loss. Stronger association with severe hearing impairment – RR 12.48 (95% CI 2.69–57.82).	Low incidence of dementia (41 cases in whole sample but only 20 in those who underwent SSI-ICM (n = 821). Volunteer population.
Gates [35] (2002) (USA)	740 volunteers from Framingham cohort	Audiometry	Panel consensus diagnosis of dementia	Mean 9.7 years	40 cases of probable AD. RR 10.8 (95% CI 4.6–25.2).	Volunteers. Loss to follow up unknown.
Gates [36] (2011) (USA)	274 individuals from Adult Changes in Thought cohort. Mean age 79.6 (range 71–96)	Behavioural central auditory test – Dichotic Sentence Identification.	Neuropsychological assessment and consensus clinician diagnosis of dementia.	Mean 26.4 months (range 10–48 months)	23 incident cases dementia. HR 6.8 (95% CI 1.9–24.1) for all-cause dementia.	Small sample, short follow up. Sample were those within cohort who volunteered for hearing testing.? loss to follow up.
Golub [37] (2017) (USA)	1881 participants 65 years and older from Washington Heights-Inwood Columbia Ageing Project	Examiner determination of observed hearing loss (OHL).	Neuropsychological assessment and subsequent panel consensus diagnosis.	Mean 7.4 years.	377 incident cases. HR 1.69 (95% CI 1.3–2.3) for OHL vs no OHL.	No data on hearing aids. Subjective determination of hearing loss. Individuals with missing longitudinal data were excluded.
Gurgel [38] (2014) (USA)	4463 participants from Cache County Study on Memory, Health and Aging. Mean age 75.4 years (SD 6.9 years).	Examiner determination during assessment or self-report.	Clinical assessment and panel consensus.	Mean 4.32 (SD 4.1) years with baseline hearing loss and 6.08 (SD 4.1) years without.	575 incident cases. HR 1.27 (95% CI 1.03–1.56) of dementia for those with hearing loss.	Subjective diagnosis of hearing loss. No data on loss to follow up.
Heywood et al. [23] (Singapore)	1515 participants from the Singapore Longitudinal Ageing Study	Whispered Voice Test.	Neuropsychological and clinical assessment. Panel consensus diagnosis of MCI or dementia.	Median 3.8 years.	144 incident MCI and 11 dementia. HR 2.30 (95% CI 1.08–4.92).	Low incidence of dementia. No formal audiometry. Original cohort 2050 but reduced to 1515 as 227 died and 296 lost to follow up.
Lin et al. [29] (USA)		Audiometry via automated testing device.	Neuropsychological testing and consensus panel diagnosis of dementia.	Median 11.9 years	58 incident cases of dementia. HR 4.94 (95% CI 1.09–22.40) of dementia for	Relatively small sample size. Loss to follow up unknown.

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Table 3 (continued)

Study (country)	Participants	Auditory assessment	Diagnosis of dementia or cognitive impairment	Follow-up	Main results (all adjusted for relevant confounders)	Limitations
	639 participants of Baltimore Longitudinal Study of Ageing. Aged 36–90 years.				severe hearing loss. HR 3 (95% CI 1.43–6.3) for moderate.	
Lin et al. [15] (USA)	1626 individuals from Health ABC Study, mean age 77.4 years.	Audiometry via automated testing device.	Incident cognitive impairment defined as 3MS score of < 80 or decline of > 5 points from baseline.	6 years of follow up	609 incident cases. HR 1.24 (95% CI 1.05–1.48) of dementia for those with hearing loss.	Panel data. Hearing loss only measured at baseline. 1984 participants in original cohort but only 1626 had at least one follow up (358 presumably lost to follow up).
Su [39] (2017) (Taiwan)	4108 individuals with age-related hearing loss (ARHL) and 4013 controls extracted from a National Health Insurance Database. Mean ages 68.6 and 69 years respectively.	ICD-9 codes consistent with ARHL.	ICD-9 codes consistent with dementia.	2 years.	869 recorded cases of dementia. HR 1.29 (95% CI 1.13–1.48) for dementia in ARHL group compared to control.	No clinical assessment of dementia or hearing. Partial adjustment for relevant confounders. Loss to follow up not stated.
HIMS (Australia)	37898 community-dwelling men aged 65 years and older at baseline.	ICD-8 and ICD-9 codes consistent with hearing loss.	ICD-8 and ICD-9 coded for dementia of any cause.	Mean 11.1 (SD 5.4) years.	Adjusted HR 1.69 (95% CI 1.54–1.85) for dementia in those with hearing loss.	Low incidence hearing impairment in linked data. No clinical assessment of dementia. 9877 men available after 16 years. Competing risk analysis.

