RESEARCH ARTICLE

Treating Hearing Loss With Hearing Aids for the Prevention of Cognitive Decline and Dementia

Lachlan Cribb,[1] Margarita Moreno-Betancur,[2,3] Matthew Paul Pase,[4] Rory Wolfe,[1] Carlene Britt,[1] Zhen Zhou,[1] Raj C. Shah,[5] Gary Rance,[6] Kerry M. Sheets,[7,8] Trevor T.-J. Chong,[9,10,11] Robyn L. Woods,[1] Anne M. Murray,[12,13,14] Alice Owen,[1] and Joanne Ryan[1]

Correspondence
Mr. Cribb
lachlan.cribb@monash.edu

Neurology® 2026;106:e214572. doi:10.1212/WNL.0000000000214572

Abstract

Background and Objectives

Hearing loss is a risk factor of cognitive decline and dementia. We sought to investigate the effect of hearing aid (HA) use on cognition and dementia risk in older adults with hearing impairment.

Methods

We emulated a target trial using data from Australian participants of the ASPirin in Reducing Events in the Elderly study. In the target trial, eligible participants were dementia-free, had moderate hearing impairment, and had no previous HA use. The treatment strategies were "use HAs" and "do not use HAs." Outcomes included overall cognition, dementia (DSM-IV criteria), and cognitive impairment (cognitive decline or dementia). The emulation used new HA prescription and frequency-of-use data measured by questionnaire, as well as cognition data from semiannual assessments over 7 years. Self-reported hearing problems were used as a proxy for moderate hearing impairment. Using the parametric g-formula, we estimated observational analogs of the intention-to-treat effect, using HA prescription to emulate allocation. Analyses for cognition outcomes were restricted to survivors. Multiple imputation was used for missing covariate and cognitive outcome data. We also emulated a second target trial with treatment strategies of (1) never, (2) rarely/sometimes, and (3) often/always use HAs.

Results

Across imputed data sets, a median of 2,777 eligible individuals were included, with a median of 664 receiving a new HA prescription. The mean age was 75 years, and 48% were female. The estimated 7-year mean overall cognition scores among survivors were similar under HA prescription and no HA prescription (mean difference 0.03 SDs; 95% CI −0.14 to 0.21). The estimated 7-year risk of dementia was 5.0% under HA prescription and 7.5% under no HA prescription (risk ratio [RR] 0.67; 95% CI 0.37–0.97), and that of cognitive impairment was 36.1% under HA prescription and 42.4% under no HA prescription (RR 0.85; 95% CI 0.70–1.00). The risks of dementia and cognitive impairment were inversely associated with the frequency of HA use.

Discussion

We found that HA use in older people with hearing impairment may reduce dementia risk, although differences in age-related cognitive change were insubstantial. We cannot rule out residual confounding as an explanation for our findings. Long-term randomized trials of HAs for dementia risk are justified.

MORE ONLINE

Class of Evidence
Criteria for rating therapeutic and diagnostic studies
NPub.org/coe

Null Hypothesis
A collection of negative, inconclusive, or replication studies; in partnership with the Center for Biomedical Research Transparency
NPub.org/Null

Supplementary Material

[1]School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia; [2]Clinical Epidemiology & Biostatistics Unit, Murdoch Children's Research Institute, Melbourne, Australia; [3]Clinical Epidemiology & Biostatistics Unit, Department of Paediatrics, The University of Melbourne, Australia; [4]School of Psychological Sciences and Turner Institute for Brain and Mental Health, Monash University, Melbourne, Australia; [5]Department of Family & Preventive Medicine and the Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, IL; [6]Department of Audiology and Speech Pathology, The University of Melbourne, Australia; [7]Department of Medicine, Hennepin Healthcare, Minneapolis, MN; [8]Department of Medicine, University of Minnesota, Minneapolis, MN; [9]Turner Institute for Brain and Mental Health, School of Psychological Sciences, Monash University, Melbourne, Australia; [10]Department of Neurology, Alfred Health, Melbourne, Australia; [11]Department of Clinical Neurosciences, St Vincent's Hospital, Melbourne, Australia; [12]Berman Center for Outcomes & Clinical Research, Hennepin HealthCare Research Institute, Minneapolis, MN; [13]Department of Medicine, Geriatrics Division, Hennepin Healthcare, Minneapolis, MN; [14]Departments of Medicine and Neurology, University of Minnesota, Minneapolis, MN.

This Null Hypothesis article is published as part of a collaborative effort between *Neurology*® and CBMRT.

Glossary

3MS = Modified Mini-Mental State Examination; **ACHIEVE** = Aging and Cognitive Health Evaluation in Elders; **AD** = Alzheimer disease; **ALSOP** = ASPREE Longitudinal Study of Older Persons; **ASPREE** = ASPirin in Reducing Events in the Elderly; **ASPREE-XT** = ASPREE-eXTension; **COWAT** = Controlled Oral Word Association Test; **DSM-IV** = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; **HA** = hearing aid; **HVLT-R** = Hopkins Verbal Learning Test–Revised; **PTA** = pure tone average; **RR** = risk ratio; **SDMT** = Symbol Digit Modalities Test.

Classification of Evidence

This study provides Class III evidence that the use of hearing aids did not change overall cognitive scores in people 70 years and older with moderate hearing impairment as compared to those who used hearing aids.

Introduction

Hearing loss is highly prevalent in older age and is associated with increased dementia risk.[1] Posited mechanisms for this association include (1) a common neuropathic pathway for hearing loss and dementia; (2) sensory deprivation leading to neuronal atrophy; (3) hearing difficulty leading to social withdrawal; (4) changes to cognitive load due to increased listening effort; and (5) an interaction between the neuronal demands of difficult listening and existing Alzheimer disease (AD) pathology (citations in references 2, 3). Observational evidence suggests that treating hearing loss with hearing aids (HAs) could reduce the risk of cognitive decline.[4] Nonetheless, treatment uptake is low, with HAs used by only a small proportion of those with meaningful hearing loss.[5]

Recently, the Aging and Cognitive Health Evaluation in Elders (ACHIEVE) randomized trial investigated the effectiveness of treating hearing loss for the prevention of cognitive decline. ACHIEVE was a parallel-group, unblinded trial that compared HAs, in conjunction with other hearing assistive technologies, with a health education control among older adults in the United States with untreated hearing loss (aged 70–84 years; n = 977).[6] After 3 years, the intervention had no effect on cognitive decline relative to control (mean difference in change in overall cognition score 0.00 SD, 95% CI −0.08 to 0.08) and had ambiguous effects on cognitive impairment (hazard ratio 0.90, 95% CI 0.61–1.33). There was, however, a substantial reduction in cognitive decline associated with HAs in a subgroup recruited into ACHIEVE from the Atherosclerosis Risks in Communities cohort, who were more likely to be older, female, have lower educational attainment, poorer cardiometabolic health, and poorer cognition relative to other participants.[6]

Given the relatively short duration of follow-up in ACHIEVE, it could not address some important questions. These include the effect of HAs on incident dementia risk and the long-term effect of HAs on cognition.[7] In this study, we sought to complement the evidence provided by ACHIEVE by addressing these gaps. Specifically, our primary aim was to investigate the longer term (7-year) effect of HA use on cognition and dementia risk using observational data from the ASPirin in Reducing Events in the Elderly (ASPREE) study[8] and associated substudies. Secondary aims were to investigate (1) the effect of HA use frequency on cognition and dementia risk and (2) effect modification by pretreatment age, hearing function, cognition, and physical health.

