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The Relationship between Hearing Impairment and Dementia in Primary Care: A Nested Case-Control Study

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ABSTRACT

Background: *Dementia is a major cause of morbidity and mortality in older persons, and it has socio-economic impact on the society. Globally, it is the fifth leading cause of mortality, and the prevalence has been projected to triple by 2050. There is increasing evidence of a link between dementia and hearing loss, but the direction of cause and effect, and strength of association is unclear. Therefore, a nested case control study within one of the largest available databases of primary care records in the UK was used to check the association between hearing impairment and dementia.*

Aim: *To estimate the proportion of exposure to hearing impairment in dementia cases and, to quantify the association by estimating the risk ratio. To establish whether the calculated risk ratio varies according to the timing of exposure from less than one month to over three years in cases compared to controls.*

Methods: *A Nested Case-Control study was used to investigate the association between dementia, and hearing impairment and other closely related hearing problems by following-up 137,270 incident cases of dementia with 450,704 matched controls by age and gender who were 50 years and above in the UK primary care setting. Conditional logistic regression was used for the unadjusted risk ratio while multiple conditional logistic regression analysis was used to find an independent association between hearing impairment and dementia.*

Results: *From the sample population, 25.7% of the cases and 23.9% of the controls were exposed to hearing impairment. There was a 10% (RR=1.10, 95% CI=1.08-1.12) increased risk of dementia after exposure to hearing impairment and this risk was greatest within four weeks of exposure (RR=1.68, 95% CI=1.52-1.85). However, the association was confounded by referral to ENT.*

Conclusion: *This study shows that hearing impairment could precedes the development of dementia, and it could increase the risk of dementia by 10%, but this link is greatest within a month of exposure to hearing impairment. Consequently, hearing impairment could be an indicator to screen for before the development of dementia.*

Keywords

Dementia, Hearing loss, Nested case control, Primary care data, Incidence density sampling.

Introduction

Dementia is a condition that affects the brain, and it is characterised by a decline in cognitive ability such as memory, executive functions, attention, language, psychomotor speed, visuoperceptual or visuospatial abilities. Notably, cognitive impairment is not part of the normal ageing process, and it substantially interferes with a person's performance of the activities of daily living (ADL) [1].

Globally, about 46.8 mllion people live with dementia, and it has projections of 74.7 million by 2030 and 131.5 million by

2050 [2]. This condition also impacts negatively on caregivers, families, and societies through its physical, psychological, and economi consequences [3]. In 2017, deaths secondary to dementia accounted for 4·4% (CI=4.4– 4.5) of total deaths. Dementia ranks as the sixth leading cause of deaths (2.5 million deaths, CI=2.4-2.5), but the second in adults age 70 and above (2.3 million deaths, CI=2.3-2.4) [4,5]. In the UK, the age-standardised prevalence of dementia was 7.1% among adults age 65 and over, equivalent to a total of 815,827 people living with dementia [4]. Likewise, the annual cost of dementia is 26.3 billion pounds [5].

The aetiology of dementia is not well known, but there are several identified modifiable and non-modifiable risk factors. There is an increased risk of dementia in adults above 65 years, females, and the presence of APOE3/4 genes [6]. Traumatic head injury is associated with a three-fold increased risk of dementia [7]. Among the established modifiable risk factors are lower education attainment and hypertension. The other modifiable risk factors of dementia are vascular diseases, senile cataract [10], and severe mental health problems [11].

Notably hearing impairment affects 17% of the UK population (11 million). The prevalence of hearing loss increases with increasing age; it affects about 40% of those over 50 years and 70% of those over 70 years [12]. Both hearing loss and dementia are gradually progressive, with an increasing prevalence from the age of 65 and above. There is evidence of an increased prevalence of hearing loss (60%) in older people with cognitive impairment [13]. Conversely, in people with severe hearing impairment and profound hearing impairment, the prevalence of dementia is 73% and 65%, respectively [14]. Hearing impairment picked during Mild Cognitive Impairment (MCI) could erroneously lead to a conclusion that hearing impairment increases the risk of developing dementia. Mild Cognitive Impairment is the prodrome of dementia, and progression to dementia is unpredictable with varying conversion rates as it could take up to three years to develop dementia [15].

There are three hypotheses on the link between hearing impairment and dementia in adults. Firstly, there is a common-cause pathway hypothesis. Both hearing impairment and dementia are consequences of neurodegenerative mechanism that is mediated through a direct effect of blood vessel changes affecting the cognitive and sensory areas of the brain [16,17]. Secondly, there is a cascade hypothesis, which states that the buildup to developing dementia in those with hearing impairment is as a result of deprivation of sensory input from the auditory system. Also, social isolation brought about by hearing impairment compounds this problem [16]. Lastly, the cognitive-load hypothesis posits that hearing impairment leads to cognitive decline by limiting the efforts necessary for recall, understanding, and responding to an incoming hearing stimulus [18,19].

There is a link between hearing impairment, and both cognitive impairment and dementia. Some studies show a positive association between hearing impairment and dementia [20-24]. A study reported noted an improvement in cognition with the use of hearing aid [25]. Although some studies have shown positive impacts gained from treatment of hearing loss in adults with dementia, this treatment has not directly improved cognition. However, it has improved the Behavioural and Psychological Symptoms of Dementia (BPSD) [26–29]. In contrast, some studies showed no significant cognitive improvement in dementia patients with hearing problem who use hearing aids [30,31].

