McMaster University | HEALTH FORUM

Rapid Evidence Profile

Examining the association between hearing loss and dementia

3 July 2024

[MHF product code: REP 76]

Appendices

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Appendix 1: Methodological details

We use a standard protocol for preparing rapid evidence profiles (REP) to ensure that our approach to identifying research evidence is as systematic and transparent as possible in the time we were given to prepare the profile.

Engaging subject matter experts

At the beginning of each rapid evidence profile and throughout its development, we engage a subject matter expert, who helps us to scope the question and ensure relevant context is taken into account in the summary of the evidence.

Identifying research evidence

For this REP, we searched ACCESSSS and PubMed for:
1) evidence syntheses
2) protocols for evidence syntheses that are underway
3) single studies.

We searched ACCESSSS using an open text search for (hearing loss AND dementia). We searched PubMed using an open text search for ("dementia"[MeSH Terms] OR "dementia"[Title/Abstract] OR "Alzheimer's"[Title/Abstract]) AND ("hearing loss"[MeSH Terms] OR "hearing loss"[Title/Abstract]) and restricted the results to systematic reviews. We ran a subsequent search in PubMed using the same search strategy but restricted it to primary studies published in the past year. Links provide access to the full search strategy.

Each source for these documents is assigned to one team member who conducts hand searches (when a source contains a smaller number of documents) or keyword searches to identify potentially relevant documents. A final inclusion assessment is performed both by the person who did the initial screening and the lead author of the rapid evidence profile, with disagreements resolved by consensus or with the input of a third reviewer on the team. The team uses a dedicated virtual channel to discuss and iteratively refine inclusion/exclusion criteria throughout the process, which provides a running list of considerations that all members can consult during the first stages of assessment. We screened 178 evidence syntheses and single studies, of which 29 went to full-text review. Seven documents were excluded following a full-text review because as they did not describe a causal relationship between hearing loss and dementia. Following this process, we included 22 evidence documents.

During this process we include published, pre-print, and grey literature, but we did not undertake a separate search for pre-print or grey literature. We do not exclude documents based on the language of a document. However, we are not able to extract key findings from documents that are written in languages other than Chinese, English, French, or Spanish. We provide any documents that do not have content available in these languages in an appendix containing documents excluded at the final stages of reviewing. We excluded documents that did not directly address the research questions and the relevant organizing framework.

Assessing relevance and quality of evidence

We assess the relevance of each included evidence document as being of high, moderate, or low relevance to the question.

Two reviewers independently appraised the quality of the guidelines we identified as being highly relevant using AGREE II. We used three domains in the tool (stakeholder involvement, rigour of development, and editorial independence) and classified guidelines as high quality if they were scored as 60% or higher across each of these domains.

Two reviewers independently appraise the methodological quality of evidence syntheses that are deemed to be highly relevant using the first version of the AMSTAR tool. Two reviewers independently appraise each synthesis, and disagreements are resolved by consensus with a third reviewer if needed. AMSTAR rates overall methodological quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality. High-quality evidence syntheses are those with scores of eight or higher out of a possible 11, medium-quality evidence syntheses are those with scores between four and seven, and low-quality evidence syntheses are those with scores less than four. It is important to note that the AMSTAR tool was developed to assess evidence syntheses focused on clinical interventions, so not all criteria apply to those pertaining to health-system arrangements or implementation strategies. Furthermore, we apply the AMSTAR criteria to evidence syntheses addressing all types of questions, not just those addressing questions about effectiveness, and some of these evidence syntheses addressing other types of questions are syntheses of qualitative studies. While AMSTAR does not account for some of the key attributes of syntheses of qualitative studies, such as whether and how citizens and subject-matter experts were involved, researchers' competency, and how reflexivity was approached, it remains the best general quality-assessment tool of which we're aware. Where the denominator is not 11, an aspect of the tool was considered not relevant by the raters. In comparing ratings, it is therefore important to keep both parts of the score (i.e., the numerator and denominator) in mind. For example, an evidence synthesis that scores 8/8 is generally of comparable quality to another scoring 11/11; both ratings are considered 'high scores.' A high score signals that readers of the evidence synthesis can have a high level of confidence in its findings. A low score, on the other hand, does not mean that the evidence synthesis should be discarded, merely that less confidence can be placed in its findings and that it needs to be examined closely to identify its limitations. (Lewin S, Oxman AD, Lavis JN, Fretheim A. SUPPORT Tools for evidence-informed health Policymaking (STP): 8. Deciding how much confidence to place in a systematic review. *Health Research Policy and Systems* 2009; 7 (Suppl1): S8.)

Preparing the profile

Each included document is cited in the reference list at the end of the REP. For all included guidelines, evidence syntheses, and single studies (when included), we prepare a small number of bullet points that provide a summary of the key findings, which are used to summarize key messages in the text. Protocols and titles/questions have their titles hyperlinked, given that findings are not yet available.

We then draft a summary that highlights the key findings from all highly relevant documents (alongside their date of last search and methodological quality).

Upon completion, the REP is sent to a subject matter expert for their review.