Methods

Observational Data Source

Data were obtained from Australian participants of the ASPREE trial and its observational follow-up called the ASPREE-eXTension (ASPREE-XT).[8,9] ASPREE was a randomized, placebo-controlled trial investigating low-dose aspirin for disability-free survival in 19,114 older individuals (aged ≥70 years for Australian participants) in Australia and the United States. In Australia, participants were recruited through collaboration with their primary care physician between 2010 and 2014. Within 3–6 months of randomization (although 15% were delayed by up to 18 months), approximately 90% of the Australian ASPREE participants completed questionnaires on medical and social health factors, including the prescription and use of HAs, as part of ASPREE Longitudinal Study of Older Persons (ALSOP), a cohort study nested within the subsample of Australian ASPREE participants.[10] Follow-up ALSOP questionnaires were completed approximately 3 years later.[10] ASPREE participants were followed prospectively until the trial ended in 2017. Participants were then invited to participate in ASPREE-XT, which continued to assess participants annually for 7 years.[11] A subset of ASPREE participants (n = 1,270) underwent baseline audiometry assessments as part of the ASPREE-Hearing substudy.[12]

In Australia, HAs are provided free of charge to aged and disability cardholders through the Hearing Services Program. Funding is also provided by the Australian Department of Veterans' Affairs and private health insurers. Most or all HAs during the study period would have been provided within a hearing clinic by an audiologist.

Protocol for the Target Trials and Their Emulation Using Observational Data

We designed the analysis of these data to emulate 2 target trials (i.e., the hypothetical, pragmatic randomized trials that would be conducted to answer our research questions, were they feasible and timely to conduct).[13] The protocols for the target trials and their emulation using observational data are presented in Table 1. The protocols of the target trials are similar to that of the ACHIEVE trial, except that the target trials are pragmatic (i.e., performed in conditions similar to routine clinical care; eTable 1 gives a comparison).

Eligibility Criteria

Inclusion criteria for the target trials included age 70+ years, moderate hearing impairment (better-ear 4-frequency [0.5–4 kHz] pure tone average [PTA] of ≥30 dBHL and <70 dBHL), and being free of dementia (Table 1). Exclusion criteria included past HA use and contraindications for HAs (e.g., fluctuating conductive hearing loss).

In the observational emulation, we assessed participants for eligibility based on their data at recruitment into ALSOP/ASPREE, except for survival and remaining event-free (for

Table 1 Protocol for the Target Trial and Observational Emulation

Protocol component	Target trials	Observational emulation
Eligibility criteria	Inclusion criteria: • Aged 70+ y • Moderate hearing impairment[a] • 3MS score >77 • Community dwelling Exclusion criteria: • Dementia • Inability/severe difficulty or requiring assistance in performing any activities of daily living • Previous HA use or cochlear implant • Poor visual acuity[b] • Medical contraindication to/unwillingness to wear HAs	Inclusion criteria: Same as target trial, except (1) self-reported hearing impairment is used instead of moderate hearing impairment and (2) consent for participation in ASPREE and ALSOP is required Exclusion criteria: Same as target trial, except (1) no exclusion for medical contraindication to/unwillingness to wear HAs (data unavailable) and (2) other ASPREE study exclusion criteria[c]
Treatment strategies	Target trial 1 • Use HAs • Do not use HAs Target trial 2 • Never use HAs • Use HAs rarely or sometimes (>0 and ≤3 times per month) • Use HAs often or always (>3 times per month)	Same as target trial
Assignment procedure	Participants are randomly allocated to one of the treatment strategies without blinding	Participants are assigned to strategies consistent with their observed data
Outcome	• Overall cognition score over follow-up, estimated as the single factor from a confirmatory factor analysis model including all tests from cognitive battery • Scores on individual cognitive tests over follow-up • Time to dementia (DSM-IV criteria) • Time to cognitive impairment (cognitive decline and dementia composite)	Same as target trial
Follow-up	Follow-up begins once treatment is assigned. Follow-up ends after 7 y, death, or loss to follow-up (whichever occurs first)	Follow-up begins at the third year of the ASPREE study (when the second ALSOP questionnaire is completed and new HA prescriptions and use frequency were reported). Follow-up ends after 7 y (i.e., 10 y after recruitment into ASPREE/ALSOP), death, or loss to follow-up (Figure 1)
Causal contrast	Intention-to-treat effect and per-protocol effect For cognitive scores, comparisons at a given follow-up point are restricted to only those who survive until at least that point (i.e., partly conditional effects).[14] For time-to-event analyses, the total effect (cause-specific cumulative incidence) is estimated.[15] Main text provides details	Same as target trials except only observational analogs of the intention-to-treat effect are estimated
Statistical analysis	Effects are estimated using the parametric g-formula	Missing data in eligibility criteria, covariates, and cognitive scores are imputed by fully conditional specification. Effects are estimated using the parametric g-formula, with adjustment for baseline confounders and time-varying predictors of censoring (for survival outcomes)

Abbreviation: 3MS = Modified Mini-Mental State Examination; ALSOP = ASPREE Longitudinal Study of Older Persons; ASPREE = ASPirin in Reducing Events in the Elderly; HA = hearing aid.
[a] Better-ear 4-frequency (0.5–4 kHz) pure tone average of ≥30 dBHL and <70 dBHL.
[b] Visual limitation in completing the 3MS.
[c] Including previous cardiovascular disease events and not being expected to survive for the next 5 years (original trial report provides details[9]).

time-to-event analyses), which were assessed at the third year of the ASPREE study (Figure 1). Because audiometry data were only available for a subset of participants, we used self-reported hearing problems as our criterion for moderate hearing loss in the primary analysis (eFigure 1 displays the distribution of audiometric hearing loss of those self-reporting hearing problems, in the subset with audiometry data available). Some criteria, such as the exclusion of those with contraindications for HAs, could not be emulated because these data were unavailable in the observational data set (Table 1).

Treatment Strategies

First Target Trial

The treatment strategies for the first target trial were (1) use HAs over follow-up and (2) do not use HAs over follow-up.

Second Target Trial

The treatment strategies for the second target trial were use HAs with the following frequencies over follow-up: (1) never, (2) rarely/sometimes (>0 and ≤3 times per month), and (3) often/always (>3 times per month). The strategies were the same in the observational emulation.

Assignment

In each target trial, participants are randomly assigned to a given strategy and are aware of their assignment. In the emulation of the first target trial, we assigned participants to the "use HAs" strategy if they reported a new HA prescription in the second ALSOP questionnaire, and to the "do not use HAs" strategy otherwise. In the emulation of the second target trial, participants who reported a new HA prescription in the second ALSOP questionnaire were assigned to strategies according to their reported frequency of HA use, which we assume represented their typical pattern of HA usage over the months before time zero. Those without a HA prescription were assigned to the "never" strategy.