Hearing impairment could be a modifiable risk factor for dementia because a range of treatments and devices are available to treat and prevent this condition. There is a need for evidence on the direction of the association between hearing impairment and dementia at the population level. This might help with advocacy for routine testing for hearing ability in the older persons to prevent or delay the development of dementia. However, there remain questions about the nature and strength of the association and the direction of cause and effect [32].

Methods

Data Source

The Health Improvement Network (THIN) database is one of the largest routinely collected primary care electronic health records from 587 general practices in the UK [33]. Read codes, developed by the NHS, code for signs and symptoms of diseases, investigations, diagnoses, treatment, and drugs [34]. Only four tables of THIN were useful for the current study.

Table 1: Component of each THIN dataset table used.

Tables	Description
Patient	Age, Sex, region, country, practice
Therapy	Medication prescription
Medical	Diagnoses, visits, episodes, referrals
Additional Health Data	Continuous data like blood pressure reading, the number of cigarettes

Study Design

The study adopted the nested case-control study design to investigate the association between dementia and hearing impairment. The cases were those with a diagnosis of dementia. The study start date was taken as the earliest of any of the patient's registration date or the agreed mortality recording (AMR) date or the agreed computer usage (ACU) date at their practice. The end date of the study for each patient taken as any of the dates of death or transfer out of THIN database or the date of the last data collection (07/01/2019).

Case and Control Selection

Only incident cases of dementia were identified using dementia specific Read codes from the therapy and medical tables of THIN. Any patient with a record of dementia one year after the start date, earliest of any of the patient's registration date or the agreed mortality recording (AMR) date or the agreed computer usage (ACU) date at their practices, was retained using dementia date.

Four eligible controls from the remaining pool of patients, that is, those who were alive and registered on the date of diagnosis of the case and therefore at risk of dementia on the event date, were selected and matched to cases by age, sex, General Practitioner (GP) practice and duration of follow-up using an incidence density sampling technique.

Exposure

Exposure to hearing impairment was identified against a list of Read codes identifying hearing impairment and related problems. Only the earliest record of exposures from the start date, but before the event date (dementia) got included in the study population. There was a need to subdivide the various forms of exposure into six categories to be able to investigate the longitudinal association between hearing impairment and dementia with respect to the length of exposure.

Confounders

The Read codes for the confounders such as hypertension, diabetes mellitus, coronary heart disease, alcohol, cigarette, stroke, were generated through QOF (Quality and Outcomes Framework) code enhancement and merged with the AHD (Additional Health Data) and medical tables.

Statistical Analysis

Conditional logistic regression was used for the unadjusted risk ratio while multiple conditional logistic regression analysis was used to find an independent association between hearing impairment and dementia. The Wald's statistic and Likelihood Ratio Test (LRT) was used to estimate the p-value of the risk ratio (RR) for binary and categorical variables, respectively. All analyses were done using STATA version 15.0 (STATA Corp LP, College Station TX).

Ethical Consideration

Approval for the study was obtained from the University of Nottingham's Scientific Research Committee with ID 19THIN014.

Results

Demographic Characteristics

There were 137,270 incident cases of dementia during a median follow-up period of approximately 10 years. There were more females (RR=1.10, CI=1.07-1.12) than males (RR=1.10, CI=1.07-1.12) with a diagnosis of dementia, and the mean age of the sample population is 81.2 ± 8.1 years.

Confounders

Table 2 shows the frequency count and proportion of cases and controls with comorbid diagnosis of the potential confounders. Approximately 12% of cases had a diagnosis of Transient Ischaemic Attack (TIA) and 11% had haemorrhagic stroke compared to 9.3% of controls with TIA and 8.4% with haemorrhagic stroke. However, there was a lower prevalence of hypertension (46.4%) and alcohol consumption (85.4%) in cases compared to controls with a diagnosis of hypertension (52.3%) or alcohol consumption (87.4%). There were no marked differences between cases and controls with diabetes mellitus, coronary heart disease, and a current smoker.

Table 2: Demographic and Clinical Characteristics of Matched Cases of Dementia and Controls in the THIN dataset.