2–16.8 years). The summary HR was 1.58 (95% CI 1.34–1.82; $I^2 = 48.5\%$, p = 0.042) for those averaging over 5 years (Fig. 7) and HR 1.29 (95% CI 1.15–1.44, $I^2 = 0\%$, p = 0.566) in those less than 5 years in duration (Fig. 8). The funnel plot (Fig. 9) indicated that population bias and heterogeneity may have been an issue in the meta-analysis (all 14 studies included) with positive studies more likely to be published.

4. Discussion

We found a significant association between hearing loss and incident dementia in our prospective cohort of community-dwelling older men. The hazard of dementia increased by 69% (95% CI 54%–85%) in men with self-reported hearing impairment compared to those with normal hearing once age and medical conditions common in later life were taken into account. This result is largely consistent with previous longitudinal studies with a pooled HR of 1.49 (95% CI 1.30–1.67) in the meta-analysis for 14 studies. The duration of hearing loss and type of dementia did not appear to impact significantly on the findings.

There are a number of strengths and limitations worth highlighting. Our findings were drawn from a large community-representative sample (n = 37898) of older men at risk of developing dementia. We excluded prevalent cases of dementia and the period of follow up was over 11 years in total. Our analyses were adjusted for age and common diseases and we allowed for the competing risk of death in the statistical models (i.e., participants who die early cannot develop dementia). Exposure data were obtained from health records and under-diagnosis of hearing loss was most likely a problem [25]. This may explain the relatively low prevalence of hearing loss (3.7%) in our study compared with others [6] and with the World Health Organization estimates [5]. This could potentially have biased our results, with only the most severe cases of hearing loss being recorded in WADLS, in which case it would not be possible to generalize the findings of our study to the population of older people with mild to moderate hearing loss. The analysis of other observational studies suggests a dose-effect of the association between hearing loss and dementia, with higher risk being often linked to the most severe cases (Table 3). In addition, the cumulative incidence of dementia in our sample was comparatively high (18.3%), most likely because the duration of our follow up was substantially longer than that of other studies. The approach that we used in our study enabled us to maintain attrition to a minimum, as the migratory movement of this Western Australian age group is fairly limited [20] and we were able to track all deaths. Survivorship bias is a frequent concern in longitudinal studies, as those who are more frail are less likely to return for assessment [26]. In this case, the association between hearing loss and dementia could be weakened because of 'healthy participant bias'.

The restriction of the HIMS sample to men affects the generalizability of the findings, but it is difficult to imagine a mechanism by which gender would mediate the effect of hearing loss on the risk of dementia. Moreover, our results are in keeping with those of studies that included women. Lastly, we adjusted our analyses for age and common medical conditions, but residual confounding and confounding due to unmeasured factors (e.g., education) cannot be dismissed. We did, however, examine the effect of chronicity of hearing loss on dementia incidence and found no difference in longstanding hearing impairment (e.g. from childhood) as opposed to ARHL.

The systematic review that we completed as part of this study produced 14 other prospective cohort studies (n = 72,831 individuals) and provided a quantitative summary of the effect of hearing loss on incident dementia in diverse populations of both genders. The findings were consistent with our own data, although some statistical heterogeneity and publication bias (as indicated by the funnel plot) were apparent. Limiting the review to studies published in English was a further limitation. The findings are also consistent with recent systematic reviews and meta-analyses on this topic [12,27]. Livingstone and colleagues [12] included 13 prospective studies in their review and

Table 4
Quality rating of studies included in the systematic review.

