McMaster University | HEALTH FORUM

Rapid Evidence Profile

Examining the association between hearing loss and dementia

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Context

- Several epidemiological studies have assessed the relationship between hearing loss and dementia given hearing loss tends to precede the clinical onset of dementia by five to 10 years.
- In 2017, and in a 2020 update, The Lancet Commission of dementia prevention, intervention, and care identified hearing impairment as "the most important modifiable risk factor for dementia."(1)
- This rapid evidence profile examines evidence on the association between hearing loss and dementia in efforts to determine whether it meets the six causal criteria of 1) temporality; 2) strength of association; 3) dose-response relationship; 4) consistency of evidence, 5) specificity; and 6) biological plausibility.

Questions

- Is there a causal relationship between hearing loss and dementia?
- What is the nature of the relationship, if any, and what impact do mitigation measures have on it?

Box 1: Evidence and other types of information

+ Global evidence drawn upon

Evidence syntheses selected based on relevance, quality, and recency of search

+ Forms of domestic evidence used (= Canadian)

Evaluation

*** Additional notable features**

Prepared in the equivalent of five-business days using an 'all hands on deck' approach

High-level summary of key findings

- We identified 22 evidence documents, of which 19 were highly relevant, including 13 evidence syntheses and six single studies.
- Generally, the highly relevant evidence documents report an association between hearing loss and all-cause dementia that meets some of the causal criteria.
- We are unable to determine whether this association exists for hearing loss and other forms of dementia due to, in some cases, a lack of included evidence documents (e.g., for Lewy body dementia, frontotemporal dementia, and vascular dementia) and in the case of Alzheimer's disease due to variable findings.
- For **temporal relationships**, consistent findings from evidence syntheses and cohort studies (both prospective and retrospective) establish hearing loss as preceding the onset of dementia.
- For the **strength of association**, evidence syntheses and single studies reported positive, statistically significant associations between hearing loss and cognitive decline and between hearing loss and all-cause dementia.
- Relatively few evidence documents addressed **dose-response relationships**, making it difficult to determine whether this criterion is fulfilled.

- Across included evidence documents, a positive association was **consistently** reported between hearing loss and cognitive impairment, and between hearing loss and all-cause dementia, with the associations generated in different evidence syntheses stemming from different study methods.
- The criterion of **specificity** was partially met for the association between hearing loss and all-cause dementia, whereby included evidence syntheses undertook sub-analyses to identify other exposures that may result or contribute to dementia.
  - However, additional information regarding the causal mechanism is needed.
- Few evidence documents directly addressed **biological plausibility**, but one evidence synthesis found that hearing loss and Lewy body dementia share a high neuritic plaque burden, while hearing loss and all-cause dementia share radiological and biomolecular similarities.

Framework to organize what we looked for

- Types of hearing loss
  - Sensorineural hearing loss (i.e., resulting from inner ear or auditory nerve dysfunction)
  - Mixed hearing loss (i.e., sensorineural hearing loss with a conductive component overlaying all or part of the audiometric range tested)
  - Central hearing loss (i.e., caused by a problem with the auditory nerve or sound centres)
  - Not specified
- Extent/level of hearing loss
  - Mild
  - Moderate
  - Moderately severe
  - Severe
- Cause of hearing loss
  - Congenital
  - Occupational
  - Recreational
  - Age-related deterioration

Box 2: Approach and supporting materials

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.

We identified evidence addressing the question by searching ACCESSSS and PubMed. All searches were conducted on 11 June 2024. The search strategies used are included in Appendix 1. In contrast to synthesis methods that provide an in-depth understanding of the evidence, this profile focuses on providing an overview and key insights from relevant documents.

We searched for full evidence syntheses (or synthesis-derived products such as overviews of evidence syntheses) and protocols for evidence syntheses.

We appraised the methodological quality of evidence syntheses that were deemed to be highly relevant using the first version of the AMSTAR tool. AMSTAR rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality, medium-quality evidence syntheses are those with scores between four and seven, and low-quality evidence syntheses are those with scores less than four. The AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to evidence syntheses pertaining to delivery, financial, or governance arrangements within health systems or implementation strategies.

A separate appendix document includes:
1) methodological details (Appendix 1)
2) key findings from evidence syntheses and single studies related to the six criteria for establishing causality for hearing loss (Appendix 2)
3) details about each identified synthesis (Appendix 3)
4) details about each identified single study (Appendix 4)
5) documents that were excluded in the final stages of review (Appendix 5).

This rapid evidence profile was prepared in the equivalent of five days of a 'full court press' by all involved staff.