Demographic and Clinical Variables	Case* n=137,270	Control* n= 450,704	Total* n= 587,974
Sex			
Male	50,537 (36.8)	164,769 (36.6)	215,306 (36.6)
Female	86,733 (63.2)	285,935 (63.4)	372,668 (63.4)
Age in year, mean (SD)	81.7 (8.3)	81.1 (8.1)	81.2 (8.1)
Age at diagnosis (years)**			
50-54	907 (0.7)	3,052 (0.7)	3,959 (0.7)
55-59	1,512 (1.1)	5,171 (1.2)	6,683 (1.1)
60-64	2,904 (2.1)	10,038 (2.2)	12,942 (2.2)
65-69	6,976 (5.1)	24,317 (5.4)	31,293 (5.3)
70-74	13,838 (10.1)	48,387 (10.7)	62,225 (10.6)
75-79	25,033 (18.2)	86,986 (19.3)	112,019 (19.1)
80-84	34,434 (25.1)	117,699 (26.1)	152, 133 (25.9)
85-89	32,003 (23.3)	103,974 (23.1)	135,977 (23.1)
90 and above	19,663 (14.3)	51,080 (11.3)	70,743 (12.0)
HI exposure duration in years, median (IQR)	9.6 (4.3-14.9)	10.23 (5.1-15.4)	10.1 (5.0-15.3)
Region			
Cheshire & Mersey	2,251(1.6)	7,225 (1.6)	9,476 (1.6)
East Midlands	3,302 (2.4)	11,226 (2.5)	14,528 (2.5)
East of England	6,559 (4.8)	21,163 (4.7)	27,722 (4.7)
Greater Manchester	11,573 (8.4)	38,401 (8.5)	49,974 (8.5)
London	12,775 (9.3)	39,236 (8.7)	52,011 (8.9)
North East	2,815 (2.1)	9,602 (2.1)	12,417 (2.1)
Northern Ireland	7,133 (5.2)	24,747 (5.5)	31,880 (5.4)
Scotland	26,227 (19.1)	87,873 (19.5)	114,100 (19.4)
South East Coast	13,735 (10.0)	44,072 (9.8)	57,807 (9.8)
South West	7,969 (5.8)	25,350 (5.6)	33,319 (5.7)
Thames Valley	4,758 (3.5)	15,184 (3.4)	19,942 (3.4)
Wales	15,362 (11.2)	52,211 (11.6)	67,573 (11.5)
Wessex	8,739 (6.4)	28,633 (6.4)	37,372 (6.4)
West Midlands	10,949 (8.0)	35,548 (7.9)	46,497 (7.9)
Yorkshire & The Humber	3,123 (2.3)	10,233 (2.3)	13,356 (2.3)
Stroke			
Transient Ischaemic attack	15,913 (11.6)	41,916 (9.3)	57,829 (9.8)
Haemorrhagic stroke	15,049 (11.0)	37,680 (8.4)	52,729 (9.0)
Diabetes diagnosis	22,195 (16.2)	70,759 (15.7)	92,954 (15.8)
Coronary Heart Disease	30,327(22.1)	104,100 (23.1)	134,427(22.9)
Hypertension	63,685 (46.4)	235,836 (52.3)	299,521 (50.9)
Alcohol Consumption	117,246 (85.4)	393,906 (87.4)	511,152 (86.9)
Smoking status			
Never	1,712 (1.3)	5,994 (1.3)	7,706 (1.3)
Non-smoker	392 (0.3)	1,408 (0.3)	1,800 (0.3)
Current smoker	22,673 (16.5)	71,338 (15.8)	94,011 (16.0)
Ex-smoker	768 (0.6)	2,521 (0.6)	3,289 (0.6)
Exception	756 (0.6)	2,297 (0.5)	3,053 (0.5)
Unknown	110,969 (80.8)	367,146 (81.5)	478,115(81.3)

* Number (percentages in parenthesis) of participants except where otherwise stated.

** Pseudo-diagnosis age for controls; the age of controls at matching.

Exposure

Table 3 shows the proportion of cases and controls with exposure to hearing impairment and other hearing-related problems. Exposure

to hearing impairment was more in cases (24.7%) compared to controls (23.9%). However, the cases had a marginally higher duration of exposure compared to controls. The majority of the sample population have had exposure to the hearing problem for more than three years (14.8%). Furthermore, in comparison to controls (16.1%), the cases had more referral from primary care to a specialist for ear or hearing-related problems (22.4%).

Table 3: Proportion of matched dementia cases and control with varying exposure to hearing impairment and other ear-related variables.

Exposure and exposure-related variables	Cases n=137,270	Control n=450,704	Total n=587,974
Hearing impairment	35,254 (25.7)	107,490 (23.9)	142,744 (24.3)
Hearing impairment subdivided by time			
Up to 1 month	893 (0.6)	1,831 (0.4)	2,724 (0.5)
> 4 weeks to < 6 months	2,399 (1.8)	6,983 (1.6)	9,382 (1.6)
≥ 6 months to ≤ 1 year	2,483 (1.8)	7,741 (1.7)	10,224 (1.7)
> 1 year to ≤ 3 years	8,303 (6.1)	25,055 (5.6)	33,385 (5.7)
Above 3 years	21,176 (15.4)	65,880 (14.6)	87,056 (14.8)
Other related exposures			
Ear disease	53,593 (39.0)	176,764(39.2)	230,357(39.2)
Symptoms of HI	26,775 (19.5)	85,277 (18.9)	112,052 (19.1)
Referral to ENT	30,783 (22.4)	72,591 (16.1)	103,374(17.6)
Hearing aid	5,447 (4.0)	15,701 (3.5)	21,148 (3.6)
Ear infection	2,594 (1.9)	7,930 (1.8)	10,524 (1.8)

Number (percentages in parenthesis) of participant except where otherwise stated.
ENT: Ear, Nose and Throat specialist. HI: Hearing Impairment.

Longitudinal Analyses

From Table 4, those exposed to hearing impairment had a significant 10% increased risk of developing dementia compared to those without exposure to hearing impairment (RR = 1.10, 95% CI=1.09-1.12). There were positive and negative independent associations between each of the confounders and dementia. Those with haemorrhagic stroke had a 42% risk of dementia (RR=1.42, 95% CI=1.39-1.45) while those with TIA had a 34% risk (RR=1.34, CI=1.31-1.37). Being a current smoker significantly increased the risk of dementia by 13% (RR=1.13, 95% CI=1.04—1.21), and diabetes mellitus significantly increased the risk of dementia by 4% (RR=1.04, CI=1.02-1.06). Notably, none of the confounders was an important independent confounder because none changed the risk ratio by more than 10%.

Table 4: The result of the analysis for the association between dementia hearing- impairment, and potential confounders.