Study	Audiometry testing		Direct clinical assessment of dementia or cognitive impairment		Valid measurement of confounding			Appropriate statistical analysis			Other source of bias		
	Yes	No	Yes	No	Yes	No	?	Yes	No	?	Yes	No	?
Davies et al. [31]		X		X	X			X					X
Deal et al. [28]	X			X	X			X				X	
Fischer [33] (2016)	X			X	X			X			X		
Fritze et al. [24]		X		X			X	X					X
Gallacher et al. [30]	X		X		X			X			X		
Gates [34] (1996)		X	X				X	X			X		
Gates [35] (2002)	X		X		X			X					X
Gates [36] (2011)	X		X				X	X					X
Golub [37] (2017)		X	X		X			X				X	
Gurgel [38] (2014)		X	X		X			X				X	
Heywood et al. [23]		X	X		X			X					X
Lin et al. [29]	X		X		X			X			X		
Lin et al. [15]	X			X	X			X			X		
Su [39] (2017)		X		X			X	X				X	
HIMS		X		X	X			X				X	

studyname	Hazard Ratio (95% CI)	% Weight
Davies_2017	1.57 (1.12, 2.02)	8.96
Deal_2017	1.55 (1.10, 2.19)	6.47
Fischer_2016	2.09 (1.29, 3.39)	1.92
Gallacher_2012	2.67 (1.38, 5.18)	0.60
Gates_1996	2.74 (0.72, 10.03)	0.10
Gates_2002	10.80 (4.60, 25.20)	0.02
Gates_2011	6.80 (1.90, 24.10)	0.02
Golub_2017	1.69 (1.30, 2.30)	7.51
Gurgel_2014	1.27 (1.03, 1.56)	19.40
Heywood_2017	2.30 (1.08, 4.92)	0.59
Lin_2011	4.94 (1.09, 22.40)	0.02
Lin_2013	1.24 (1.05, 1.48)	24.60
Su_2017	1.29 (1.13, 1.48)	29.79
Overall (I-squared = 18.0%, p = 0.262)	1.38 (1.23, 1.53)	100.00

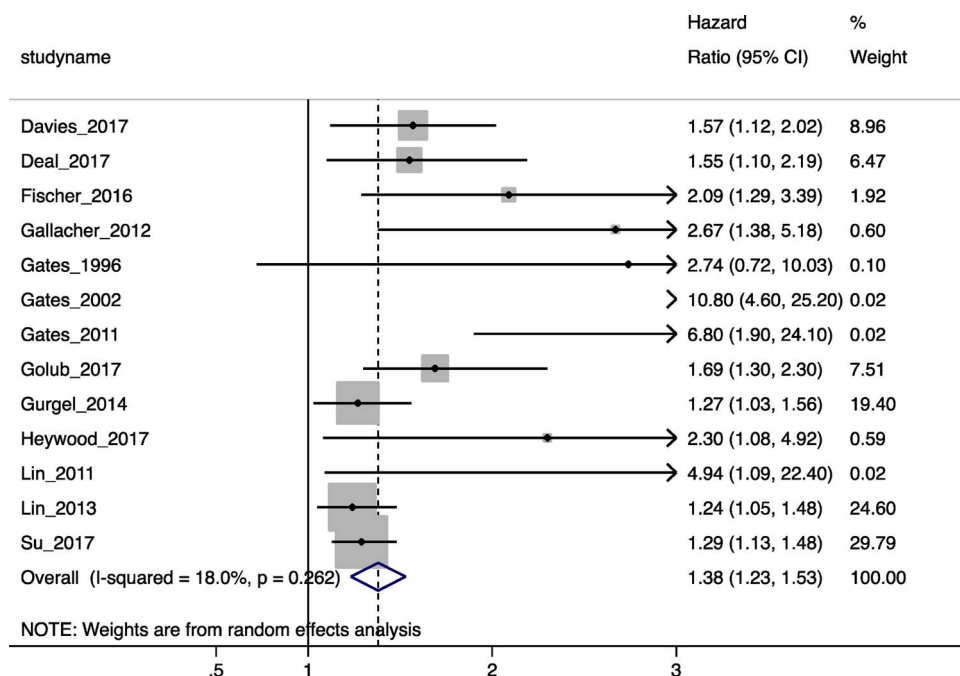NOTE: Weights are from random effects analysis.