Appendix 2: Key findings from evidence syntheses and single studies related to the six criteria for establishing causality for hearing loss and dementia

Causal criteria	Cognitive decline	Alzheimer's disease	Lewy body dementia	Vascular dementia	Dementia (general)
Temporal relationship	• An older high-quality evidence synthesis of cohort studies found an association between age-related hearing loss and cognitive decline (1)	• An older high-quality evidence synthesis of cohort studies and cross-sectional studies found no association between age-related hearing loss and dementia (1) • An older low-quality evidence synthesis of prospective cohort studies reported an association between hearing impairment and the development of Alzheimer's disease, but it was based on findings from three studies (2) • A retrospective cohort study found 8.6% of participants developed Alzheimer's disease over a median follow-up period of 22.6 months, demonstrating that the exposure (concurrent visual and hearing impairment) preceded the Alzheimer's disease diagnosis (3) • A retrospective cohort study found that the risk of Alzheimer's disease in hearing impaired individuals remained elevated across various follow-up periods, from 0–24 months to beyond 60 months (4)		• A retrospective cohort study found that the risk of vascular dementia in hearing impaired individuals remained elevated across various follow-up periods, from 0–24 months to beyond 60 months (4)	• An older high-quality evidence synthesis of cohort studies found an association between age-related hearing loss and dementia (1) • A prospective cohort study included in a recent high-quality evidence synthesis of other prospective studies found men with hearing loss were more likely to develop dementia than men without (5) • A recent high-quality evidence synthesis of prospective cohort studies found a positive association between hearing loss and dementia (6) • A recent medium-quality evidence syntheses of prospective cohort studies found hearing loss to be associated with increased risk of dementia (7) • A prospective cohort study found a significant positive association between hearing loss and the development of all-cause dementia (8) • A recent retrospective cohort study found over 14.4 years, 1% of those with hearing loss (adjusted for age and sex) developed dementia compared to 0.4% of those without hearing loss (9) • A retrospective cohort study found that the risk of

Causal criteria	Cognitive decline	Alzheimer's disease	Lewy body dementia	Vascular dementia	Dementia (general)
					dementia in hearing impaired individuals remained elevated across various follow-up periods, from 0–24 months to beyond 60 months (4)
Strength of association	• A recent medium-quality evidence synthesis found a combined hazard ratio of 1.30 (95% Confidence Interval [CI] 1.16–1.45) for age-related hearing loss and cognitive impairment (10) • A recent medium-quality evidence synthesis found a hazard ratio of 1.11 (95% CI 1.06–1.15) for cognitive impairment due to hearing loss (11) • A recent medium-quality evidence synthesis reported hazard ratios of 1.29 (95% CI 1.11–1.50) and 1.56 (95% CI 1.17–1.42) for the development of mild cognitive impairment and non-specified cognitive decline, respectfully, among those with hearing loss (7) • A recent medium-quality review found a pooled risk ratio for the development of hearing loss and mild-cognitive impairment was 1.44 (95% CI 1.27–1.64) (12)	• A recent medium-quality evidence synthesis found a statistically significant increase in hearing thresholds of 4.5 dB among those with Alzheimer's disease as compared to those without (13) • An older low-quality evidence synthesis reported an overall risk ratio of 4.87 (95% CI 0.09–26.35) for those with hearing impairment developing Alzheimer's disease, but the meta-analysis was conducted on only three studies (2) • A cross-sectional study found that moderate to frequent densities of neuritic plaques were associated with higher odds of hearing impairment, but overall amyloid deposition, neurofibrillary tangle staging, and overall Alzheimer's disease neuropathology level were not clearly associated with increased risks of hearing impairment (14) • A retrospective cohort study found that dual sensory impairment (concurrent visual and hearing impairment) was significantly associated with a higher risk of developing Alzheimer's disease compared to no sensory impairment, while visual impairment alone and hearing impairment alone were not significantly associated with increased Alzheimer's disease risk (3) • A cross-sectional cohort study found that no statistically significant correlations between objective	• A cross-sectional study found that the presence of any Lewy body pathology was associated with a significantly increased likelihood of hearing impairment (odds ratio of 2.10, 95% CI 1.27–3.48) (14)	• One older high-quality evidence synthesis found a non-significant association was found between age-related hearing loss and vascular dementia (1) • A cross-sectional cohort study found that there were no statistically significant associations between any aspects of cerebrovascular disease and presence of hearing impairment (7)	• An older high-quality evidence synthesis reported an odds ratio of 1.28 (95% CI 1.02–1.59) for the development of dementia among those experiencing age-related hearing loss (1) • One recent high-quality evidence synthesis found an aggregated hazard ratio of 1.49 (95% CI 1.30–1.67) of developing dementia among men with hearing loss (5) • A recent high-quality evidence synthesis reported a hazard ratio of 1.59 (95% CI 1.37–1.86) for the development of dementia among those with hearing loss (6) • A recent medium-quality evidence synthesis found a hazard ratio of 1.21 (95% CI 1.11–1.31) for incident dementia due to hearing loss (11) • A recent medium-quality evidence synthesis reported a hazard ratio of 1.35 (95% CI 1.26–1.45) for those with hearing loss developing incident dementia (7) • A recent high-quality evidence synthesis identified an odds ratio between age-related hearing loss and cognitive impairment of 1.89 (95% CI 1.50–2.38) (16)