Exposure (variable)	RR (95%CI)	p-value	% change*
Hearing impairment	1.10 (1.09-1.12)	<0.001	NA
Stroke			
Transient Ischaemic attack	1.34 (1.31-1.37)	<0.001	0
Haemorrhagic stroke	1.42 (1.39-1.45)	<0.001	0
Diabetes Mellitus	1.04 (1.02 -1.06)	<0.001	0
Coronary Heart Disease	0.95 (0.93-0.96)	<0.001	0.9
Hypertension	0.77 (0.76-0.78)	<0.001	0.9
Alcohol consumption	0.80 (0.78-0.82)	<0.001	0.9
Smoking status			0
Current smoker	1.13 (1.04-1.21)	0.002	
Ex-smoker	1.07 (0.96-1.20)	0.244	
Non-smoker	0.94 (0.94-1.10)	0.449	
Exception	1.18 (1.04-1.33)	0.009	
Unknown	1.02 (0.95-1.10)	0.622	

*Adjustment for each confounder; RR: Risk Ratio; CI: Confidence Interval.

From Table 5, the crude risk for dementia after exposure to hearing impairment was highest within one month of exposure (RR=1.69, CI=1.53-1.86), but gradually reduced to baseline after three years of exposure to hearing impairment (RR=1.10, CI=1.07-1.12). The model containing a priori defined confounder; TIA, haemorrhagic stroke and current, smoking had the same risk ratio as the crude risk for dementia after exposure to hearing impairment (RR=1.10, CI=1.08-1.12). Conversely, there was a reduced risk of dementia in hearing impairment after adjustments for variables along the diagnostic or treatment pathway, ENT referral and hearing aid

Table 5: The result of the multivariable analysis of the association between hearing-impairment and dementia.

Exposure	Crude RR (95% CI)	P-value	Adj. RR** (95% CI)	P-value	Adj. RR*** (95% CI)		Adj. RR**** (95% CI)	P-value
Hearing impairment	1.10 (1.09-1.12)	<0.001	1.10 (1.08-1.11)	<0.001	0.97 (0.95-0.99)	0.002	1.10 (1.08-1.12)	<0.001
Hearing impairment subdivided by time		<0.0001*		<0.0001*		<0.0001*		<0.0001*
Up to 1 month	1.69 (1.53-1.86)		1.67 (1.52-1.84)		1.48 (1.34-1.63)		1.68 (1.52-1.85)	
> 4 wks. to < 6 month	1.15 (1.09-1.21)		1.14 (1.08-1.21)		0.98 (0.93-1.04)		1.14 (1.08-1.20)	
≥ 6 months to ≤ 1year	1.06 (1.0-1.12)		1.06 (1.00-1.11)		0.91 (0.86-0.96)		1.05 (1.00-1.11)	
> 1 year to ≤ 3 years	1.09 (1.06-1.12)		1.08 (1.05-1.11)		0.93 (0.90-0.96)		1.09 (1.07-1.11)	
Above 3 years	1.10 (1.07-1.12)		1.09 (1.07-1.11)		0.98 (0.96-1.00)			
Related exposures								
Symptoms of HI	1.08 (1.06-1.11)	<0.001	1.08 (1.05-1.10)	<0.001	1.04 (1.02-1.06)	<0.001		
Ear infection	1.12 (1.07-1.18)	<0.001	1.09 (1.04-1.15)	0.001	1.02 (0.97-1.08)	0.43		
Ear diseases	1.03 (1.00-1.04)	0.001	1.01 (0.99-1.03)	0.66	0.97 (0.95-0.98)	<0.001		
Hearing aid	1.12 (1.08-1.16)	<0.001			0.98 (0.95-1.02)	0.59		
Referral to ENT	1.75 (1.72-1.78)	<0.001			1.74 (1.75-1.82)	<0.001		

*P-value for estimation by Likelihood Ratio Test (LRT); **Mutually adjusted RR model for ear disease and ear infection and all confounders.
*** Mutually adjusted for Hearing aid and ENT referral; **** Adjusted *a priori* for TIA, haemorrhagic stroke, current smoking.
TIA: Transient Ischaemic Attack. Adj.: Adjusted RR: Risk ratio.
All models included potential confounders; Diabetes Mellitus, Alcohol use, Smoking status (current), Coronary heart disease, Hypertension, Haemorrhagic stroke, TIA, except the model with *a priori* confounder.

(RR=0.97, 95% CI=0.95-0.99). However, there was a 48% increased risk up to a month (RR=1.48, 95% CI=1.34-1.63).

Discussion

The approximate proportion of individuals with a diagnosis of dementia exposed to hearing impairment (26%) was higher than the proportion of individuals exposed to the same condition in matched controls (24%). However, a wider difference (6.3%) existed between the case and control groups for referral to ENT physician and a marginal increase in the proportion of cases compared to controls with corresponding exposure to hearing impairment according to duration of exposure. In the other non-specific and related exposures, there was a considerable increase in the proportion of cases with prior documented referral to ear specialist compared to those without dementia. Notably, referral for ENT consultation has 78% (Adj. RR=1.78, 95% CI:1.74-1.81) increased risk of contributing to the development of dementia.

This study was able to demonstrate an association between exposure to hearing impairment and having a diagnosis of dementia, and the direction of this association was longitudinal. There was a significant 10% increased risk of dementia with exposure to hearing impairment (RR=1.10, 95% CI=1.09-1.12) but the risk seems to be highest within one-month record of hearing impairment (RR=1.49, 95% CI=1.35-1.64) and declined over time to reach the lowest risk after three years. Since hearing impairment is a chronic problem, it appears the risk of developing dementia after three years of exposure to hearing impairment might be causal rather than part of the degenerative process of dementia itself, which has a shorter prodrome of less than 3years.

