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Commentary: Hearing loss, dementia and the danger of professional rabbit holes- a comment on Livinston et al., 2024

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Editor's Note: ENT & Audiology News, a British publication, was gracious enough to allow CanadianAudiologist to reprint this article by Doctors Munro and Dawes. Like a cup of tea, this article cuts through a labrynth of terminology and misinterpretation in this important area. Phrases such as "relative risk" are discussed to remind us that the word "relative" is not just an adjective, but that the phrase has a well-defined, and often misleading definition. The original citation of this article is ENT & Audiology News, September, 2024. Pinpoint Publishing. For additional information check out Dawes P, Munro KJ. (2024). Hearing loss and dementia: where to from here? Ear and Hearing, 45(3), 529-536.

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Background

Dementia is a major global challenge: the incidence may be decreasing in some high-income countries, such as the UK, but the number of people living with dementia is growing because of increases in life expectancy. This is a ticking time bomb with devastating consequences for patients, families and carers, and the health and care system.

The Lancet publishes Commissions on pressing issues in science, medicine, and global health, with the aim of providing recommendations that change health policy or improve practice. The most recent report comes from the standing Commission on dementia prevention, intervention, and care, originally published by Livingston *et al* in 2017 and updated in 2020. For the new report (Livingston *et al*, 2024), about half of the 27 authors are UK-based and about half are specialists in

psychiatry. Unless we are mistaken, no author has primary expertise in hearing science.

Since prevention is better than cure, the updated report highlights 14 potentially modifiable risk factors throughout the life course (up from 9 in 2017 and 12 in 2020). It also highlights advances in new liquid biomarkers, preventative interventions and treatments. Consistent with the priorities of many research funding agencies, the report is clear that ensuring consideration of all cultures and ethnicities is essential to target help to people who need it most. Ultimately, there is a need to understand how risk factors vary across diverse populations. The report represents an enormous amount of work and continues to deservedly receive widespread attention, but it is not perfect when discussing hearing loss and hearing aids (see below).

Relevance to audiology and hearing science

It is *de rigueur* in publications on hearing loss to commence with statistics on worldwide hearing loss and disease burden, followed invariably by a sentence on the association between hearing loss and dementia. Like Lewis Caroll's Alice in Wonderland, we may be in danger of going down a professional rabbit hole: the attention devoted to hearing loss and dementia may become a distraction from the evidence-based importance of healthy hearing for healthy ageing, an important social responsibility.



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Some of the key points in the report have been misunderstood or misreported by the hearing community. Here we provide three examples:

1. What does risk mean in epidemiological studies? In everyday language, risk suggests something that may <u>cause</u> another; for example, heavy rain brings risk of flooding (i.e., if it continues to rain, it will cause flooding). In epidemiology studies, risk means an <u>association</u> or marker, not

necessarily the cause. It is a logical fallacy that arises from thinking because two things co-occur, one must have caused the other. There has been a tendency to erroneously state that hearing loss causes dementia.

- 2. Modifiable and potentially modifiable risk factors. Some risk factors are <u>known</u> to modify the chances of disease; for example, Type II diabetes (disease) can be modified by changes in diet (risk). A potentially modifiable risk factor is something that <u>may</u> cause the disease and can be modified. Hearing loss is a marker for dementia. It is a <u>potentially</u> modifiable risk factor for dementia but only if it actually causes dementia and can be successfully treated (see below for more discussion). There has been a tendency to omit the word "potentially" when discussing hearing as a modifiable risk factor. This one word can make a world of difference.
- 3. Personal risk. The risk to an individual with hearing loss is reported as a relative risk (RR; the probability of developing dementia with hearing loss divided by the probability without hearing loss). However, many in our profession misuse the weighted population attributable fraction (PAF, the reduction in dementia cases that would occur if exposure to a risk factor was completely abolished) to demonstrate personal risk. The RR for the various potentially modifiable risk factors identified in the report are shown in Table 1. The report explains that removing the risk (e.g., minimise diabetes and reduce air pollution) may reduce neuropathological damage or increase and maintain cognitive reserve. This is not a competition to identify the factor with the highest RR, but we have ranked the factors in Table 1 according to the 2024 risk estimate to illustrate trends. For example, less education (a potential risk because of less cognitive reserve and less cognitively stimulating occupations) has remained unchanged over time. On the other hand, RR for both depression and diabetes has increased. Importantly, for those working in audiology, the biggest reduction in RR is for hearing loss, down from 1.9 to 1.4, based largely on the review by Yu et al (2024). The reason for the reduction in RR estimates for hearing loss is because of the inclusion of additional studies modelling dementia risk associated with hearing loss that included more extensive control for potential confounds.