Causal criteria	Cognitive decline	Alzheimer's disease	Lewy body dementia	Vascular dementia	Dementia (general)
		measures of hearing loss and cerebrospinal fluid biomarkers of Alzheimer's disease (amyloid-β and p-tau181) after adjusting for age, except for a weak correlation between amyloid-β values and the Hearing Handicap Inventory for the Elderly (15) • A retrospective cohort study found that hearing impairment was significantly associated with an increased risk of Alzheimer's disease (4)			• A recent prospective cohort study found a risk ratio of 1.04 (95% CI 1.00–1.09) for the development of all-cause dementia among individuals with hearing loss (8) • A recent retrospective cohort study reported an age and sex adjusted risk ratio (time varying) of 1.41 (95% CI 1.38–1.43)(9)
Dose-response relationship			• A cross-sectional cohort study found that the association between Lewy body pathology and hearing impairment did not increase with higher cortical pathology (14)		• A recent medium-quality evidence synthesis reported a 10 dB worsening of hearing loss to be associated with a 16% increase in dementia risk (7)
Consistency of evidence	• A recent medium-quality evidence synthesis included 11 systematic reviews and meta-analyses (10) • A recent medium-quality evidence synthesis included a range of study designs, namely prospective, cohort, cross-sectional, and matched case control studies(12)	• An older low-quality evidence synthesis included only three prospective cohort studies in its pooled analysis (2)			• An older high-quality evidence synthesis included both cohort studies (prospective and retrospective) and cross-sectional studies (1)
Specificity	• A recent medium-quality evidence synthesis report significant heterogeneity across included studies limiting the specificity in the results (12)				• An older high-quality evidence synthesis reported lower odds ratios in cohort studies as compared to those calculated from cross-sectional studies (1) • A recent high-quality evidence synthesis found the association was not affected

Causal criteria	Cognitive decline	Alzheimer's disease	Lewy body dementia	Vascular dementia	Dementia (general)
					by study characteristics including the diagnostic methods for hearing loss, validation strategy for dementia, follow-up duration, or adjustment of the apolipoprotein E genotype (6) • A recent medium-quality evidence synthesis found social isolation did not mediate the relationship between hearing loss and dementia (11) • A recent high-quality evidence synthesis found hearing loss to be the third highest unweight risk factor for dementia, behind low education and hypertension, a population attributable risk factor of 15.6% (95% CI 10.3–20.9) (17) • A recent medium-quality evidence synthesis found select modifiers, including baseline age, type of hearing assessment, and length of follow-up, were not significant in the analysis (7) • One recent prospective cohort study over an average of 21 years found a significant risk of developing dementia following hearing loss after accounting for a range of effect moderators (8) • The study also identified that given the years monitored, it is unlikely that a reverse causation is present (8)
Biological plausibility		• A cross-sectional cohort study found that the neuropsychological domains most correlated with	• A cross-sectional cohort study found some support for the		• A recent low quality evidence synthesis found hearing loss and dementia share

Causal criteria	Cognitive decline	Alzheimer's disease	Lewy body dementia	Vascular dementia	Dementia (general)
		hearing loss were executive function and processing speed, rather than memory domains typically affected in early Alzheimer's disease, suggesting that age-related hearing loss may not be directly linked to Alzheimer's disease pathology in cognitively unimpaired older adults (15)	association between dementia-related neuropathology and hearing loss, suggesting that hearing loss may be associated with a high neuritic plaque burden and more common in Lewy body disease (14)		radiological (e.g., white matter hyperintensities) and biomolecular (e.g., brain atrophy) similarities (18)

Appendix 3: Details about each identified evidence synthesis

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations

• Types of hearing loss
  ○ Not specified
• Cause of hearing loss
  ○ Age-related deterioration
• Causality criteria
  ○ Temporal relationship
  ○ Strength of association
  ○ Consistency of evidence
  ○ Biological plausibility and coherence
• Type of dementia
  ○ Alzheimer's disease
  ○ Vascular dementia
  ○ Not specified
• Contribution to dementia
  ○ Amplification of dementia
• Mitigation measures
  ○ Effects of hearing aids
	Age-related hearing loss is a possible biomarker and modifiable risk for cognitive decline, cognitive impairment, and dementia, but not for Alzheimer's disease (1)
	• The systematic review and meta-analysis aims to estimate the association between age-related hearing loss and cognitive function, cognitive impairment, and dementia
	• The review included only observational cross-sectional and cohort studies that assess hearing loss using pure tone audiometry
	• A significant association was found between age-related hearing loss and dementia in cross-sectional and cohort studies, reporting an odds ratio of 2.42 and 1.28, respectively, but no statistically significant association was found between age-related hearing loss and Alzheimer's disease for either cross-sectional or cohort studies
	• The association between age-related hearing loss and vascular dementia was also found to be not significant
	• In general,, associations became weaker with late publication dates due to greater adjustments for co-variants
	• Hypotheses for causal mechanisms include vascular dysfunction and impaired verbal communication
		High	No	8/11	2016	No	• Age

• Types of hearing loss
  ○ Not specified
• Cause of hearing loss
  ○ Age-related deterioration
• Causality criteria
  ○ Strength of association
  ○ Consistency of evidence
• Type of dementia
  ○ Not specified
• Mitigation measures
  ○ Effects of hearing aids
	Correcting hearing loss is associated with a slower decline in cognition (19)
	• The systematic review and meta-analysis aims to evaluate the associations of hearing aids and cochlear implants with cognitive decline and dementia
	• The review included randomized clinical trials or observations studies relating to the effect of hearing interventions on cognitive function, cognitive decline, cognitive impairment, and dementia in patients with hearing loss
	• Overall, participants with hearing loss who used hearing restorative devices experienced a 19% lower risk of cognitive decline compared to those with uncorrected hearing loss
	  ○ This association remained significant even after adjusting for potential confounding factors such as age, gender,
		High	No	6/11	2021	No	• Age