Follow-Up

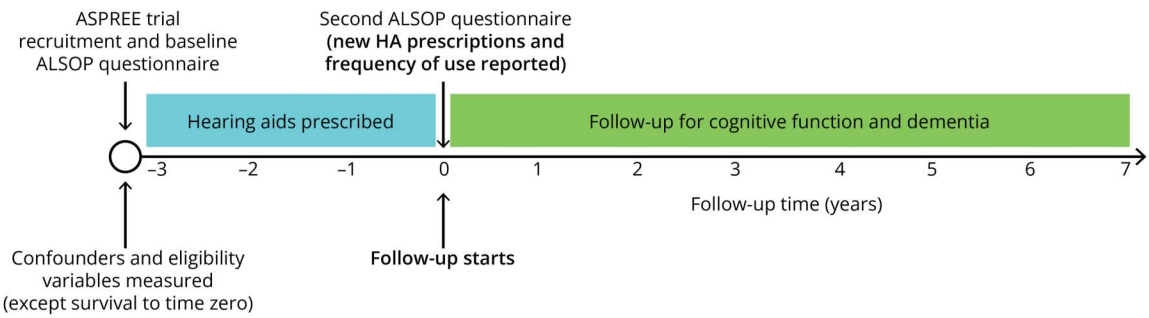
In the target trials, follow-up commences when eligibility criteria are met and treatment is assigned. In the emulation, follow-up commences at the third year of the ASPREE study, when eligibility criteria were met and new HA prescriptions and use were first reported (Figure 1).

Outcomes

In the target trials and the observational emulation, the primary outcome was the overall cognition score over follow-up, estimated as the single factor score from a confirmatory factor analysis model that included each test from the ASPREE cognitive battery (eMethods). The score was scaled to have mean 0 and SD 1 at ASPREE baseline. Larger values indicate better performance. Secondary outcomes included time to dementia, time to cognitive impairment, and scores on the individual cognitive tests (Modified Mini-Mental State Examination [3MS] for global cognition, the Hopkins Verbal Learning Test–Revised [HVLT-R] for learning and memory, the single letter [F] Controlled Oral Word Association Test [COWAT] for language and executive function, and the Symbol Digit Modalities Test [SDMT] for psychomotor speed).

The procedure for dementia diagnoses has been described previously.[16] In brief, suspected dementia diagnoses ("triggers") were made based on cognitive decline, reports of memory or cognitive problems to a specialist, or the prescription of cholinesterase inhibitors. Additional cognitive assessments were administered at least 6 weeks after the initial trigger. The available information (including any other relevant information, such as brain CT or MRI) was reviewed by a panel of neurologists, neuropsychologists, and geriatricians, with dementia adjudicated according to DSM-IV criteria. Dementia was not classified into subclasses for this study because most cases of dementia in older people are due to multiple brain pathologies.[16,17] Cognitive impairment was defined as a composite of dementia and cognitive decline, with cognitive decline determined as a reduction of 1.5 sample SDs in performance on the HVLT-R Delayed Recall, SDMT, 3MS, or COWAT for an individual, relative to baseline, which was sustained for at least 2 assessments.[16]

Figure 1 Structure of Observational Study



ALSOP = ASPREE Longitudinal Study of Older Persons; ASPREE = ASPirin in Reducing Events in the Elderly; HA = hearing aid.

Causal Contrast

The causal contrasts in the target trials are the intention-to-treat and per-protocol effects. In the observational emulation, because longitudinal data on HA adherence were not available, only observational analogs of intention-to-treat effects were estimated. For the emulation of the first target trial, the observational analog of the intention-to-treat effect is the effect of HA prescription vs no HA prescription. For the emulation of the second target trial, it is the effect of initiating HA use at frequencies of never, rarely/sometimes, or often always.

Death is a competing event for our analyses. For the cognitive outcomes, the contrast we estimate is the causal difference in means between strategies at a given follow-up time among those who survived until at least that time. This contrast is referred to as the "partly conditional effect"[14] and is written as $E\left[Y_t^z - Y_t^{z'} \mid S \geq t\right]$ in potential outcomes notation, where Y_t^z is the outcome at time t under assignment to strategy z and S represents survival time. For the time-to-event outcomes, we estimated the "total effect," also known as the cause-specific cumulative incidence,[15] which captures all paths through which exposure influences the outcome, including through the competing event itself.[18]

Identifying Assumptions

The causal contrast for the cognition outcomes is identified (i.e., can be validly estimated) under the assumptions of exchangeability (no unmeasured common causes of treatment and the outcome or of missing data and the outcome), positivity (all participant subgroups have some positive probability of receiving each treatment strategy and of having complete data), and causal consistency.[19,20] Identification of the total effect for the survival outcomes further requires these assumptions for censoring.[15]

We assumed that exchangeability for treatment held (i.e., that there was no residual confounding) after adjusting for selected confounders at ASPREE baseline, including demographic, clinical (e.g., diabetes), social, mental health, cognition, and hearing variables (e.g., better-ear 4-frequency PTA and tinnitus severity) and APOE ε4 genotype (eTable 2 provides detail on covariates, and information on handling of missing data is provided below). Confounders were identified from guidelines on dementia risk factors[1] and previous studies that have examined factors associated with HA use in similar populations.[21,22] The other identifying assumptions underpinning our analysis are described in the directed acyclic graph and associated text in eFigure 2.

Statistical Analysis

The data analysis for the observational emulation followed a prespecified plan, although the analysis deviated from the plan due to computational limitations. These changes are described in the eMethods. Data analysis was performed using R version 4.4.2. All analysis code is available online.[23]

Missing Data

Missing data in the exposures, covariates, and outcomes are summarized in eTables 1 and 2. Missing data in exposures and covariates were generally infrequent, although audiometry data were only available for 10% of the sample. Outcome missingness was principally due to withdrawal (n = 464 [18%] by year 7) or death (n = 326 [13%] by year 7).

Missing data were multiply imputed by the fully conditional specification approach, using R package mice.[24] Missing data models included baseline covariates, treatment variables, all cognitive outcomes,[25] time-varying auxiliary variables (e.g., depression symptoms and dementia), and nonlinear and product terms.[26] Elastic net variable selection was used to select terms for inclusion in the imputation model.[27] Cognitive data that were unavailable because the participant died before a given assessment point or because the planned annual assessment had not yet occurred (and, therefore, survival status was not yet known; n = 464 [18%] at year 7 only) were not imputed. The specification of the imputation models is described in eTable 3.

Owing to missing data in some eligibility criteria, we used bootstrapping (200 samples) followed by multiple imputation to obtain CIs.[28] Two imputed data sets were created within each bootstrap sample.[29] Point estimates and CI limits were computed by pooling across imputed data sets and bootstrap samples using established formulas.[29] Details on imputation methods can be found in eMethods.

Estimation for Cognitive Outcomes

Mean cognitive scores over time under each treatment strategy were estimated using the parametric g-formula. Outcome models were fitted using multivariable linear regression and included restricted cubic splines for continuous variables, including time, as well as treatment by time, covariate by time, covariate by treatment, covariate by treatment by time, and covariate by covariate product terms (eTable 1). Effect modification by prespecified baseline characteristics was assessed by standardizing to the confounder distribution within subgroups of a given effect modifier.