Fig. 3. Forest plot showing hazard of dementia (and 95% confidence intervals) for those with hearing impairment compared to normal hearing.

found a positive association between even mild hearing impairment and incident dementia in 11 of the studies. They subsequently completed a meta-analysis on three of these studies [28–30] and found a pooled RR of 1.94, (95% CI 1.38–2.73) for dementia in those with hearing loss over 9–17 years of follow up. In addition, the same authors have proposed a life-course model of the contribution of risk factors from different phases of the life span to dementia and they estimate that around 9.1% of dementia cases could be attributable to midlife hearing loss.

The included studies in our review varied considerably in size, duration of follow up and recruitment. Methods used for assessment of hearing were fairly diverse with self-report, observations by researchers, health records and more robust audiometry being used. Assessment of dementia also varied with the use cut-off scores on cognitive tests, reported diagnoses, use of cognitive enhancing

medication, health records and in-person detailed clinical assessment. In order to account for this heterogeneity, we performed a series of post-hoc analyses and found similar results in studies that met a more stringent quality criteria. Dementia-type did not substantially change the findings of the meta-analysis (e.g., generic diagnosis of dementia/cognitive impairment or Alzheimer's disease), but the possible bias associated with the publication of studies with large positive effects raises concern that the overall impact of hearing loss on dementia risk may be currently overestimated. Finally, it is also important to consider that the use of observational data to ascertain causality has limitations. Hearing loss in later life could simply be another marker of increasing frailty and be a concurrent association rather than a true cause of dementia.

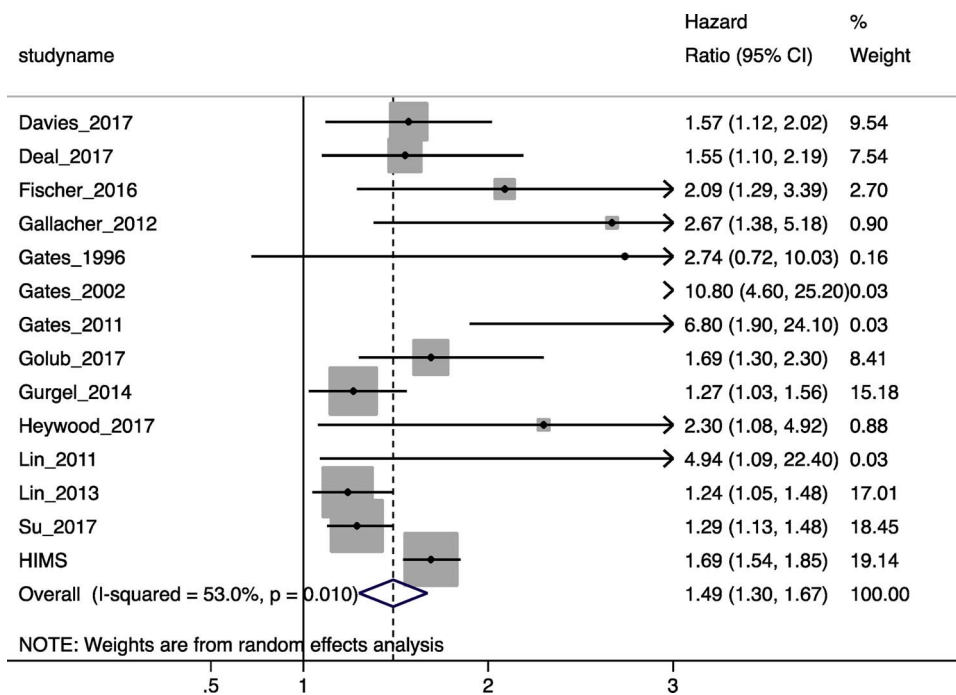The finding of increased dementia risk in association with hearing