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ Effects of cochlear implants	education, socio-economic status, and other health conditions • The use of hearing restorative devices was significantly associated with a 3% improvement in cognitive test scores assessing general cognition • These findings were robust in sub-group analyses, quantitative assessments of publication bias, as well as cumulative and leave-one-out meta-analyses						
• Types of hearing loss ○ Central hearing loss • Causality criteria ○ Strength of association ○ Consistency of evidence ○ Biological plausibility and coherence • Type of dementia ○ Alzheimer's disease	Alzheimer's disease is associated with hearing loss in frequencies associated with normal speech communication and the loss of hearing is increased at higher frequencies (13) • This review aims to estimate the degree to which Alzheimer's disease patients have impaired hearing by performing a meta-analysis • It reviewed 248 published studies that quantified peripheral hearing function using pure-tone audiometry for subjects with Alzheimer's disease • Six studies met the inclusion criteria with a combined total of 171 subjects with Alzheimer's disease compared to 222 age-matched controls • Findings suggest that subjects with Alzheimer's disease have higher hearing thresholds at 0.5–2 kHz pure-tone average (PTA) and 0.5–4 kHz PTA compared to age-matched controls • These findings confirm that individuals with Alzheimer's disease have diminished hearing ability, provided a quantitative measure of the extent of hearing loss, and indicated that the impairment is more pronounced at higher sound frequencies	High	No	5/11	2021	No	• Age
• Types of hearing loss ○ Not specified • Cause of hearing loss ○ Age-related hearing loss ○ Noise-induced • Causality criteria ○ Temporal relationship ○ Strength of association ○ Consistency of evidence	This synthesis found a positive association between hearing impairment and incident dementia in both the longitudinal cohort of older men and in the meta-analysis of available prospective studies (5) • This synthesis investigated the association of hearing loss and dementia through two 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 ▪ 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	High	No	8/11	2017	No	• Sex/gender

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ Biological plausibility and coherence • Type of dementia ○ Not specified	impairment (Hazard Ratio [HR] was found to be 1.69, 95% Confidence Interval [CI] 1.54–1.85) ○ A systematic review and meta-analysis of 14 included studies (n = 72,831 individuals) provided a quantitative summary of the effect of hearing loss on incident dementia in diverse populations of both genders (HR 1.49, 95% CI 1.30–1.67)						
• Types of hearing loss ○ Not specified • Causality criteria ○ Temporal relationship ○ Strength of association ○ Consistency of evidence ○ Biological plausibility and coherence • Type of dementia ○ Not specified	This comprehensive umbrella review highlights the strong link between age-related hearing loss and cognitive impairment, including dementia (10) • This study aims to explore and validate the association between age-related hearing loss with cognitive impairment and dementia through summarizing and evaluating existing evidence • A total of 11 systematic reviews and meta-analyses met the inclusion criteria • The results of the pooled meta-analysis suggested a strong association of age-related hearing with cognitive impairment and dementia • The combined hazard ratio for age-related hearing loss and cognitive impairment was 1.30 (95% CI 1.16–1.45) • For older adults experiencing hearing issues, regular cognitive assessments could facilitate the early detection of neurodegenerative conditions • Similarly, those with mild cognitive impairment might significantly benefit from prompt audiological evaluations	High	No	6/11	2023	No	• Age
• Types of hearing loss ○ Not specified • Causality criteria ○ Temporal relationship ○ Strength of association ○ Consistency of evidence ○ Biological plausibility and coherence • Type of dementia ○ Not specified	Hearing loss may be an independent risk factor for dementia in a community-derived general population (6) • The meta-analysis aims to clarify the relationship of hearing loss and dementia • Fourteen cohort studies investigating the association between hearing loss and the incidence of dementia in a community-derived population including 726,900 participants were analyzed • Particular types of hearing loss were not specified • Hearing loss was independently associated with dementia (HR 1.59, 95% CI 1.37–1.86) • Sub-group analyses showed that this association seemed to not be affected by study characteristics such as the diagnostic methods for hearing loss, validation strategy for	High	No	8/11	2021	No	• None reported

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	dementia, follow-up duration, and adjustment of the apolipoprotein E genotype						

• Types of hearing loss
  ○ Not specified
• Cause of hearing loss
  ○ Age-related deterioration
• Causality criteria
  ○ Biological plausibility and coherence
• Type of dementia
  ○ Alzheimer's disease
• Mitigation measures
  ○ Effects of hearing aids
	In middle-aged and older patients with hearing loss and Alzheimer's disease (AD) or dementia, hearing aids were not found to increase cognitive function, and authors were unable to find a causal relationship between hearing loss and AD (20)
	• Limited effectiveness of hearing aids in patients with AD or dementia is attributed to factors including the specific mechanism underlying AD and hearing loss and the choice of an endpoint
	  ○ Both the included studies chose the Mini-Mental State Examination (MMSE) score or Alzheimer's Disease Assessment Scale–Cognitive subscale (ADAS–Cog) as the assessments
	  ○ Both scores were ineffective when calculating the minimum detectable effect size in change from baseline
	• One study found a significant genetic overlap but not a causal relationship between hearing loss and AD
	• Since it is hard to determine whether hearing loss or AD comes first, a hearing aid might not be an appropriate therapeutic method because the development trajectory or causal relationship between hearing loss and AD is unclear
	• In AD or dementia patients with hearing loss, cognitive decline is attributed not only to decreased sensory input but also to the deteriorated ability of information processing and output, which cannot be modified by hearing aids
		High	No	7/11	2022	No	• Age