Estimation for Survival Outcomes

Cause-specific risks of dementia and cognitive impairment for each treatment strategy were estimated using the parametric g-formula estimator for the total effect.[15] The algorithm has been described in detail previously.[15,30] In brief, we constructed a person-period data set, which we used to fit pooled over time generalized linear models for the event, for death, and for time-varying predictors of censoring (cardiovascular disease, cancer, frailty, polypharmacy, Short Form-12 physical and mental health component scores, and depression symptoms).[15] We then set treatment to a particular strategy and then sequentially, across 1-year intervals, simulated values of the time-varying covariates conditional on the assigned treatment, baseline covariates, and the simulated time-varying covariates from the previous year. Predicted hazards of the

event and of death were computed as functions of the assigned treatment, baseline covariates, and the simulated time-varying covariates from the previous year. Risks were then estimated from these hazards. This process was repeated for each treatment strategy to estimate strategy-specific risks. The validity of these risk estimates relies on the above-mentioned causal assumptions and no model misspecification.

Sensitivity Analyses

Benchmarking

We informally "benchmarked" our analysis by comparing our estimates for the overall cognition score outcome after 3 years with the primary results reported in the ACHIEVE trial.[31] The reasoning behind such benchmarking is that, if the findings are similar to the benchmark trial (here, ACHIEVE), then we can be more confident that the assumptions underlying the observational analysis are plausible (notably that there is little residual baseline confounding) and, therefore, also in the extension of the analysis to complementary questions that the benchmark trial did not address.[31]

Other Sensitivity Analyses

We also performed the following sensitivity analyses:

1. We applied the same moderate objective hearing loss inclusion criterion as the target trials, based on audiometry data, using multiple imputation to handle missingness in these data across the whole sample.
2. To assess potential residual confounding (e.g., by health care engagement/access), we compared the overall cognition score between those prescribed HAs who "never" use them and those not prescribed HAs, adjusting for selected confounders.
3. We used (1) cancer and (2) consent for participation in ASPREE-XT as negative outcome controls, given the lack of hypothesized effect of HAs on these events.
4. The restriction to survivors for the cognitive outcomes could result in selection bias if mortality rates differ between HA strategies (DAG in eFigure 1). To assess the potential for this bias, we compared the risk of death between HA strategies.
5. To assess potential model misspecification for time-to-event outcomes, we estimated outcome risks using an inverse probability–weighted estimator of the total effect[15] (eMethods).

Standard Protocol Approvals, Registrations, and Participant Consents

ASPREE and ASPREE-XT were approved by the ethics review board at each participating institution. All participants provided written informed consent.

Data Availability

Data from the ASPREE study are available to researchers who have submitted and received approval for an expression of interest in the ASPREE access management system (ams.aspree.org/public/request-data/access-aspree-data/).

Results

Characteristics of the eligible sample are listed in Table 2. Across imputed data sets, a median of 2,777 eligible participants were included in the sample. A flow diagram for sample selection is displayed in eFigure 3. A median of 664 participants reported receiving a new HA prescription during the 3 years preceding time zero. HAs were reported as never used (or not prescribed) by 2,196 (79%), rarely or sometimes used by 188 (7%), and often or always used by 402 (14%). By the end of follow-up, there was a median of 51 deaths, 25 dementia cases, and 131 cognitive impairment cases among

Table 2 Demographic and Clinical Characteristics of the Sample[a]

	New hearing aid prescription	
Characteristic[b]	**Yes**	**No**
N[c]	664 (646, 686)	2,113 (2,079, 2,143)
Age, y	75.1 (71.8, 77.3)	74.2 (71.4, 76)
Sex, woman	327 (49)	1,015 (48)
Education, y		
<9	106 (16)	285 (14)
9–11	207 (31)	662 (31)
12	78 (12)	236 (11)
13–15	97 (15)	332 (16)
16	55 (8)	179 (8)
>16	121 (18)	415 (20)
White race	653 (98)	2,091 (99)
APOE ε4 positivity	156 (23)	568 (27)
Smoking		
Current	16 (2)	52 (2)
Former	277 (42)	913 (42)
Never	372 (56)	1,144 (54)
Diabetes	57 (9)	149 (7)
History of cancer	124 (19)	424 (20)
3MS overall score	93.8 (91.2, 97)	94.1 (92.0, 97.0)
Overall cognition score	−0.1 (−0.7, 0.7)	0.0 (−0.6, 0.7)
Better-ear 4-frequency PTA (db HL)	32.7 (25.0, 40.0)	26.8 (19.1, 33.6)

Abbreviations: 3MS = Modified Mini-Mental State Examination; PTA = pure tone average.
[a] Measured at recruitment into the ASPREE/ALSOP study. Summary statistics are the mean over imputed data sets.
[b] Median (Q1, Q3); n (%) for categorical variables.
[c] Median over imputed data sets.

those prescribed HAs and 123 deaths, 92 dementia cases, and 411 cognitive impairment cases among those not prescribed HAs.