The Lancet report year	2024	2020	2017
Depression	2.2 (1.7-3.0)	1.9 (1.6-2.3)	1.9 (1.6-2.3)
Traumatic brain injury	1.7 (1.4-1.9)	1.8 (1.5-2.2)	-
Diabetes	1.7 (1.6-1.8)	1.5 (1.3-1.8)	1.5 (1.3-1.8)
Less education	1.6 (1.3-2.0)	1.6 (1.3-2.0)	1.6 (1.3-2.0)
Social isolation	1.6 (1.3-1.8)	1.6 (1.3-1.9)	1.6 (1.3-1.9)
Untreated vision loss	1.5 (1.4-1.6)	-	-
Hearing loss	1.4 (1.0-1.9)	1.9 (1.4-2.7)	1.9 (1.4-2.7)
Obesity	1.3 (1.0-1.7)	1.6 (1.3-1.9)	1.6 (1.3-1.9)
High LDL cholesterol	1.3 (1.3-1.4)	-	-
Smoking	1.3 (1.2-1.4)	1.6 (1.2-2.2)	1.6 (1.2-2.2)
Excessive alcohol consumption	1.2 (1.0-1.5)	1.2 (1.1-1.3)	
Hypertension	1.2 (1.1-1.4)	1.6 (1.2-2.2)	1.6 (1.2-2.2)
Physical inactivity	1.2 (1.2-1.3)	1.4 (1.2-1.7)	1.4 (1.2-1.7)
Air pollution	1.1 (1.1-1.1)	1.1 (1.1-1.1)	-

Table 1. Potentially modifiable risk factors, ranked according to relative risk for dementia (95% CI) in the 2024 Lancet commission on dementia, intervention, prevention and care (Livingston *et al*, 2024).

It is noteworthy that the RR for untreated vision loss, an addition in the 2024 report, is very similar to the RR for hearing loss. The top five personal risks for dementia are: depression, traumatic brain injury, diabetes, less education and social isolation. This may change over time because the report identifies several potential risk factors where there is currently insufficient evidence (e.g., diet is relevant for healthy ageing and relevant to the risk factors of obesity and diabetes) - definitely an area to watch. In our experience, public facing documents and websites containing statements such as, "hearing loss is the single greatest risk factor for dementia" are misleading because the public generally assume this is referring to personal risk.

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Each author in the report wrote at least one section and "unanimously agreed on the best available evidence and its consistency." Therefore, it takes a brave person to dispute the contents of the report. However, we would like to highlight three issues to stimulate discussion and encourage critical thinking.

- 1. *Population attributable fraction (PAF)*. To our mind, the calculation of PAF is probably the most methodologically problematic part of the report.
 - The updated PAF is 7% (down from 9% and 8% in the 2017 and 2020 reports, respectively). This means 7% of dementia cases could be avoided, assuming hearing loss causes dementia and all hearing loss could be completely eliminated or entirely mitigated. However, risk factors may co-occur in a clinically meaningful way in some individuals (Xiong et al, 2024). The Lancet report does not account for this co-occurrence, or if different combinations lead to different clinical outcomes. Therefore, we do not know if PAF has been over or underestimated.
 - The 2017 and 2020 reports estimated the size of the population with 'midlife hearing loss' to be 31.7%. The 2024 report a substantially increased population estimate of 59% without any explanation for the increase (see Table 2). It is not clear that 59% is a realistic estimate of the proportion of the general population that is relevant to hearing loss as a 'potentially modifiable risk factor'. The PAF would be considerably lower than 7% if the 2017 prevalence estimate of 31.7% had been used.
 - The report assumes that all risk factors are causal and can be completely eliminated (Kivipelto *et al*, 2024). We do not know if hearing loss causes dementia and most people with hearing loss do not own hearing aids. The best available evidence so far (from a single study) suggests that hearing aids may mitigate cognitive decline, but only among those with hearing loss worse than 30 dB HL who also have other risks for dementia (i.e. a 'high risk' subgroup characterised by high levels of diabetes; the ACHIVE trial; Lin *et al*, 2024). It is not clear to us that the improvement in audibility and/or social interactions for relatively mild hearing losses are sufficient to explain the findings. This suggests that *if* it is possible to mitigate cognitive decline and dementia risk, it is only potentially feasible in a fraction of the population with hearing loss.

In summary, questionable assumptions and uncertainties about the validity of data used to calculate PAF means we are inclined to treat it with a "pinch of salt". In any case, it is RR that is important to both the individual and the health care professional (see our earlier point three, above).