• Types of hearing loss
  ○ Sensorineural hearing loss
  ○ Not specified
• Extent/level of hearing loss
  ○ All
• Causality criteria
  ○ Dose-response relationship
• Type of dementia
  ○ Not specified
• Contribution to dementia
	Evidence shows a dose-dependent association between hearing threshold levels in adults and later cognitive impairment or incident dementia (11)
	• The systematic review and meta-analysis aims to examine the role of social isolation as a mediator in the relationship between hearing loss and cognition, but only one study included social isolation as a mediator and it was found not to be a contributing factor
	• Pure tone audiometry (conventional or screening method) was the method of obtaining hearing levels in all included studies
	• Of 15 included studies, two exclusively used dementia diagnosis as an outcome, 12 used cognitive scores, and one study used both
		High	No	7/11	2023	No	• None identified

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
○ Amplification of dementia	• The most frequent cognitive test used was the Mini-Mental State Examination (MMSE), which is not specific enough to detect lower levels of cognitive domains associated with various dementias ○ The Digit Symbol Substitution Test (a processing speed test) was sometimes also used which can be better suited to detect problems with recall and processing speed associated with dementia • A causal relationship between hearing loss (40 dB hearing loss or greater) and incidence of dementia and cognitive impairment was found in 11 out of 15 studies ○ The pooled hazard ratio for incident dementia due to hearing loss was 1.21, and there was a high percentage of total variability due to between-study heterogeneity • There were differences in the severity of hearing loss across groups, which may limit the validity of results • There is a need to use more standardized methods and analyses to study the effect of hearing loss on dementia incidence and cognitive decline in longitudinal studies so that a pooled effect can be measured						
• Types of hearing loss ○ Not specified • Causality criteria ○ Biological plausibility and coherence • Type of dementia ○ Alzheimer's disease ○ Vascular dementia • Contribution to dementia ○ Amplification of dementia	In meta-analyses, hearing loss was found to be the third highest unweighted risk factor for dementia behind low education and hypertension, and third highest weighted risk factor behind low education and physical inactivity (17) • The systematic review and meta-analysis aims to estimate the population attributable fraction (PAF) for dementia associated with modifiable risk factors • Specifically, later-life dementia was searched for (prevalent or incident in people aged 60+), but no restrictions were made on dementia subtype, the sex or baseline age of participants, or the period of study • The mechanisms linking hearing loss to dementia are not well understood, but proposed pathways include: ○ shared pathology (i.e., accumulation of amyloid-β in auditory regions) ○ hearing loss resulting in structural and functional brain changes and imposing increased cognitive load, leading to reduced cognitive resources and decline, reduced social interaction, and increased dementia risk	High	No	8/11	2023	No	• Age • Place of residence • Socio-economic status

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	• Compared with high-income countries, low-income and middle-income countries had higher unweighted and weighted PAF values for education and hearing loss						

• Types of hearing loss
  ○ Not specified
• Causality criteria
  ○ Temporal relationship
  ○ Strength of association
  ○ Consistency of evidence
  ○ Biological plausibility and coherence
• Type of dementia
  ○ Alzheimer's disease
	Hearing loss is associated with an increased risk of cognitive impairment (2)
	• This study assessed the association between hearing impairment and Alzheimer's disease
	• This study included prospective cohort studies; three were regarding Alzheimer's disease and one was general cognitive impairment
	• The overall combined relative risk of people with hearing impairment developing Alzheimer's disease, compared to controls, was 4.87 (95% CI 0.90–26.35, p = 0.066)
	• However, when an additional study on general cognitive impairment was added, the overall risk of people with hearing impairment developing Alzheimer's disease, compared to controls, was 2.82 (95% CI 1.47–5.42, p =0.002)
	• These findings suggest that hearing impairment can increase the risk of cognitive disorders
	• There are still more factors that need to be considered such as the type, cause, or severity of hearing loss as these factors were not specified in this meta-analysis
		High	No	3/9	2016	No	• None reported

• Types of hearing loss
  ○ Not specified
• Causality criteria
  ○ Temporal relationship
  ○ Consistency of evidence
  ○ Dose-response relationship
  ○ Biological plausibility and coherence
• Type of dementia
  ○ Alzheimer's disease
  ○ Vascular dementia
	Hearing loss is associated with an increased risk of developing a cognitive impairment, including dementia and Alzheimer's; this relationship may be modified by the intensity of hearing loss (7)
	• This systematic review and meta-analysis assessed the association between hearing impairment and dementia subtypes
	• This review included cohort studies of participants without dementia, a minimum two year follow up, and follow up cognitive outcomes
	• This study included 50 cohorts, with a total sample of 1,548,754 participants
	• Hearing loss was captured as a dichotomous variable across studies (yes/no)
	• Hearing loss was associated with risk for various types of dementia
	  ○ Incident dementia (HR 1.35, 95% CI 1.26–1.45)
	  ○ Mild cognitive impairment (HR 1.29, 95% CI 1.11–1.50)
		High	No	6/11	2023	No	• None reported