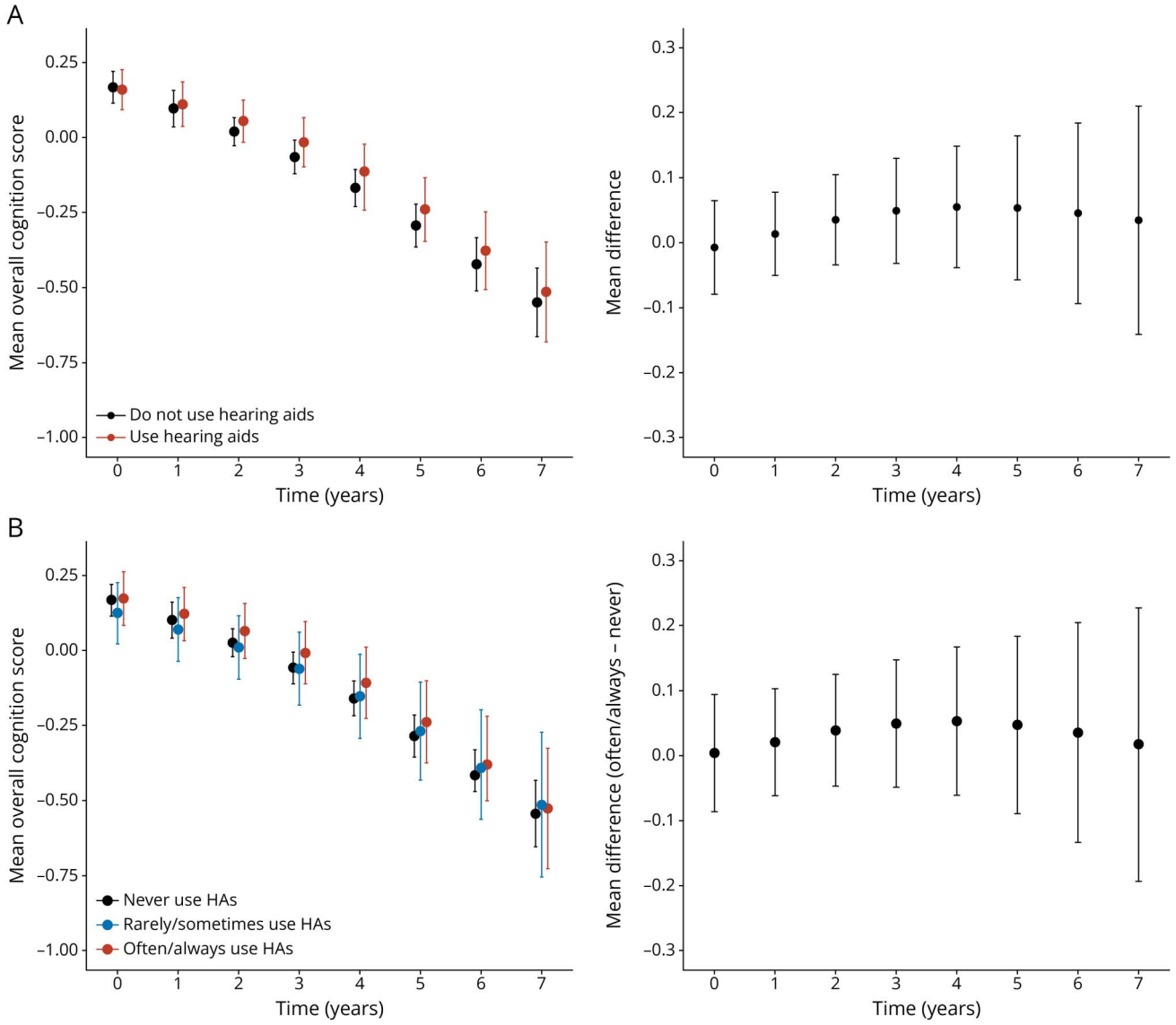
Cognitive Outcomes

Figure 2 shows the estimated observational analogs of the intention-to-treat mean overall cognition scores over follow-up, conditional on survival, under the different treatment strategies. Among survivors at year 7, the estimated mean scores under HA prescription and no HA prescription were similar (mean difference 0.03 SD; 95% CI −0.14 to 0.21), as were the estimated means under initiation of often/always and never using HAs (mean difference 0.02 SD; 95% CI −0.19 to 0.23). Results for the individual cognitive tests are displayed in eFigures 4–10. In general, outcomes were similar between strategies or modestly better under HA prescription, relative to no HA prescription.

Dementia and Cognitive Impairment

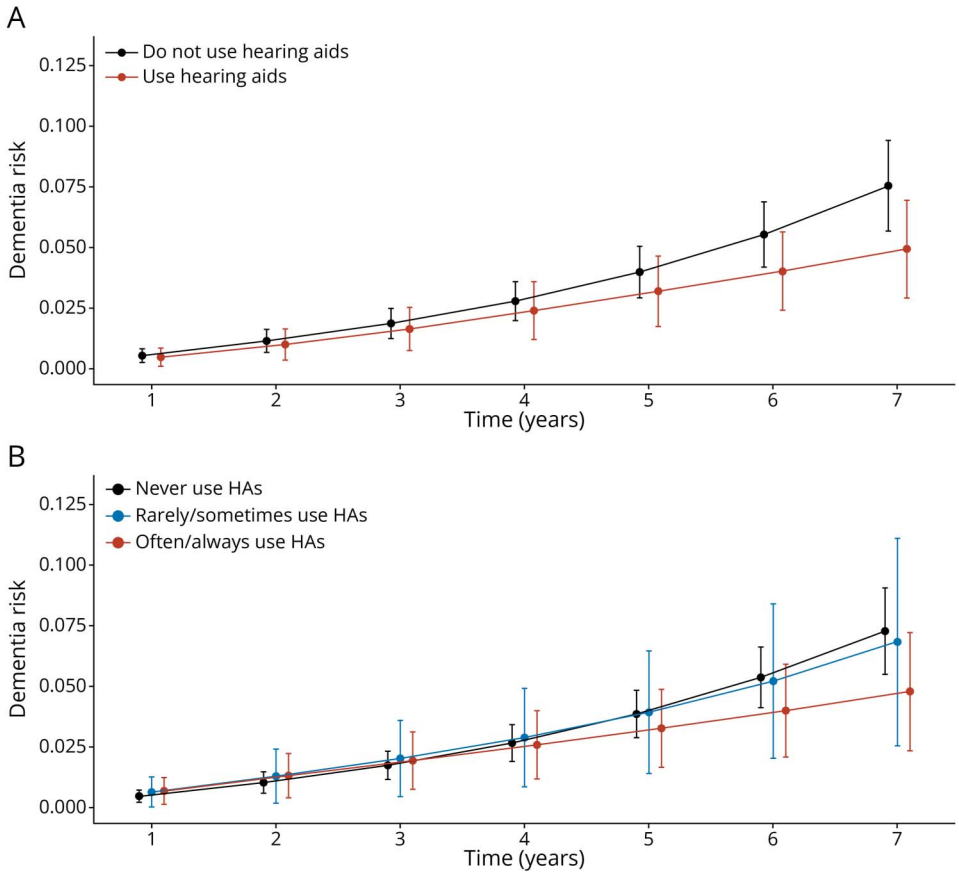
Figure 3 shows the estimated observational analogs of the intention-to-treat risk of dementia over follow-up under the different treatment strategies. By year 7, the estimated risk of dementia was 5.0% under HA prescription and 7.5% under no HA prescription (risk ratio [RR] 0.67; 95% CI 0.37–0.97). Estimated 7-year dementia risks were 7.3%, 6.8%, and 4.8% under initiation of never, rarely/sometimes, and often/always

Figure 2 Estimated Observational Analog of Intention-to-Treat Mean Overall Cognition Score Over Follow-Up Among Survivors Under Different Treatment Strategies



The overall cognition score was estimated by confirmatory factor analysis and is scaled to have mean 0 and SD 1 at ASPREE baseline. Larger values indicate better performance. Estimated means at a given follow-up point are conditional on surviving to at least that follow-up point. (A) Observational analog of intention-to-treat estimates for the strategies (1) use hearing aids and (2) do not use hearing aids. (B) Observational analog of intention-to-treat estimates for the strategies (1) never, (2) rarely/sometimes, and (3) often/always use hearing aids. Error bars represent 95% CIs. ASPREE = ASPirin in Reducing Events in the Elderly; HA = hearing aid.

Figure 3 Estimated Observational Analogs of Intention-to-Treat Risk of Dementia Under Different Treatment Strategies



(A) Observational analog of intention-to-treat risk for strategies (1) use hearing aids and (2) do not use hearing aids. (B) Observational analog of intention-to-treat risk for strategies (1) never, (2) rarely/sometimes, and (3) often/always use hearing aids. Error bars represent 95% CIs. HA = hearing aid.

using HAs, respectively (RR for often/always vs never 0.67; 95% CI 0.29–1.06).

Figure 4 shows the estimated observational analogs of the intention-to-treat risk of cognitive impairment over follow-up. By year 7, the estimated risk was 36.1% under HA prescription and 42.4% under no HA prescription (RR 0.85; 95% CI 0.70–1.00). Estimated risks under initiation of never, rarely/sometimes, and often/always using HAs were 41.5%, 39.2%, and 35.7%, respectively (RR for often/always vs never 0.86; 95% CI 0.66–1.06).