A cohort study of 68,061 community-dwelling patients with dementia, and 259,337 matched controls followed up for 11 years investigating the inequalities in receipt of mental and physical healthcare in people with dementia estimated that 37% of males and 63% of females had a diagnosis of dementia [48]. According to the age categories, those within the age category of 50-59 years constituted the lowest proportion (2%) whilst those within the age category of 80-84 years constituted the highest proportion of cases (26%). It is not unsurprising that these figures are similar to the findings of the current study because both studies used the same database and are likely to have similar limitations about misclassification of cases. Similarly, in another population-based cohort study of 6,154 participants with a median follow-up of 6 years, a computer-based personal interview of participants or their informants, questionnaire-generated, or physician diagnosis found dementia to be 64% in females, and the mean age was 77.3 years (SD=8.6) [49]. The findings are also similar to the findings of the current study considering the difference in the source of both data.

The English Longitudinal Study of Ageing (ELSA) examined each of self-reported hearing problem (Wave 7), objective hearing problem (Wave 7), and dementia cross-sectionally. Participants who reported moderate and poor hearing were 1.6 (95% CI, 1.05-2.37) and 2.6 (95% CI=1.74-3.93) times more likely to develop dementia compared with those with normal hearing. In the objective assessment for hearing ability, participants who had moderate and poor hearing were 1.6 (95% CI, 0.93-2.84) and 4.4 (95% CI=1.94-9.91) times more likely to develop dementia compared with those with normal hearing. These results are different from the current study probably because the cross-sectional analysis would have included prevalent cases of dementia and potentially magnify the measure of effect. Furthermore, in a cohort study design with a 10-year follow-up where the researchers got information on exposure to hearing problems retrospectively in 2004 (Wave 2), participants who reported moderate and poor hearing were 39% (95% CI, 1.01-1.92) and 57% (1.12-2.02) more likely to develop dementia compared to those who reported normal hearing [50]. Some factors could be responsible for the higher measure of effect seen in the longitudinal analysis of the ELSA study due to a smaller cohort sample size (8,780 participants) and a small incident dementia case (269). There is also the possibility of recall bias on exposure and undue sensitisation of the participants.

The current study estimated that being referred to an ENT specialist by a GP was significantly associated with developing dementia (RR=1.78, 95% CI=1.74-1.81). It is possible for those referred to ENT specialist to eventually get a confirmatory diagnosis of hearing impairment and get treatment for it before returning to primary care. A similar longitudinal study, of 154,783 incident cases of dementia age 65 years and above using secondary data from health insurance claims, found that cases treated by ENT professionals were less likely to develop dementia during a four-year follow-up (HR=0.74, 0.001) [51]. This result is a sharp contrast to the current finding, and this could be due to having access to specialist care database.

The use of hearing aid is one of the treatments offered to people with hearing impairment by ENT specialists, but there is conflicting evidence over its effectiveness in improving dementia directly or indirectly through Quality of Life (QOL) [52-56]. A randomised controlled trial (RCT) found no significant improvement in the memory of patients with dementia compared to the placebo group [53]. This result could be due to the short follow-up period of 6 months, small sample size lacking enough power to detect any real change and questionable compliance with the use of hearing aid by the participants, inadequate blinding of audiologist capable of introducing confirmation bias [57]. However, the current study found a negligible protective association between the use of hearing aid and the development of dementia (RR=0.99, 95% CI=0.95-1.03) but this association was not significant. This finding could be due to the lack of access to specialist data, with more accurate data on prescription of hearing aid, therefore, possibly increasing the measure of effect.

Furthermore, this is similar to the findings of another population-based study of 3,777 community-dwelling participants followed up for 25 years to investigate the relationship between self-reported hearing problems, and each of death, depression, disability, and dementia. The study found that participants who reported hearing problems were 1.18 (HR=1.18, 95% CI=1.02-1.36) times more likely to develop dementia compared to those who did not report

hearing problems. The use of hearing aid in those with a hearing problem was 14% (HR=0.86, 95% CI=0.59-1.26) less likely to develop dementia compared to those with hearing problems but without hearing aids [58]. The reason for this similarity could be because both studies used the clinician-based diagnosis to identify cases and binary self-report hearing problem for cases, the severity of hearing impairment was not considered to establish dose-response association and the long follow-up.

Study Strengths

This study involved a large sample of national primary care data from the THIN dataset. The sample population comprises individuals age 50 and above, which is generalisable to the UK population; therefore, it increases the external validity of this study [37]. Some studies show THIN to be valid for pharmaco-epidemiological studies [38-40], and specifically for studies with a focus on dementia [41]. This large dataset provided a measure of effect with a narrow margin of error and increased statistical power to the study.

The use of prospectively recorded dataset taken at the point of consultation eliminated the risk of recall bias in the cases and observer bias in the controls. Also, it is easier to conduct this type of study because it saves time and money that would have gone into contacting cases of dementia to obtain information on exposure(s). The incidence density sampling technique provided an additional advantage by reducing bias in a case-control design and gives a measure of effect obtainable in cohort design studies. Moreover, the risk ratio is not biased by any differential loss to follow-up, such as death of cases or transfer out of THIN, among the exposed compared to the unexposed [42]. Recorded cases of dementia for this study were clinician diagnosis and this offered prevention of response bias and confirmation bias for self-administered, and researcher administered questionnaires, respectively.