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	○ Non specified cognitive decline (HR 1.56, 95% CI 1.17–1.42) ○ A 10 dB worsening of hearing loss was associated with 16% increase in dementia risk (95% CI 1.07–1.27), suggesting a dose-response • Only three studies included vascular dementia, limiting statistical power of the results (HR 1.30, 95% CI 0.83–2.05) • No selected modifiers (baseline age, type of hearing assessment, and length of follow up) were significant in the analysis						
• Types of hearing loss ○ Not specified • Causality criteria ○ Biological plausibility and coherence • Type of dementia ○ Not specified • Mitigation measures ○ Effects of hearing aids ○ Effects of cochlear implants • Effects of treatment	There are radiological (e.g., white matter hypersensitises) and biomolecular (e.g., brain atrophy) relationships between dementia and hearing loss; this relationship can be mitigated by treatment for hearing devices (18) • This review explored the radiological and biomolecular relationships between dementia and hearing loss, as well as potential treatments to mitigate the relationship • The type, extent, and cause of hearing loss was not specified • Both conditions show white matter hyperintensities ○ White matter hypersensitivities is correlated with difficulty in understanding auditory words and increased risk of dementia in older adults ○ This may be due to gliosis disrupting synaptic transmission • Brain atrophy and gliosis have been seen in both conditions ○ Atrophy was seen in the temporal region and may accelerate the risk of dementia ○ Diffused atrophy was seen in dementia, and could possibly lead to hearing loss • Treatments have found that restoring auditory function (e.g., with hearing devices and cochlear implants) could stimulate brain connectivity required for memory ○ Digital hearing aids are less invasive than other treatments, but people with memory impairments may forget to wear them ○ Bone anchored hearing implants stimulate the cochlea and can allow better word understanding to support memory • Cochlear implant is effective for profound hearing loss and some evidence shows improvement in cognitive function, but it is invasive and expensive	High	No	1/9	2020	No	• None reported

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations

• Types of hearing loss
  ○ Not specified
• Causality criteria
  ○ Strength of association
  ○ Biological plausibility and coherence
• Type of dementia
  ○ Not specified
	Central and peripheral hearing loss is associated with mild cognitive impairment (12)
	• This synthesis explored the relationship between age-related hearing loss and mild cognitive impairment
	• Types of hearing loss included were central, peripheral, or general self-reported
	• The pooled risk ratio across 23 studies for developing hearing loss and mild cognitive impairment was 1.44 (95% CI 1.27-1.64)
	• The risk ratio of peripheral hearing loss and mild cognitive impairment in two cross-sectional study was 2.06 (95% CI 1.35 – 3.15)
	• The authors reported significant heterogeneity across studies and noted that longitudinal studies would be helpful to confirm results
		High	No	6/11	2020	No	• Age

• Types of hearing loss
  ○ Not specified
• Causality criteria
  ○ Temporal relationship
  ○ Strength of association
  ○ Consistency of evidence
  ○ Biological plausibility and coherence
• Type of dementia
  ○ Not specified
	Hearing loss is associated with declined cognitive function and dementia in older adults (16)
	• This synthesis and meta-analysis examined the relationship between age-related hearing loss and cognitive decline and dementia
	• Across studies, the effect size of cognitive function with hearing loss was –0.26
	• The odds ratio between age-related hearing loss and cognitive impairment was 1.85
	• Sub-group analyses demonstrated that the pooled effect size was larger for cognitive impairment (1.95) than dementia (1.45)
		High	No	8/11	2022	No	• Age

• Types of hearing loss
  ○ Not specified
• Causality criteria
  ○ Temporal relationship
  ○ Strength of association
  ○ Consistency of evidence
  ○ Biological plausibility and coherence
• Type of dementia
  ○ Not specified
	Across 17 studies, hearing loss is associated with risk of developing dementia or cognitive decline, with peripheral auditory functioning being the primary focus of most studies (21)
	• The objective of this systematic review was assessing the relationship between hearing loss and dementia
	• All studies found a relationship between hearing loss and dementia or cognitive decline
	• Peripheral auditory function was the most researched hearing type
	• The methodology used across studies was variable, creating challenges with systematic cross study comparison
		Medium	No	3/9	2016	No	• None reported

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Living status	Quality (AMSTAR)	Last year literature searched	Availability of GRADE profile	Equity considerations
	• A total of 17 studies measured cardiovascular disease as a risk factor, but none found any significant modifying effects • The authors conclude that more prospective studies are needed to help identify potential causation, rather than just correlation between hearing loss and dementia/cognitive decline						

• Types of hearing loss
  ○ Not specified
• Causality criteria
  ○ Dose-response relationship
• Type of dementia
  ○ Not specified
	Evidence suggests that hearing impairment negatively impacts cognition, but diversity within studies, small sample sizes, and other limitations prevent causal conclusions between hearing loss and dementia (22)
	• Some but not all studies demonstrate a faster rate of decline in cognition and increased risk of incident all-cause dementia
	• Data reveal a dose-response relationship between the degree of hearing impairment (whether in those being treated or not) and general cognition, but dementia remains unspecified
	• While the study revealed an association between hearing impairment and cognition, further causal conclusions are premature
		Medium	No	6/11	2015	No	• Age