Estimated observational analogs of the intention-to-treat risk, risk differences, and risk ratios at the end of follow-up, along with CIs for each quantity, are summarized for both survival outcomes in eTable 4.

Effect Modification

The estimated 7-year mean differences in the overall cognition score among survivors, comparing HA prescription and no HA prescription, were greater in those with 3MS overall score <95 (0.17 SD; 95% CI −0.07 to 0.40) and better-ear 4-frequency PTA ≥30 dbHL (0.12 SD; 95% CI −0.12 to 0.36) at baseline (eFigures 11 and 12). There was modest or no indication of effect modification by frailty, age, or self-rated physical health (eFigures 13–15).

Sensitivity Analyses

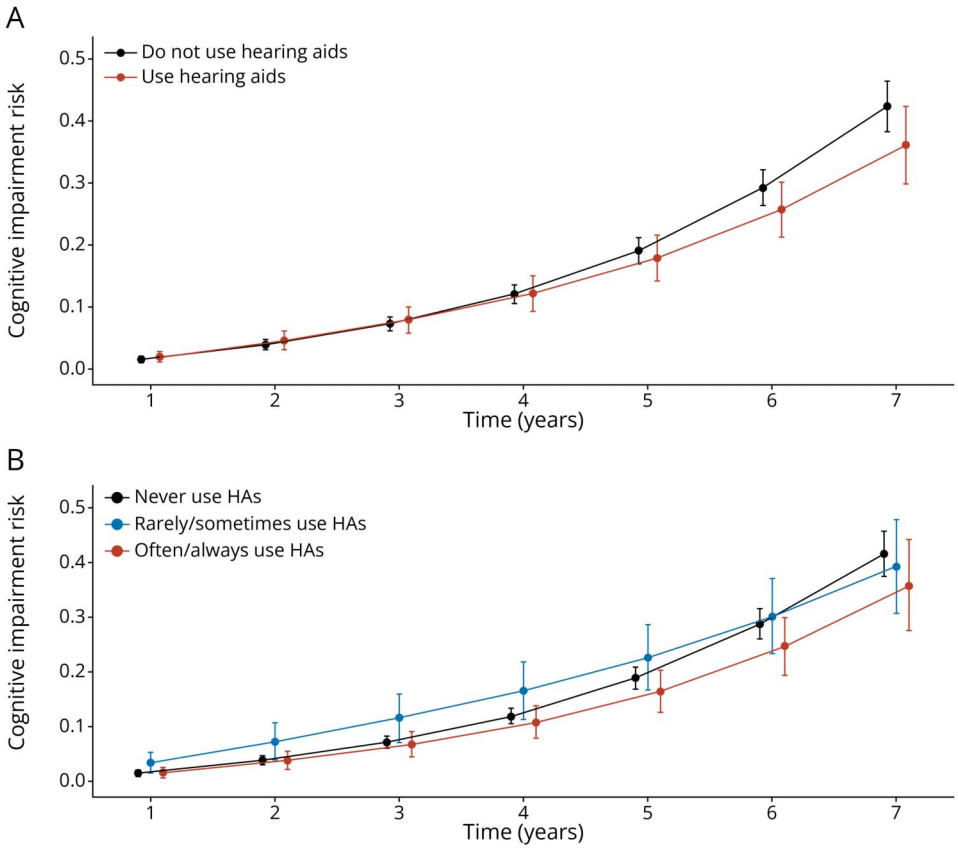
Benchmarking

The estimated 3-year mean difference in the overall cognition score, comparing initiation of often/always using HAs vs never using HAs, was 0.04 SDs (95% CI −0.05 to 0.13), similar to the ACHIEVE intention-to-treat mean difference of 0.00 SDs (95% CI −0.08 to 0.08).

Other Sensitivity Analyses

When using (multiply imputed) audiometry data to define moderate hearing loss, the estimated 7-year mean difference in the overall cognition score among survivors, comparing HA prescription and no HA prescription, was greater (0.14 SD; 95% CI −0.08 to 0.35), as was the overall rate of cognitive decline regardless of treatment strategy (eFigure 16). For the dementia and cognitive impairment analyses, results were similar to those of the main analysis, although overall risks were considerably greater (eFigures 17 and 18, respectively). For instance, the estimated dementia risk was 10.1% under no HA prescription and 7.8% under HA prescription (RR 0.80; 95% CI 0.48–1.12).

Figure 4 Estimated Observational Analogs of Intention-to-Treat Risk of Cognitive Impairment Under Different Treatment Strategies



(A) Observational analog of intention-to-treat risk for strategies (1) use hearing aids and (2) do not use hearing aids. (B) Observational analog of intention-to-treat risk for strategies (1) never, (2) rarely/sometimes, and (3) often/always use hearing aids. Error bars represent 95% CIs. HA = hearing aid.

There was little difference in overall cognition scores between those who were prescribed HAs but reported no HA use and those not prescribed HAs (eFigure 19). Estimated observational analogs of the intention-to-treat risks of cancer (eFigure 20), of consenting to participation in ASPREE-XT (e.g., 95% and 95% under initiation of often/always and never use HAs, respectively), and of death (eFigure 21) were similar by treatment strategy. Finally, estimated risks from the inverse probability–weighted estimator were similar to the main g-formula results for dementia (eFigure 22) and cognitive impairment (eFigure 23).

Classification of Evidence

This study provides Class III evidence that the use of hearing aids did not change overall cognitive scores in people 70 years and older with moderate hearing impairment as compared to those who used hearing aids.

Discussion

We used data from the ASPREE study, and 2 of its ancillary studies, to investigate whether the use of HAs in older people with hearing impairment could improve neurocognitive health. After 7 years of follow-up, we found that the estimated mean overall cognition score among survivors was similar under HA prescription and no HA prescription. Similarly, there was little difference in the overall cognition score under initiation of different frequencies of HA use. In subgroup analyses, we found that those with poorer hearing function and poorer cognition may experience greater benefit. This is consistent with the findings of ACHIEVE, which found benefit only in a subgroup with relatively poor baseline cognition and a higher risk of cognitive decline.[6] For the dementia outcome, we estimated that the 7-year risk was 33% lower under HA prescription than under no HA prescription. Estimated dementia risks decreased proportionally to the frequency of HA use. For cognitive impairment, we estimated that the 7-year risk was 15% lower under HA prescription than under no HA prescription.

Despite differences in study design and in the duration of treatment and follow-up, our findings for the dementia outcome are consistent with a recent meta-analysis of 4 observational studies, which reported a 17% reduction in the dementia hazard rate in those treated with HAs compared with those with uncorrected hearing loss.[4] Our findings for cognitive impairment were also similar to the 10% reduction in the hazard rate of cognitive impairment over 3 years found in ACHIEVE[6] and to the 19% reduction in the hazard rate of

cognitive decline in a meta-analysis of 8 longitudinal observational studies.[4]

The finding of lower dementia risk under HA prescription but little corresponding reduction in overall age-related cognitive change is somewhat unexpected but would align with some proposed mechanisms linking sensory loss to dementia risk. The first of these is the interaction between the neurologic effects of hearing loss and existing neuropathology.[2,3] In brief, hearing loss produces altered neuronal activity as a consequence of the demands of listening in difficult environments. This change in neuronal activity could interact with existing AD pathology in the medial temporal lobe in a manner that ultimately leads to the worsening of that pathology.[3] If this were true, it could be plausible that the improvement in audibility through amplification (thus minimizing the neuronal sequelae of hearing loss) could prevent or delay dementia onset in those with existing AD pathology but offer less corresponding benefit in the subpopulation without AD pathology. Alternatively, our findings could be consistent with the sensory deprivation hypothesis, wherein that sensory deprivation caused by hearing loss affects regional brain volume.[3,32] This would be consistent with our findings of a reduction in overall cognitive impairment (not just dementia) in those receiving HAs.