Study limitations

Both cases and controls stand the risk of being misclassified with potential for type 1 error. The definitive diagnosis of hearing impairment or hearing loss made by specialists who might not be available at the level of primary care [43]. It is not surprising that this study found a large proportion of cases and controls referred to specialists but is not clear whether they eventually had a diagnosis of hearing impairment and were classified as such in the secondary care or tertiary care. If the cases that were referred to ENT had more confirmed hearing impairment diagnoses, then this study could have underestimated the measure of effect and the reverse if the referred controls had more confirmed diagnoses of hearing impairment.

There is rarity of studies on the validation of THIN codes for hearing impairment. Triangulation of the codes for hearing loss through manual review of computer profiles of the individuals in this study could not be done due to the constraint of time [47]. This limitation could affect the internal validity of this study, but this is understandable as the process of validation could take up to one year. The study population was not surveyed systematically for hearing impairment. The study relied on presentation of patients to primary care, and consequently, may have missed some cases of hearing impairment. Differential missing of hearing impairment in one of the two groups could lead to bias. The trend of the association between exposure to hearing impairment and dementia could not be tested to know the effect of the gradient of exposure on the outcome. The estimated measure of effect in this study gave a universal weight to all possible degree of exposure that could have differed if hearing impairment was a continuous variable.

Future Research

Other researchers could consider building on the preliminary findings of the current study to investigate the outcome (QOL) in those elderly population with hearing impairment who received screening test for dementia and subsequently treated in comparison to those with a hearing impairment without screening for dementia but later developed dementia. A stand-alone validation study could be a step in the right direction to build on the findings of this study. The validation study would help to confidently identify the Read codes that are highly specific for picking those with hearing impairment through a systematic sampling of the GPs entering records of hearing impairment in the THIN database.

Public Health Impact

The current study found 10% (RR=1.10, CI=1.08-1.12) increased risk of developing dementia in those exposed to hearing impairment. This estimate translates to a number needed to harm (NNH) of 50 [59]. From a public health perspective, screening 50 individuals with a hearing impairment for dementia might be able to identify one person with a risk of later developing dementia, which is dependent on the sensitivity and specificity of the screening instrument. However, the time of 49 people with hearing impairment but without developing dementia and that of the GP would have been wasted. Just like the breast screening programme in the UK, false positive and false-negative results from this screening could lead to over-diagnosis and over-treatment. However, there remains a question of whether the cost of preventing dementia outweighs the cost of treating dementia at population level.

Assume findings confirmed elsewhere, this suggests that complaints of hearing difficulty by patients or when picked up by the GP should be followed by screening for dementia. Early identification of dementia and prompt referral could help to slow down the disease process leading to a better outcome for the patient and saving money for the government and families.

Conclusion

What is Already Known

There is a relationship between hearing impairment and dementia, but the direction of association is blurred. Some authors argue that the observed association could be due to reverse causality. In addition to this, studies have also shown a dose-response effect of hearing impairment on dementia.

New Insights from this Study

Higher proportion of people with dementia were exposed to hearing impairment compared to matched controls. The highest proportion with a diagnosis of dementia first had a recorded exposure to hearing impairment for more than three years, and the cases had more referral to ENT compared to their controls. There was an increased risk of developing dementia after exposure to hearing impairment, but the risk was highest within 4 weeks of exposure.

Recommendation

To raise awareness of screening test for dementia at the primary care level for older adult patients with hearing impairment. The focus should not only be for correcting the hearing impairment but for early recognition of dementia.