• Types of hearing loss
  ○ Not specified
• Cause of hearing loss
  ○ Age-related deterioration
• Causality criteria
  ○ Consistency of evidence
• Type of dementia
  ○ Alzheimer's disease
  ○ Not specified
• Contribution to dementia
  ○ Acceleration of dementia
  ○ Amplification of dementia
• Mitigation measures
  ○ Effects of hearing aids
	Hearing impairment was prioritized as a modifiable factor in dementia risk scores (23)
	• The primary aim of this review was to examine modifiable risk factors for dementia risk reduction
	• The review consisted of a four-phased approach, including an umbrella review, a Delphi consensus study – first round, synthesis of information, and a Delphi consensus study – second round
	• 14 of 18 studies on hearing impairment found a significant increase in dementia risk or cognitive decline
	• The included cohort studies found the use of hearing aids to reduce the risk/progression of dementia in hearing impaired adults
		Low	No	6/11	2021	No	• Age

Appendix 4: Details about each identified single study

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristic	Equity considerations

• Types of hearing loss
  ○ Not specified
• Cause of hearing loss
  ○ Age-related deterioration
• Causality criteria
  ○ Strength of association
  ○ Biological plausibility and coherence
• Type of dementia
  ○ Alzheimer's disease
  ○ Lewy body dementia
  ○ Vascular dementia
	The study suggests that age-related hearing loss may be a factor predicting increased risk of Lewy body dementia and Alzheimer's dementia but not for cerebrovascular dementia (14)
	• The study aimed to examine whether the presence of dementia-related neuropathy was associated with hearing impairment later in life using clinical and post-mortem neuropathological data
	• Within a cohort of 432 participants, 64.2% were cognitively impaired but had normal hearing while 51.6% were cognitively impaired and had impaired hearing
	• The presence of moderate neuritic plaques and frequent neuritic plaques both had a significant association with hearing impairment, an odds ratio of 3.11 and 3.65 respectively, but for sparse neuritic plaques the result was non-significant
	• Alzheimer's-related neuropathological change was not associated with significantly increased odds of hearing impairment in comparison to those without Alzheimer's-related neuropathology; similarly no significant association was found between increasing amyloid deposition and presence of hearing impairment
	• The presence of any Lewy body pathology was associated with significant increases in the likelihood of hearing impairment
	• There were no statistically significant associations between any aspects of cerebrovascular disease and presence of hearing impairment
		High	*Focus of study:* Examining the association between age-related hearing loss and different types of dementia
			
			Publication date: 2023
			
			Jurisdiction: United Kingdom
			
			Methods: Cross-sectional study
				• Age

• Types of hearing loss
  ○ Not specified
• Cause of hearing loss
  ○ Age-related deterioration
• Causality criteria
  ○ Temporal relationship
  ○ Strength of association
• Type of dementia
  ○ Alzheimer's disease
	The study found dual sensory impairment (concurrent visual and hearing impairment) was associated with a significantly higher risk of developing Alzheimer's disease compared to no sensory impairment, while single sensory impairments alone were not significantly associated with increased Alzheimer's disease risk in the fully adjusted model (3)
	• This study aimed to investigate the impact of sensory impairment, particularly visual impairment, hearing impairment, and dual sensory impairment, on the incidence of Alzheimer's disease in a cohort of Japanese adults who had newly applied for long-term care needs certification
	• Among the 14,186 participants (mean age 80.4 years, 57.9% women) over a median follow-up period of 22.6 months, those with dual sensory impairment had a 56% higher risk of developing Alzheimer's disease (Hazard Ratio: 1.6, with a 95% CI 1.1–2.2, p = 0.008) compared to those with no sensory impairment
		High	*Focus of study:* Association between sensory impairment and Alzheimer's disease
			
			Publication date: 2024
			
			Jurisdiction: Japan
			
			Methods: Retrospective cohort study
				• Age

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristic	Equity considerations
	• Visual impairment alone (HR: 1.0, CI 0.9–1.2, p = 0.60) and hearing impairment alone (HR: 1.2, CI 0.9–1.5, p = 0.21) were not significantly associated with increased Alzheimer's disease risk in the fully adjusted model. • Kaplan-Meier curves showed that the risk of Alzheimer's disease onset was higher in the hearing impairment only group compared to those with no sensory impairment, although not as high as the dual sensory impairment group, which suggests that individuals with hearing impairment, especially when combined with visual impairment, may be potential targets for Alzheimer's disease prevention			

• Types of hearing loss
  ○ Not specified
• Cause of hearing loss
  ○ Age-related deterioration
• Causality criteria
  ○ Strength of association
  ○ Biological plausibility and coherence
• Type of dementia
  ○ Alzheimer's disease
	Age-related hearing loss was not linked to pathological markers of Alzheimer's disease nor to neuropsychological domains (15)
	• Study aimed to examine the biomarkers for dementia among individuals with hearing loss
	• No statistically significant correlations were identified between amyloid-β and p-tau-level and any of the objective auditory measures after adjusting for age
	• A weak but significant correlation was found between amyloid-β values and the hearing handicap inventory
		High	*Focus of study:* Biomarkers for Alzheimer's disease among individuals with age-related hearing loss
			