- Causality criteria
  - Temporal relationship (e.g., exposure must precede the occurrence of the outcome)
  - Strength of association (e.g., association should meet statistical significance to demonstrate that it was not simply a chance occurrence)
  - Dose-response relationship (e.g., evidence that increasing exposure increases the risk of the outcome)
  - Consistency of evidence (e.g., similar or the same results generated by studies using different methods in different settings)
  - Specificity (e.g., the exposure is the only cause of the outcome that can be shown)
  - Biological plausibility and coherence (e.g., the association between the exposure and outcome should be plausible and consistent with current knowledge)
- Type of dementia
  - Alzheimer's disease
  - Frontotemporal dementia
  - Lewy body dementia
  - Vascular dementia
  - All-cause dementia
- Contribution to dementia
  - Acceleration of dementia
  - Amplification of dementia
- Mitigation measures
  - Effects of hearing aids
  - Effects of cochlear implants
  - Effects of treatment

What we found

We identified 23 evidence documents, of which we determined 19 to be highly relevant, including:

- 13 evidence syntheses
- six single studies.

Coverage by and gaps in existing evidence syntheses and domestic evidence

Generally, the highly relevant evidence documents report an association between hearing loss and all-cause dementia. Very few of the included documents specified the type of hearing loss included in the evidence syntheses and single studies. The exceptions to this were five evidence syntheses and two single studies that focused exclusively on age-related hearing loss. However, these evidence documents did not differentiate whether the hearing loss was sensorineural, mixed, or central.

The included evidence documents covered all causality criteria, with most of the included documents providing evidence for three of the causality criteria: 1) temporal relationship (i.e., associations identified in evidence syntheses of longitudinal prospective cohort studies); 2) strength of association (i.e., finding statistically significant associations between hearing loss and dementia); and 3) consistency of evidence (i.e., similar results reported across types of studies). We found limited evidence that provided explicit insight about the remaining three causality criteria of specificity, dose-response relationship, or biological plausibility.

Most of the included evidence documents examined the association between hearing loss and all-cause dementia, with relatively fewer providing findings about cognitive impairment (i.e., impairment that doesn't meet the level of a dementia diagnosis), Alzheimer's disease, vascular dementia, and Lewy body dementia. No evidence documents addressed frontotemporal dementia.

The included evidence documents did not make definite statements about the causal path between hearing loss and dementia or whether hearing loss accelerated or amplified dementia. Three evidence documents – two evidence syntheses and one single study – identified the effects of hearing aids on the association between hearing loss and dementia. A summary of this evidence is included following an overview of the causality criteria.

Key findings from included evidence documents on causality criteria

Temporal relationship

Five evidence syntheses (two recent high-quality, one older high-quality, one recent medium-quality, and one older low-quality) and four recent single studies provided evidence of the temporal relationship between exposure and outcome.(2-10) The findings from evidence syntheses and single studies were largely based on cohort studies – including prospective, retrospective and cross-sectional designs – which may be used to establish temporality between exposure (hearing loss) and the outcomes of interest (dementia). There is consistent evidence of a temporal relationship between hearing loss and cognitive decline,(2) as well as for hearing loss and all-cause dementia.(2; 5-10) However, we found mixed results for hearing loss and Alzheimer's disease,(2-5) and insufficient evidence to determine the temporal relationship between hearing loss and vascular dementia, though the single included study noted an elevated risk.(5)

Strength of association

Ten evidence syntheses (three recent high-quality, one older high-quality, five recent medium-quality, and one older low-quality)(2; 3; 6-8; 11-15) and five single studies (one prospective cohort, three retrospective cohort, and one cross-sectional) provide findings on the strength of association between hearing loss and dementia.(4; 5; 9; 10; 16)

Evidence syntheses found a positive statistically significant association between hearing loss and cognitive impairment and non-specific cognitive decline, with hazard ratios ranging from 1.11 (95% CI 1.06–1.15) to 1.44 (95% CI 1.27–1.64).(8; 12; 14) One of the evidence syntheses specifically examined age-related hearing loss and cognitive impairment and found a positive statistically significant association, reporting a hazard ratio of 1.30 (95% CI 1.16–1.45).(13)

Evidence syntheses and single studies did not conclusively provide evidence of the strength of the association between hearing loss and Alzheimer's disease. While two evidence syntheses (one recent medium-quality and one older low quality) and one retrospective cohort study reported positive statistically significant associations,(3; 5; 15) others, including one older high quality evidence synthesis and two cross-sectional studies, did not identify an association.(2; 16; 17)

One 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).(17)

One evidence synthesis and one cross-sectional cohort study found no statistically significant association between hearing loss and vascular dementia.(2; 8)

Four evidence syntheses (two recent high-quality and two recent medium-quality) (6-8; 12) and two recent cohort studies (one prospective and one retrospective) (9; 10) found a statistically significant association between hearing loss and developing all-cause dementia, with hazard ratios ranging from 1.21 (95% CI 1.11–1.31) to 1.59 (95% CI 1.37–1.86) and risk ratios ranging from 1.04 (95% CI 1.00–1.09) to 1.41 (95% CI 1.38–1.43).