References

1. ICD-11 - Mortality and Morbidity Statistics. Available from: https://icd.who.int/dev11/l-m/en#/http://id.who.int/icd/entity/546689346
2. Prince M, Wimo A, Guerchet M, et al. World Alzheimer Report 2015: The Global Impact of Dementia-An analysis of prevalence, incidence, cost and trends. Alzheimer's Dis Int. 2015; 1-84. Available from: https://kclpure.kcl.ac.uk/portal/en/publications/world-alzheimer-report-2015--the-global-impact-of-dementia(ae525fda-1938-4892-8daa-a2222a672254)/export.html
3. WHO | Dementia: a public health priority. WHO. 2012;
4. Prince M, Knapp M, Guerchet M, et al. Alzheimer's Society - Dementia UK: Second edition - overview. 2014.
5. Prince MD, Knapp M, Guerchet A, et al. Title Dementia UK: Update Second edition. Alzheimer's Society. 2014; 1-142. Available from: https://www.alzheimers.org.uk/sites/default/files/migrate/downloads/dementia_uk_update.pdf
6. Neu SC, Pa J, Kukull W, et al. Apolipoprotein E Genotype and Sex Risk Factors for Alzheimer Disease. JAMA Neurol. 2017; 74: 1178.
7. Lee Y-K, Hou S-W, Lee C-C, et al. Increased Risk of Dementia in Patients with Mild Traumatic Brain Injury: A Nationwide Cohort Study. Zhang XY, editor. PLoS One. 2013; 8: e62422.
8. Rizzi L, Rosset I, Roriz-Cruz M. Global Epidemiology of Dementia: Alzheimer's and Vascular Types. Biomed Res Int. 2014; 2014: 1-8.
9. Stern Y. Cognitive reserve in ageing and Alzheimer's disease. Lancet Neurol. 2012; 11: 1006-10012.
10. Wen Y-H, Wu S-S, Lin C-HR, et al. A Bayesian Approach to Identifying New Risk Factors for Dementia: A Nationwide Population-Based Study. Medicine (Baltimore). 2016; 95: e3658.
11. Diniz BS, Teixeira AL, Cao F, et al. History of Bipolar disorder and the risk of dementia: a systematic review and meta-analysis. Am J Geriatr Psychiatry. 2017; 25: 357.
12. Facts and figures | Action on Hearing Loss. Available from: https://www.actiononhearingloss.org.uk/about-us/our-research-and-evidence/facts-and-figures/
13. Nirmalasari O, Mamo SK, Nieman CL, et al. Age-related hearing loss in older adults with cognitive impairment. Int Psychogeriatrics. 2017; 29: 115-121.
14. Kim SY, Lim J-S, Kong IG, et al. Hearing impairment and the risk of neurodegenerative dementia: A longitudinal follow-up study using a national sample cohort. Sci Rep. 2018; 8: 15266.
15. Defrancesco M, Marksteiner J, Kemmler G, et al. Severity of Depression Impacts Imminent Conversion from Mild Cognitive Impairment to Alzheimer's Disease. J Alzheimer's Dis. 2017; 59: 1439-1448.
16. Lin FR, Niparko JK, Ferrucci L. Hearing Loss Prevalence in the United States. Arch Intern Me. 2011; 171: 1851.
17. Golub JS. Brain changes associated with age-related hearing loss. Curr Opin Otolaryngol Head Neck Surg. 2017; 25: 347-352.
18. Rudner M. Cognitive Spare Capacity as an Index of Listening Effort. Ear Hear. 2016; 37: 69S-76S.
19. Pichora-Fuller MK, Kramer SE, Eckert MA, et al. Hearing Impairment and Cognitive Energy. Ear Hear. 2016; 37: 5S-27S.
20. Wei J, Hu Y, Zhang L, et al. Hearing impairment, mild cognitive impairment, and dementia: A meta-analysis of cohort studies. Dementia and Geriatric Cognitive Disorders Extra. Karger Publishers. 2017; 7: 440-452.
21. Lin FR, Albert M. Hearing loss and dementia - who is listening? Aging Ment Health. 2014; 18: 671-673.
22. Lin VYW, Black SE. Linking Deafness and Dementia: Challenges and Opportunities. Otol Neurotol. 2017; 38: e237-239.
23. Deal JA, Betz J, Yaffe K, et al. Hearing impairment and incident dementia and cognitive decline in older adults: The health ABC study. Journals Gerontol - Ser A Biol Sci Med Sci. 2017; 72: 703-709.
24. Teipel S, Fritze T, Ovari A, et al. Regional Pattern of Dementia and Prevalence of Hearing Impairment in Germany. J Am Geriatr Soc. 2015; 63: 1527-1533.
25. Taljaard DS, Olaithe M, Brennan-Jones CG, et al. The relationship between hearing impairment and cognitive function: a meta-analysis in adults. Clin Otolaryngol. 2016; 41: 718-729.
26. Deal JA, Albert MS, Arnold M, et al. A randomized feasibility pilot trial of hearing treatment for reducing cognitive decline: Results from the Aging and Cognitive Health Evaluation in Elders Pilot Study. Alzheimer's Dement Transl Res Clin Interv. 2017; 3: 410-415.
27. Palmer C V, Adams SW, Bourgeois M, et al. Reduction in caregiver-identified problem behaviors in patients with Alzheimer disease post-hearing-aid fitting. J Speech Lang Hear Res. 1999; 42: 312-328.
28. Haque R, Chowdhury FH, Islam S, et al. Large cerebellopontine angle tuberculoma: a case report. Neurol Neurochir Pol. 2019; 46: 196-199.

29. Palmer C V, Adams SW, Durrant JD, et al. Managing hearing loss in a patient with Alzheimer disease. J Am Acad Audiol. 1998; 9: 275-284.

30. Adrait A, Perrot X, Nguyen M-F, et al. Do Hearing Aids Influence Behavioral and Psychological Symptoms of Dementia and Quality of Life in Hearing Impaired Alzheimer's Disease Patients and Their Caregivers? J Alzheimer's Dis. 2017; 58: 109-121.

31. Nguyen M-F, Bonnefoy M, Adrait A, et al. Efficacy of Hearing Aids on the Cognitive Status of Patients with Alzheimer's Disease and Hearing Loss: A Multicenter Controlled Randomized Trial. J Alzheimer's Dis. 2017; 58: 123-137.

32. Thomson RS, Auduong P, Miller AT, et al. Hearing loss as a risk factor for dementia: A systematic review. Laryngoscope Investig Otolaryngol. 2017; 2: 69-79.

33. The Health Improvement Network | re3data.org. Available from: https://www.re3data.org/repository/r3d100011282

34. Read Codes-NHS Digital. Available from: https://digital.nhs.uk/services/terminology-and-classifications/read-codes

35. Robins J, Greenland S, Breslow NE. A General Estimator For The Variance Of The Mantel Haenszel Odds Ratio. Am J Epidemiol. 1986; 124: 719-723. Available from: http://citeseerx.ist.psu.edu/viewdoc/summary?doi=10.1.1.228.3832

36. Pearce N. Analysis of matched case-control studies. BMJ. 2016; 352: i969.

37. Blak BT, Thompson M, Dattani H, et al. Generalisability of the Health Improvement Network (THIN) database: Demographics, chronic disease prevalence and mortality rates. Inform Prim Care. 2011; 19: 251-255.