			Publication date: 2024
			
			Jurisdiction: Spain
			
			Methods: Cross-sectional study
				• Age

• Types of hearing loss
  ○ Not specified
• Cause of hearing loss
  ○ Age-related deterioration
• Extent/level of hearing loss
  ○ Mild
  ○ Severe
• Causality criteria
  ○ Strength of association
  ○ Consistency of evidence
  ○ Biological plausibility
• Type of dementia
  ○ Alzheimer's disease
  ○ Vascular dementia
• Other dementias (specified as ICD-10: F02.F03)
	The study found individuals with hearing impairment, regardless of severity, had a higher risk of developing dementia compared to those without hearing impairment, and this increased risk was observed across different types of dementia and follow-up periods (4)
	• The aim of the study was to examine the association between hearing impairment and the risk of dementia among old adults
	• This retrospective cohort study analyzed data from 44,728 participants (22,364 with hearing impairment and 22,364 matched controls) in South Korea
	• Individuals with hearing impairment had a significantly higher risk of developing dementia compared to those without (HR: 1.28, 95% CI 1.23–1.34)
	• Both severe (HR: 1.25, 95% CI 1.16–1.35) and mild (HR: 1.29, 95% CI 1.23–1.35) hearing impairment were associated with an increased risk of dementia
	  ○ This increased risk was observed across different types of dementia: Alzheimer's disease (HR: 1.29, 95% CI 1.22–1.37), vascular dementia (HR: 1.25, 95% CI 1.08–1.44), and other dementias (HR: 1.36, 95% CI 1.23–1.50)
		High	*Focus of study:* Association between dementia and hearing loss
			
			Publication date: 2024
			
			Jurisdiction: South Korea
			
			Methods: Retrospective cohort study
				• Not reported

Dimension of organizing framework	Declarative title and key findings	Relevance rating	Study characteristic	Equity considerations
	• The risk remained elevated across various follow-up periods: 0–24 months (HR: 1.28, 95% CI 1.18–1.39), 25–60 months (HR: 1.30, 95% CI 1.19–1.41), and beyond 60 months (HR: 1.20, 95% CI 1.13–1.27)			

• Types of hearing loss
  ○ Not specified
• Extent/level of hearing loss
  ○ Mild
  ○ Moderate
  ○ Moderately severe
  ○ Severe
• Cause of hearing loss
  ○ Congenital
  ○ Occupational
  ○ Recreational
  ○ Age-related deterioration
• Causality criteria
  ○ Temporal relationship
  ○ Strength of association
  ○ Consistency of evidence
• Type of dementia
  ○ Alzheimer's disease
  ○ Not specified
• Contribution to dementia
  ○ Acceleration of dementia
  ○ Amplification of dementia
	Acquired hearing impairment is a risk factor for all-cause dementia; a moderate association was found between hearing impairment and dementia (relative risk of 1.04), with a higher risk ration identified in the less than 85 years age group (8)
	• The primary aim of this cohort study was to utilize audiometric testing and dementia diagnostic testing to determine whether hearing impairment was an independent risk factor for all-cause dementia
	• The study featured 7,135 individuals who were followed over 20.3–23.3 years
	• A moderate 12% increased risk was associated with 10 dB hearing loss in those under 85 years of age (relative risk of 1.12)
	• No association was found in the age group of 85 years and older (possibly due to competing risk of death)
	• The findings of this study (i.e., association and magnitude) are consistent with the existing literature
		High	*Focus of study:* To investigate whether hearing impairment was an independent risk factor for all-cause dementia
			
			Publication date: December 2023
			
			Jurisdiction: Norway
			
			Methods: Prospective cohort study
				• Age

• Types of hearing loss
  ○ Not specified
• Causality criteria
  ○ Consistency of evidence
• Type of dementia
  ○ Not specified
• Contribution to dementia
  ○ Acceleration of dementia
  ○ Amplification of dementia
	Participants with hearing loss in this cohort study had a higher adjusted hazard ratio for dementia (9)
	• The primary objective of this study was to investigate the association between hearing loss and clinical outcomes
	• This retrospective population-based cohort study, conducted in Alberta between April 2004 and March 2019, featured a total of 4,724,646 residents
	• During the median follow-up of 14.4 years, 2.9% of participants developed dementia
	• The hazard ratio of dementia after age-sex adjustments (time varying) was found to be significant at 1.41
		High	*Focus of study:* Investigating the association between hearing loss and clinical outcomes
			
			Publication date: July 2023
			
			Jurisdiction: Alberta
			
			Methods: Retrospective cohort study
				• Age

Appendix 5: Documents excluded at the final stages of reviewing

Document type	Hyperlinked title
Evidence syntheses	Cortical auditory evoked potentials in cognitive impairment and their relevance to hearing loss: A systematic review highlighting the evidence gap
	Effects of cochlear implantation on cognitive decline in older adults: A systematic review and meta-analysis
Single studies	Hearing intervention versus health education control to reduce cognitive decline in older adults with hearing loss in the USA (ACHIEVE): A multicentre, randomised controlled trial
	A pragmatic clinical trial of hearing screening in primary care clinics: Effect of setting and provider encouragement
	Association between hearing loss and clinical outcomes: Population-based cohort study
	Recruitment and baseline data of the aging and cognitive health evaluation in elders (ACHIEVE) study: A randomized trial of a hearing loss intervention for reducing cognitive decline
	Hearing loss, hearing aid use, and risk of dementia in older adults

Waddell K, DeMaio P, Wu N, Dass R, Grewal E, Alam S, Wilson MG. Rapid evidence profile #76: Examining the association between hearing loss and dementia. Hamilton: McMaster Health Forum, 3 July 2024.

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