Fig. 4. Forest plot showing hazard of dementia (and 95% confidence intervals) for those with hearing impairment compared to normal hearing, including data from HIMS.
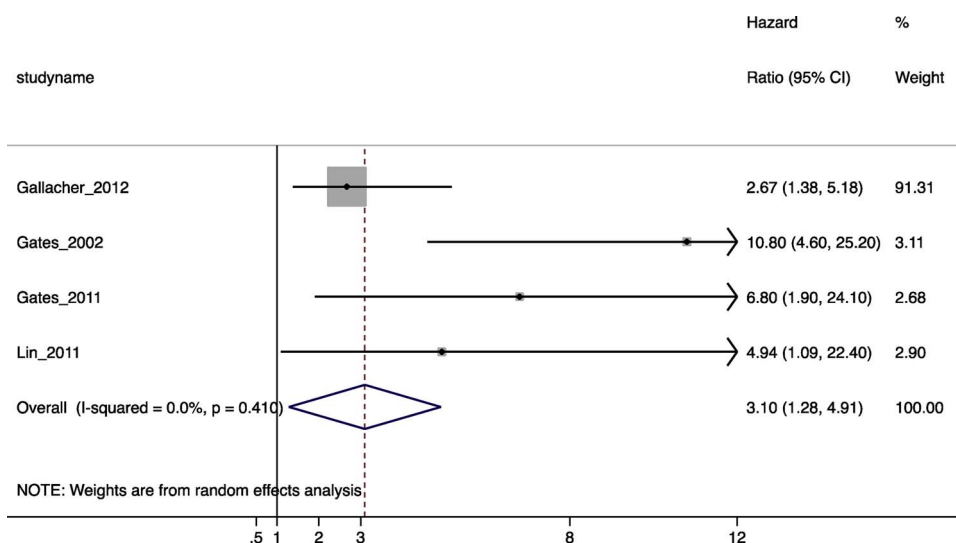

Fig. 5. Forest plot showing hazard of dementia (and 95% confidence intervals) for those with hearing impairment compared to normal hearing in studies that had robust measures of hearing and dementia i.e. 'good quality studies'.

loss is interesting and could have important public health implications, should future studies prove this link to be causal. One of the unanswered questions raised by our studies though is whether this effect may be modifiable in any way i.e. would hearing aids reduce risk or change the trajectory of cognitive decline. Davies et al. [31] studied 8780 individuals as part of the English Longitudinal Study of Ageing. Participants self-reported hearing performance in 2004/2005 and were assessed for dementia through to June 2015. Six and a half percent (n = 561) of the population reported using hearing aids and whilst the risk of dementia was higher in those with poor hearing (HR 1.57, 95% CI 1.12–2.02), this was not associated with an obvious change in the risk of dementia among those using hearing aids (HR 0.99, 95% CI 0.61–1.42). Participants did, however, rate their hearing when using the aids so this negative finding is not surprising.

Lin et al. [29], in another study, examined 639 individuals as part of the Baltimore Longitudinal Study of Aging and found a HR of 4.94 (95%

CI 1.09–22.40) for dementia in those with severe hearing loss compared to normal. In addition, they reported a univariate HR of 5.3 (95% CI 2.9–9.6) for dementia in those using hearing aids (9.9% of the sample) suggesting that this does not have much obvious effect on reducing dementia risk. Hearing was assessed via audiometry and was presumably done without hearing aids in place so this finding is perhaps not so surprising and is merely just an alternative measure of hearing performance. Nonetheless, these results raise concerns that the fitting of hearing aids may not substantially change the risk of dementia, in the same way that the use of antidepressants fails to modify the risk of dementia associated with depression [32]. Well designed randomized controlled trials targeting older people with hearing loss who are at risk of cognitive impairment are needed to determine if the link between hearing loss and cognitive impairment is causal and can be reversed with appropriate treatment.