Another explanation for the lack of clear benefit on age-related cognitive change relates to the characteristics of the sample. ASPREE participants were in relatively good cognitive health at recruitment, thus potentially minimizing the scope for improvement. This would be consistent with the findings of ACHIEVE, wherein only the subgroup with relatively poor physical and cognitive health benefited from the intervention.[7] Finally, this finding could be explained by the heterogeneity of age-related cognitive change, which can be driven by a wide range of factors, not just brain atrophy and neuropathology, including declining physical and mental health, specific medications, hormone imbalances, and vitamin deficiencies.

Strengths of the study include the availability of longitudinal cognitive follow-up, the consensus-led diagnosis of dementia, extensive measurement of confounders, and the use of an observational study design approach (target trial emulation) which helps to define a clear target estimand and avoid common biases.[33,34] Limitations are apparent in differences between our observational analysis and the target trials it sought to emulate. First, not all data required to emulate the eligibility criteria of the target trials were available. For instance, we could not exclude those with contraindications to HAs. There is thus the possibility that some participants in the study sample would never receive a HA and the "effect" of HAs is, therefore, undefined in this subgroup (i.e., the positivity assumption is violated). Second, to be included in the observational analysis, participants must have met the eligibility criteria of the ASPREE trial, such as being free from cardiovascular disease.[9] These additional criteria would have resulted in a sample that differed from the target population, especially regarding physical health, which could result in bias if these criteria were also effect modifiers. Third, objective hearing function data were only available for a small proportion of participants (10%). We used multiple imputation to handle missing data in this important confounder, but residual confounding may thus be present. Further residual confounding may also arise as participants receiving HAs may have differed from those not receiving HAs in other aspects of hearing function, such as speech-in-noise ability, which may also be dementia risk factors.[3]

Another potential source of bias is that those who sought out and used HAs must have had the cognitive capacity to do so. This group, therefore, may have tended toward better pretreatment cognitive function compared with those not receiving HAs. We do not expect this to be a major source of bias in this study, however, for 2 reasons: (1) eligible participants were cognitively healthy at baseline (3MS overall score >77) and hence had sufficient cognitive capacity to seek out and use a HA, and (2) in our analyses, we adjusted for several measures of baseline cognition (thus accounting for pretreatment differences). A further issue is that the start of follow-up was not precisely aligned with HA prescription (which could occur up to 3 years before time zero). This nonalignment could result in residual confounding if the confounders measured at ASPREE/ALSOP baseline were not a good proxy for those same confounders at the time of HA prescription.[34] Because we did not have longitudinal data on HA adherence available, we were also not able to estimate per-protocol effects. Finally, because our study differed in some important respects from ACHIEVE, there were limitations in the benchmarking procedure we used to assess the no unmeasured confounding assumptions underpinning our analysis.[31] For instance, the ACHIEVE trial compared a best-practice audiological intervention with a health education control, whereas we compared HAs as prescribed under routine clinical care with no HA prescription.[6]

In conclusion, we found that treating hearing loss with HAs may reduce dementia risk, although it may have limited influence on age-related cognitive change in relatively healthy older people with hearing impairment. Long-term randomized trials and observational studies in populations at high risk of cognitive decline would be a valuable next step.

Acknowledgment

The authors thank the ASPREE study participants and the ASPREE study staff for their essential contributions.

Author Contributions

L. Cribb: drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data. M.M. Betancur: drafting/revision of the manuscript for content, including medical writing for content; study concept or design. M.P. Pase: drafting/revision of the manuscript for content,

including medical writing for content; study concept or design. R. Wolfe: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design. C. Britt: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design. Z. Zhou: drafting/revision of the manuscript for content, including medical writing for content. R.C. Shah: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. G. Rance: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. K.M. Sheets: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. T.T.-J. Chong: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. R.L. Woods: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. A.M. Murray: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. A. Owen: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. J. Ryan: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design.

Study Funding

This research was supported by an Australian Government Research Training Program Scholarship and Monash Graduate Excellence Scholarship. The ASPREE project, comprising 2 components of ASPREE and ASPREE-XT, was led by Monash University in Australia and the Berman Centre for Outcomes and Clinical Research in the United States. Funding for the ASPREE project was provided by Australian and US governments; the Australian National Health and Medical Research Council (NHMRC) (grants 334047 and 1127060); the National Institute on Aging; the National Cancer Institute at the US NIH (grants U01AG029824 and U19AG062682); Monash University (Australia); and the Victorian Cancer Agency (Australia). ALSOP received funding support from Monash University, ANZ Trustees, the Wicking Trust, and the Mason Foundation. M.M. Betancur was supported by an Australian NHMRC Investigator Grant (ID 2009572). M.P. Pase received an Australian National Health NHMRC Investigator Grant Fellowship (GTN2009264). G. Rance is supported by the Graeme Clark Chair in Audiology and Speech Science. J. Ryan is funded by Leadership 1 Investigator Grant 2016438 from the NHMRC.

Disclosure

R. Shah reports being the site principal investigator or subinvestigator for Alzheimer disease clinical trials for which his institution (Rush University Medical Center) is compensated (Athira Pharma, Inc.; Edgewater NEXT; Eisai, Inc.; Eli Lilly & Co., Inc.; and Genentech, Inc.). T.T.-J. Chong has received honoraria from Roche for lectures. All other authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

Publication History

Received by *Neurology*® May 16, 2025. Accepted in final form November 14, 2025. Submitted and externally peer reviewed. The handling editor was Associate Editor Linda Hershey, MD, PhD, FAAN.