38. Langley TE, Szatkowski LC, Wythe S, et al. Can primary care data be used to monitor regional smoking prevalence? An analysis of The Health Improvement Network primary care data. BMC Public Health. 2011; 11: 773.

39. Lo Re V, Haynes K, Forde KA, et al. Validity of The Health Improvement Network (THIN) for epidemiologic studies of hepatitis C virus infection. Pharmacoepidemiol Drug Saf [Internet]. 2009; 18: 807-814.

40. Lewis JD, Schinnar R, Bilker WB, et al. Validation studies of the health improvement network (THIN) database for pharmacoepidemiology research. Pharmacoepidemiol Drug Saf. 2007; 16: 393-401.

41. Walters K, Hardoon S, Petersen I, et al. Predicting dementia risk in primary care: development and validation of the Dementia Risk Score using routinely collected data. BMC Med. 2016; 14: 6.

42. Furie KL, Kasner SE, Adams RJ, et al. Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: A guideline for healthcare professionals from the American Heart Association/American stroke association. Stroke. 2011; 42: 227-276.

43. Vandenbroucke JP, Pearce N. Case-control studies: basic concepts. Int J Epidemiol. 2012; 41: 1480-1489.

44. Martin-Merino E, Fortuny J, Rivero E, et al. Validation of Diabetic Retinopathy and Maculopathy Diagnoses Recorded in a U.K. Primary Care Database. Diabetes Care. 2012; 35: 762-767. http://www.ncbi.nlm.nih.gov/pubmed/22357184

45. Ruigómez A, Martín-Merino E, Rodríguez LAG. Validation of ischemic cerebrovascular diagnoses in the health improvement network (THIN). Pharmacoepidemiol Drug Saf. 2010; 19: 579-585. http://www.ncbi.nlm.nih.gov/pubmed/20131328

46. Meal A, Leonardi-Bee J, Smith C, et al. Validation of THIN data for non-melanoma skin cancer. Qual Prim Care. 2008; 16: 49-52. http://www.ncbi.nlm.nih.gov/pubmed/18700078

47. García Rodríguez LA, Ruigómez A. Case validation in research using large databases. Br J Gen Pract. 2010; 60: 160-161. http://www.ncbi.nlm.nih.gov/pubmed/20202361

48. Cooper C, Lodwick R, Walters K, et al. Inequalities in receipt of mental and physical healthcare in people with dementia in the UK. Age Ageing. 2017; 46: 393-400. http://www.ncbi.nlm.nih.gov/pubmed/27916749

49. Deckers K, Cadar D, van Boxtel MPJ, et al. Modifiable Risk Factors Explain Socioeconomic Inequalities in Dementia Risk: Evidence from a Population-Based Prospective Cohort Study. J Alzheimer's Dis. 2019; 1-9. Available from: https://www.medra.org/servlet/aliasResolver?alias=iospress&doi=10.3233/JAD-190541

50. Davies HR, Cadar D, Herbert A, et al. Hearing Impairment and Incident Dementia: Findings from the English Longitudinal Study of Ageing. J Am Geriatr Soc. 2017; 65: 2074-2081. http://www.ncbi.nlm.nih.gov/pubmed/28734053

51. Fritze T, Teipel S, Ovari A, et al. Hearing Impairment Affects Dementia Incidence. An Analysis Based on Longitudinal Health Claims Data in Germany. PLoS One. 2016; 11: e0156876.

52. Dawes P, Emsley R, Cruickshanks KJ, et al. Hearing loss and cognition: the role of hearing AIDS, social isolation and depression. PLoS One. 2015; 10: e0119616.

53. Nguyen M-F, Bonnefoy M, Adrait A, et al. Efficacy of Hearing Aids on the Cognitive Status of Patients with Alzheimer's Disease and Hearing Loss: A Multicenter Controlled Randomized Trial. J Alzheimer's Dis. 2017; 58: 123-137. http://www.ncbi.nlm.nih.gov/pubmed/28387664

54. Jerger J, Chmiel R, Florin E, et al. Comparison of conventional amplification and an assistive listening device in elderly persons. Ear Hear. 1996; 17: 490-504. http://www.ncbi.nlm.nih.gov/pubmed/8979037

55. Dawes P, Emsley R, Cruickshanks KJ, et al. Hearing Loss and Cognition: The Role of Hearing Aids, Social Isolation and Depression. Johnson B, editor. PLoS One. 2015; 10: e0119616. https://dx.plos.org/10.1371/journal.pone.0119616

56. Amieva H, Ouvrard C, Giulioli C, et al. Self-Reported Hearing Loss, Hearing Aids, and Cognitive Decline in Elderly Adults: A 25-Year Study. J Am Geriatr Soc. 2015; 63: 2099-2104.

57. McCormack A, Fortnum H. Why do people fitted with hearing aids not wear them? Int J Audiol. 2013; 52: 360-368. http://www.ncbi.nlm.nih.gov/pubmed/23473329

58. Amieva H, Ouvrard C, Meillon C, et al. Death, Depression, Disability, and Dementia Associated with Self-reported Hearing Problems: A 25-Year Study. Journals Gerontol - Ser A Biol Sci Med Sci. 2018; 73: 1383-1389. https://academic.oup.com/biomedgerontology/article/73/10/1383/4783130

59. Cordell WH. Number needed to treat (NNT). Ann Emerg Med. 1999; 33: 433-436. https://www.cebm.net/2014/03/number-needed-to-treat-nnt/