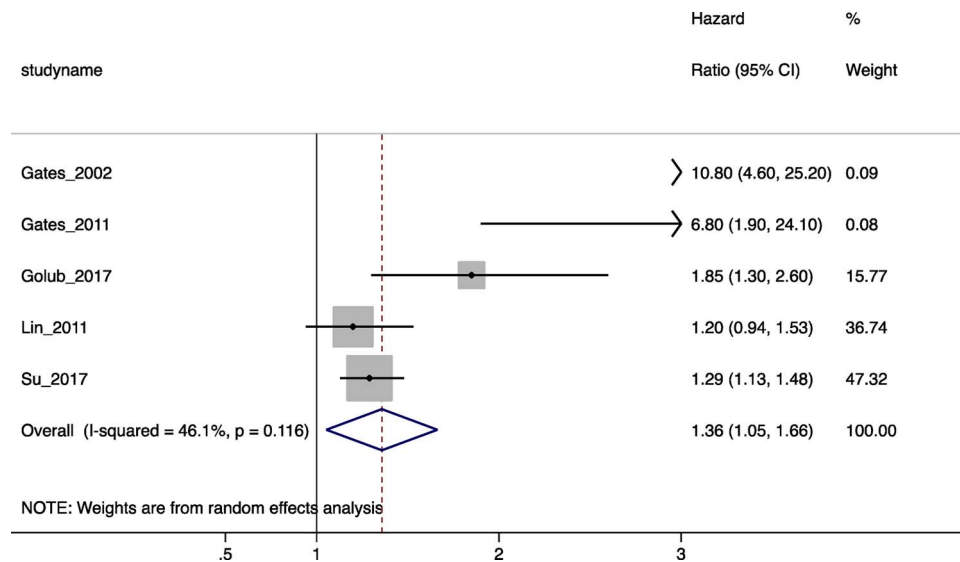In summary, we found a positive association between hearing

Fig. 6. Forest plot showing hazard of Alzheimer's type dementia (and 95% confidence intervals) for those with hearing impairment compared to normal hearing.
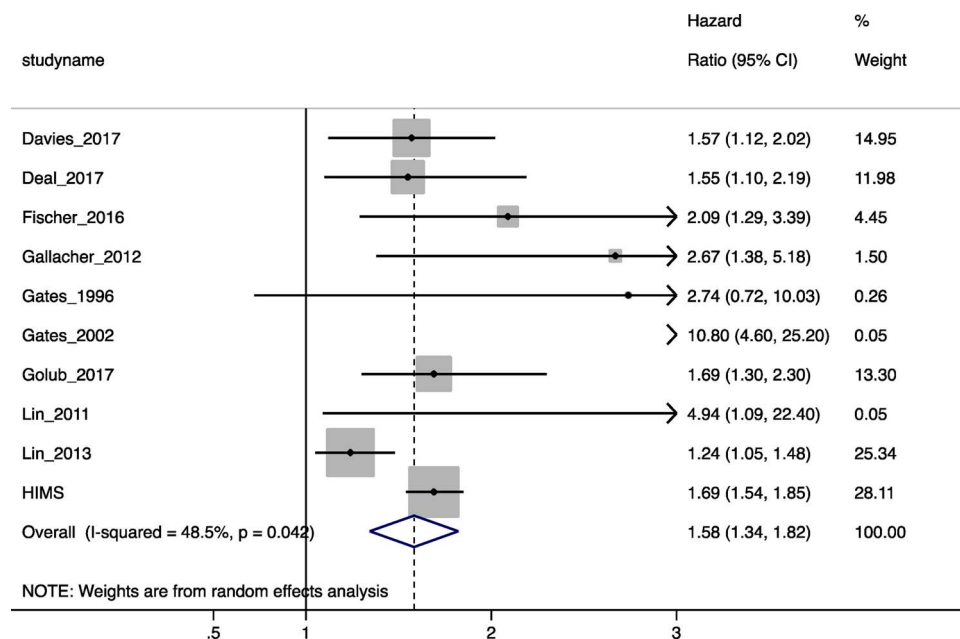

Fig. 7. Forest plot showing hazard of dementia (and 95% confidence intervals) for those with hearing impairment compared to normal hearing where the follow-up period of the study was on average at least 5 years.

impairment and incident dementia in both our longitudinal cohort of older men and in the meta-analysis of available prospective studies. Hearing loss is common and its risk increases with age, leading to a number of unwanted social and health consequences and reduced quality of life for the individual concerned. Whilst direct causality remains uncertain, the link between hearing and dementia seems plausible and efforts to reduce its impact should continue to be explored.