The Lancet report year	2017	2020	2024
RR for dementia	1.9 (1.4-2.7)	1.9 (1.4-2.7)	1.4 (1.0-1.9)
Prevalence estimate for "mid-life" hearing loss	31.7%	31.7%	59%
Population attributable fraction for mid-life" hearing loss	9.1%	8.2%	7%

Table 2. Relative risk for dementia, prevalence estimates, and population attributable fraction associated with 'mid life hearing loss' from *The Lancet* commission on dementia intervention, prevention and care (Livingston *et al*, 2024).

2. Association is not causation. The report states that evidence from observational studies comparing outcomes for hearing aid users versus non-users continues "to suggest a causal association with the clinical expression of dementia." Likewise, the executive summary states that, "The evidence that treating hearing loss decreases the risk of dementia is now stronger than when our previous Commission report was published." Also, the key message section (second page) states that specific actions to reduce dementia risk across the life course includes making hearing aids accessible for people with hearing loss. These are bold statements and clinician scientists in audiology like us would have preferred a more nuanced approach.

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There is a danger that these statements will lead to policy-based decisions, which will then be used as evidence, instead of the evidence-base informing policy. The association between hearing loss and dementia/cognitive decline is based primarily on observational studies. Even if there is: (i) consistency across studies, (ii) evidence that one (hearing loss) precedes the other (dementia), and (iii) a dose effect (more hearing loss means greater risk of dementia), this does not rule out a common cause. For example, we think it possible that a vascular pathology could affect the inner ear first because of the high demand for oxygen. Additionally, pathological changes in hearing may be detected earlier because of massively redundant parallel, neural pathways that may delay the ability to detect the damage that causes dementia. This is not to deny the *possibility* that hearing loss may cause dementia either directly (changes to the brain because of reduced auditory input or the impoverished auditory input meaning greater reliance on finite cognitive reserves) or indirectly (e.g., via lack of social stimulation). There is currently a lack of good quality evidence to settle the question [but see Griffiths *et al* (2024) for a discussion on likely mechanisms].

3. Benefit of hearing intervention. The Lancet report discusses the long-awaited outcome of the ACHIEVE trial, an impressive large scale randomised controlled trial (RCT) of a hearing aid intervention on reducing cognitive decline among a group of people with hearing loss. The Lancet report could benefit from providing more critical scrutiny of the results from ACHIEVE. The main finding of ACHIEVE was negative – no effect of hearing aids in reducing cognitive

decline. But *The Lancet* report does not offer any discussion of this finding. The Lancet report focuses on the results of a post-hoc secondary analysis that appears to show a benefit of hearing aids in reducing cognitive decline among a subgroup of people characterised by the ACHIEVE authors as a 'high risk' group. *The Lancet* report could have offered more scrutiny of this secondary result because there are several reasons to be cautious that this secondary result may be spurious e.g., small effect size [Cohen's d = 0.25; 0.2-0.5 are considered small], lack of a dose response and potential comorbidity (Dawes and Munro, 2024). The evidence on effective interventions for dementia appears to be pointing towards the need for multidomain interventions, personalised to the risk profile of the individual.

What we know and what we don't know

We know that:

- Hearing loss is a marker of brain health (as is vision, balance, smell, touch and taste; Albers *et al* (2015) and there is consistent evidence of an association with cognitive decline/dementia.
- Current estimates of individual risk of dementia associated with hearing loss are lower than with depression, traumatic brain injury, diabetes, low education and social isolation. Individual risk for dementia with hearing loss is generally similar to the risk associated with untreated vision loss, obesity, high LDL cholesterol and smoking.
- Hearing loss is important in its own right: (i) it ranks third for Years Lived with a Disability (YLD), (ii) first for sensory loss in over 70-year-olds, and (iii) impacts Quality of Life.
- Hearing aids have proven benefits for improving communication and social interactions. They facilitate well-being and an active, engaged, independent & healthier older age.
- Negative messaging that links hearing loss to risk of dementia is not socially responsible and may result in stigma and discourage help-seeking.

We do not know:

- If hearing loss causes dementia because any mechanisms linking peripheral hearing loss and cortical degeneration are unknown.
- If hearing aids reduce the risk of dementia. Although low-quality evidence (from observational studies) suggests interventions for hearing loss may reduce the risk of dementia, there are few high RCTs. One high quality hearing intervention RCT did not show any reduction in cognitive decline in the general population. A secondary analysis showing a small effect in a "high risk" population awaits replication.

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