References

1. Livingston G, Huntley J, Liu KY, et al. Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. *Lancet*. 2024;404(10452):572-628. doi:10.1016/S0140-6736(24)01296-0
2. Sarant J, Lemke U, Giroud N, Scherpiet S, Weinstein B. Promoting hearing and cognitive health in audiologic rehabilitation for the well-being of older adults. *Int J Audiol*. 2024;63(10):761-771. doi:10.1080/14992027.2023.2260099
3. Griffiths TD, Lad M, Kumar S, et al. How can hearing loss cause dementia? *Neuron*. 2020;108(3):401-412. doi:10.1016/j.neuron.2020.08.003
4. Yeo BSY, Song HJJMD, Toh EMS, et al. Association of hearing aids and cochlear implants with cognitive decline and dementia: a systematic review and meta-analysis. *JAMA Neurol*. 2023;80(2):134-141. doi:10.1001/jamaneurol.2022.4427
5. Sugiura S, Uchida Y, Nishita Y, et al. Prevalence of usage of hearing aids and its association with cognitive impairment in Japanese community-dwelling elders with hearing loss. *Auris Nasus Larynx*. 2022;49(1):18-25. doi:10.1016/j.anl.2021.03.017
6. Lin FR, Pike JR, Albert MS, et al. 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. *Lancet*. 2023;402(10404):786-797. doi:10.1016/S0140-6736(23)01406-X
7. Liu K. Hearing intervention and cognitive decline: the ACHIEVE trial. *Lancet*. 2024;404(10447):29-30. doi:10.1016/S0140-6736(24)00712-8
8. ASPREE Investigator Group. Study design of ASPirin in Reducing Events in the Elderly (ASPREE): a randomized, controlled trial. *Contemp Clin Trials*. 2013;36(2):555-564. doi:10.1016/j.cct.2013.09.014
9. McNeil JJ, Woods RL, Nelson MR, et al. Effect of aspirin on disability-free survival in the healthy elderly. *N Engl J Med*. 2018;379(16):1499-1508. doi:10.1056/NEJMoa1800722
10. McNeil JJ, Woods RL, Ward SA, et al. Cohort profile: the ASPREE Longitudinal Study of Older Persons (ALSOP). *Int J Epidemiol*. 2019;48(4):1048-1049h. doi:10.1093/ije/dyy279
11. Ernst ME, Broder JC, Wolfe R, et al. Health characteristics and aspirin use in participants at the baseline of the aspirin in reducing events in the elderly–eXTension (ASPREE-XT) observational study. *Contemp Clin Trials*. 2023;130:107231. doi:10.1016/j.cct.2023.107231
12. Lowthian JA, Britt CJ, Rance G, et al. Slowing the progression of age-related hearing loss: rationale and study design of the ASPIRIN in HEARING, retinal vessels imaging and neurocognition in older generations (ASPREE-HEARING) trial. *Contemp Clin Trials*. 2016;46:60-66. doi:10.1016/j.cct.2015.11.014
13. Hernán MA, Robins JM. Using big data to emulate a target trial when a randomized trial is not available. *Am J Epidemiol*. 2016;183(8):758-764. doi:10.1093/aje/kwv254
14. Kurland BF, Johnson LL, Egleston BL, Diehr PH. Longitudinal data with follow-up truncated by death: match the analysis method to research aims. *Stat Sci Rev J Inst Math Stat*. 2009;24(2):211. doi:10.1214/09-STS293
15. Young JG, Stensrud MJ, Tchetgen Tchetgen EJ, Hernán MA. A causal framework for classical statistical estimands in failure-time settings with competing events. *Stat Med*. 2020;39(8):1199-1236. doi:10.1002/sim.8471
16. Ryan J, Storey E, Murray AM, et al. Randomized placebo-controlled trial of the effects of aspirin on dementia and cognitive decline. *Neurology*. 2020;95(3):e320-e331. doi:10.1212/WNL.0000000000009277
17. Schneider JA, Arvanitakis Z, Bang W, Bennett DA. Mixed brain pathologies account for most dementia cases in community-dwelling older persons. *Neurology*. 2007;69(24):2197-2204. doi:10.1212/01.wnl.0000271090.28148.24
18. Rojas-Saunero LP, Young JG, Didelez V, Ikram MA, Swanson SA. Considering questions before methods in dementia research with competing events and causal goals. *Am J Epidemiol*. 2023;192(8):1415-1423. doi:10.1093/aje/kwad090
19. Moreno-Betancur M, Lee KJ, Leacy FP, White IR, Simpson JA, Carlin JB. Canonical causal diagrams to guide the treatment of missing data in epidemiologic studies. *Am J Epidemiol*. 2018;187(12):2705-2715. doi:10.1093/aje/kwy173
20. Hernán MA, Robins JM. Causal inference: What If. Boca Raton: Chapman & Hall/CRC; 2010.
21. Fisher DE, Li CM, Hoffman HJ, et al. Sex-specific predictors of hearing-aid use in older persons: the age, gene/environment susceptibility: Reykjavik study. *Int J Audiol*. 2015;54(9):634-641. doi:10.3109/14992027.2015.1024889
22. Gopinath B, Schneider J, Hartley D, et al. Incidence and predictors of hearing aid use and ownership among older adults with hearing loss. *Ann Epidemiol*. 2011;21(7):497-506. doi:10.1016/j.annepidem.2011.03.005
23. Cribb, L. Accessed November 21 2025. https://www.github.com/Lachlan-Cribb/Hearing_aids_dementia
24. van Buuren S, Groothuis-Oudshoorn K. mice: multivariate imputation by chained equations in R. *J Stat Softw*. 2011;45(3):1-67. doi:10.18637/jss.v045.i03

25. Huque MH, Moreno-Betancur M, Quartagno M, Simpson JA, Carlin JB, Lee KJ. Multiple imputation methods for handling incomplete longitudinal and clustered data where the target analysis is a linear mixed effects model. *Biom J*. 2020;62(2):444-466. doi:10.1002/bimj.201900051
26. Dashti SG, Lee KJ, Simpson JA, White IR, Carlin JB, Moreno-Betancur M. Handling missing data when estimating causal effects with targeted maximum likelihood estimation. *Am J Epidemiol*. 2024;193(7):1019-1030. doi:10.1093/aje/kwae012
27. Zahid FM, Heumann C. Multiple imputation with sequential penalized regression. *Stat Methods Med Res*. 2019;28(5):1311-1327. doi:10.1177/0962280218755574
28. Tompsett D, Zylbersztejn A, Hardelid P, De Stavola B. Target trial emulation and bias through missing eligibility data: an application to a study of palivizumab for the prevention of hospitalization due to infant respiratory illness. *Am J Epidemiol*. 2023;192(4):600-611. doi:10.1093/aje/kwac202
29. Bartlett JW, Hughes RA. Bootstrap inference for multiple imputation under uncongeniality and misspecification. *Stat Methods Med Res*. 2020;29(12):3533-3546. doi:10.1177/0962280220932189
30. *gfoRmula: An R Package for Estimating the Effects of Sustained Treatment Strategies via the Parametric g-formula: Patterns*. Accessed July 1, 2024. cell.com/patterns/fulltext/S2666-3899(20)30008-8
31. Matthews AA, Dahabreh IJ, Fröbert O, et al. Benchmarking observational analyses before using them to address questions trials do not answer: an application to coronary thrombus aspiration. *Am J Epidemiol*. 2022;191(9):1652-1665. doi:10.1093/aje/kwac098
32. Armstrong NM, An Y, Doshi J, et al. Association of midlife hearing impairment with late-life temporal lobe volume loss. *JAMA Otolaryngol Neck Surg*. 2019;145(9):794-802. doi:10.1001/jamaoto.2019.1610
33. Hernán MA, Sauer BC, Hernández-Díaz S, Platt R, Shrier I. Specifying a target trial prevents immortal time bias and other self-inflicted injuries in observational analyses. *J Clin Epidemiol*. 2016;79:70-75. doi:10.1016/j.jclinepi.2016.04.014
34. Cribb L, Moreno-Betancur M, Wu Z, Wolfe R, Pasé M, Ryan J. Moving beyond the prevalent exposure design for causal inference in dementia research. *Lancet Healthy Longev*. 2025;6(2):100675. doi:10.1016/j.lanhl.2024.100675