Contributors

Andrew H. Ford wrote the paper, performed the analyses and performed the literature review together with Osvaldo P. Almeida.

All authors contributed to data collection, study design and editorial review of the manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.
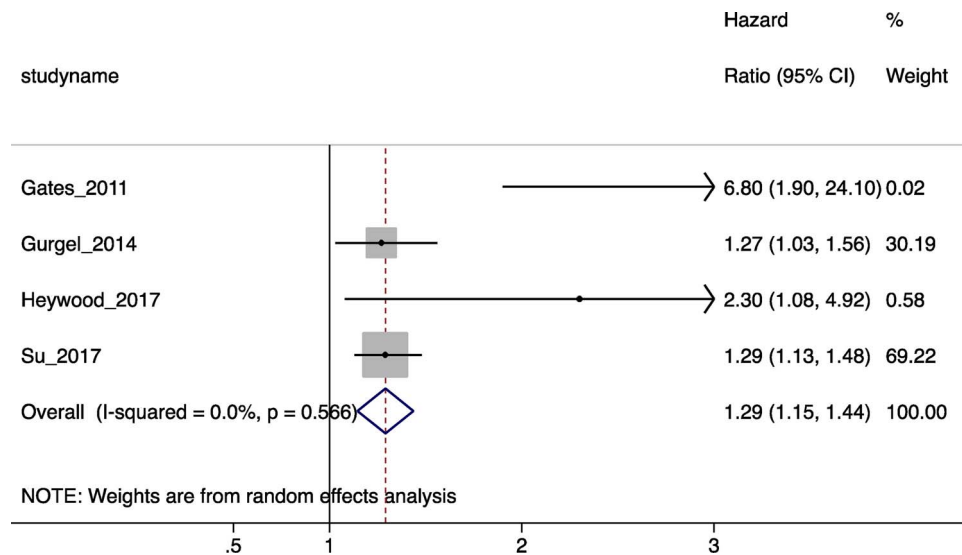
Funding

Fig. 8. Forest plot showing hazard of dementia (and 95% confidence intervals) for those with hearing impairment compared to normal hearing where the follow-up period of the study was on average < 5 years.
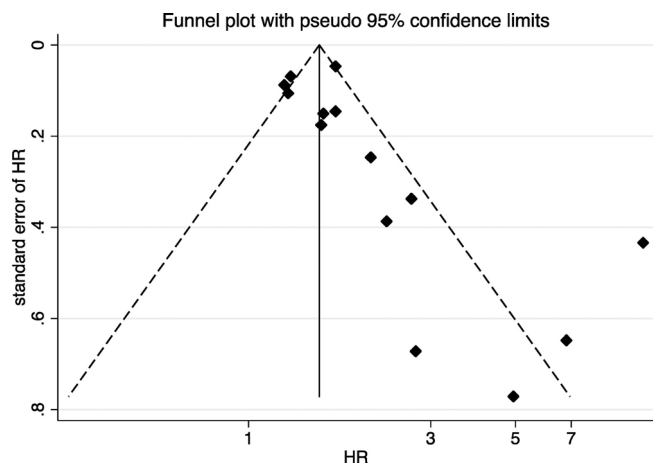

Fig. 9. Funnel plot showing the distribution of studies (diamonds) according to their hazard ratios and standard error of the hazard ratio.

Ethical approval

The Ethics Committees of the University of Western Australia and of the Department of Health of Western Australia approved the study procedures. Similarly, the Legal Data Custodian of Western Australia approved the conduction of the study – the Data Custodian is responsible for ensuring that all data are de-identified and used for the purposes of the approved medical research only. In addition, the Legal Data Custodian is responsible for ensuring that named investigators alone have access to the data.

Provenance and peer review

Peer review was directed by Margaret Rees independently of Leon Flicker (one of the authors and an Editor of *Maturitas*), who was blinded to the process.

Research data (data sharing and collaboration)

There are no linked research data sets for this paper. The authors do not have permission to share data.

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