Dose-response relationship

Two evidence documents provided findings related to a dose-response relationship between hearing loss and two different types of dementia, Lewy body dementia and all-cause dementia. The first was a cross-sectional study that found the association between Lewy body pathology and hearing impairment did not increase with higher cortical pathology.(17) The second finding came from a recent medium-quality evidence synthesis, which reported a 10 dB worsening of hearing loss to be associated with an increase in dementia risk.(8)

Consistency of evidence

Across the included evidence documents, a positive association was consistently reported between hearing loss and cognitive impairment, as well as between hearing loss and all-cause dementia. The associations generated within evidence syntheses included different methods such as an overview of systematic reviews, cohort studies (retrospective, prospective, and cross-sectional), cross-sectional studies, and matched case-control studies.(2; 6; 13; 14)

An insufficient number of documents were identified to determine the consistency of evidence for the association between hearing loss and Lewy body dementia or hearing loss and vascular dementia. Inconsistent evidence was reported for the association between hearing loss and Alzheimer's disease.(2; 3; 5; 15-17)

Specificity

Findings related to specificity were only identified for the association between hearing loss and two forms of dementia – cognitive impairment and all-cause dementia. For the association between hearing loss and cognitive impairment, one recent medium-quality evidence synthesis reported significant heterogeneity among the studies included in a pooled analysis, limiting the specificity of the results.(14)

Regarding the association between hearing loss and all-cause dementia, many of the included evidence syntheses and single studies reported adjusting for age and sex, while others included additional sub-analyses to determine that the association was not affected by study characteristics, including diagnostic methods, validation strategies for dementia, or follow-up duration.(6; 7; 9) Further, one older high-quality evidence synthesis did report lower odds ratios in cohort studies than those calculated from cross-sectional studies.(2) However, both remained statistically significant.(2) Finally, one prospective cohort study that followed individuals for over 20 years reported that it was unlikely that a reverse causation was present between hearing loss and all-cause dementia given the length of time during which individuals participated in the study.(9)

Biological plausibility

Though most of the included evidence documents spoke to the biology of dementia and hearing loss, only three evidence documents – two cross-sectional studies and one recent low-quality evidence synthesis – included findings specific to biological plausibility.

For the association between hearing loss and Alzheimer's disease, a cross-sectional study found that the neuropsychological domains most correlated with hearing loss were executive function and processing speed rather than memory typically affected in early Alzheimer's disease (e.g., amyloid deposition and p-tau), suggesting that age-related hearing loss may not be directly linked to Alzheimer's disease pathology in cognitively unimpaired older adults.(16)

For the association between hearing loss and Lewy body dementia, a cross-sectional study found some support for the association between dementia-related neuropathology and hearing loss, suggesting that hearing loss may be

associated with a high neuritic plaque burden, which is also associated with the development of Lewy body dementia.(17)

Finally, for all-cause dementia, a recent low-quality evidence synthesis found hearing loss and dementia share radiological (e.g., white matter hyperintensities) and biomolecular (e.g., brain atrophy) similarities, suggesting the potential for biological plausibility.(18)

Key findings from evidence documents on the impact of mitigation measures

Two recent medium-quality evidence syntheses reported on the effects of mitigation measures. The first synthesis included both randomized controlled trials and case-control studies and found that older participants with hearing loss who used hearing restorative devices experienced a lower risk of cognitive decline than those with uncorrected hearing loss.(19) The association remained significant after adjusting for age, sex, education, socio-economic status, and existing co-morbidities.(19)

However, the second evidence synthesis found that hearing aids did not increase cognitive function among patients with hearing loss and Alzheimer's disease, which may be due in part to underlying mechanisms of Alzheimer's disease.(20)

Next steps based on the identified evidence

- While the association between hearing loss and all-cause dementia does meet many of the causal criteria including temporality, strength of association, specificity, and consistency, additional research efforts should focus on generating evidence about other causal mechanisms, which may require additional research that examines the association by type of hearing loss.
- Additional research efforts could also focus on other forms of dementia, particularly on the relationship between hearing loss and Alzheimer's disease, which remains unclear from the included evidence.

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