ARIC Manuscript Proposal #4286

PC Reviewed: 6/13/23	**Status: _____**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Effect of best-practices hearing intervention on self-reported hearing handicap: Findings from the ACHIEVE Study

b. Abbreviated Title (Length 26 characters): Hearing intervention and Hearing Handicap

2. Writing Group:
Writing group members as of 5/23/2023; additional steering committee members may elect to join authorship.

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__VAS___ **[please confirm with your initials electronically or in writing]**

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3. Timeline:

Proposal timeline	May-June 2023	June-July 2023	July-August 2023
Proposal approval	X		
Data Analysis		X	
Manuscript preparation and submission			X

4. Rationale:

The Aging and Cognitive Health Evaluation in Elders study (ACHIEVE; Clinicaltrials.gov Identifier: NCT03243422) is a multicenter randomized controlled trial to determine efficacy of a best-practice hearing intervention on reducing cognitive decline and other functional declines in older adults. Novel approaches for reducing cognitive/functional decline in older adults are needed given the aging of the population and the personal, socioeconomic, and public health implications of poor health among older adults. Epidemiologic data now strongly suggest that age-related peripheral hearing loss in older adults is independently associated with poorer health (cognitive and functional). Better health may be promoted by the adoption of a comprehensive hearing intervention consisting of the use of hearing assistive technologies (hearing aids, other integrated hearing assistive devices) and rehabilitative training. To date, however, there has never been a randomized trial that has investigated whether hearing loss treatment could promote better health, and, specifically reduce handicap directly attributed to hearing loss. We will evaluate the effect of hearing intervention compared to a successful aging health education control invention on hearing handicap measured with the Hearing Handicap Inventory for Elderly-Screening Version [HHIE-S,(Newman & Weinstein, 1988)].

5. Main Hypothesis/Study Questions:

Study Question:

To determine the effect of a hearing intervention versus a successful aging health education control intervention on the self-reported hearing handicap in 70-84 year-old well-functioning and cognitively-normal adults with hearing loss.

Main Hypotheses:

Hearing intervention (versus successful aging health education control) reduces hearing handicap among older adults with hearing loss.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

Study design: Randomized trial of 977 participants enrolled in the Aging and Cognitive Health Evaluation in Elders (ACHIEVE) trial from 2018-2019 and followed for 3 years. Participants were from four U.S. sites (Forsyth County, NC; Jackson, MS; Minneapolis, MN; Washington County, MD). 238 participants were recruited from the ongoing Atherosclerosis Risk in Communities Neurocognitive (ARIC-NCS) Study and the remaining 739 participants were recruited de novo from the community.

Inclusion/exclusion criteria: All eligible participants enrolled at baseline in the ACHIEVE study.

- Inclusion criteria: 1) age 70-84 years, 2) community-dwelling adults, 3) mild–to-moderate audiometric hearing impairment, defined as a better-hearing ear pure tone average (PTA) ≥30 and

<70 dB hearing level (Deal et al., 2018), 4) MMSE ≥23 for those with high school degree or less, and ≥25 for those with some college education or more, 5) Word Recognition in Quiet score ≥60% correct in the better-hearing ear, 6) fluent English-speaker, 7) older adults who plan to remain in the area during the study period.

- Exclusion criteria: 1) self-reported difficulty in ≥2 activities of daily living, 2) prior dementia diagnosis, 3) vision impairment, 4) medical contraindication to hearing treatment, 5) untreatable conductive hearing impairment, 6) unwillingness to regularly wear hearing aids; 7) self-reported hearing aid use in the past year.

Outcome Variables

The primary outcome is self-reported hearing handicap measured by the Hearing Handicap Inventory for the Elderly – Screening Version (HHIE-S). For this instrument participants responded either Yes (assigned 4 points), Sometimes (2 points), or No (0 points) to 10-questions about their hearing in different dituations. Total scores yeild a possible range from 0-40 point with higher values indicating greater handicap. If a value is missing from the 10-items, then an HHIE-S score cannot be calculated. The score ranges from 0 to 40 and can be analyzed as a continuous measure, categorized as no hearing handicap (0-8), mild to moderate hearing handicap (10-24), or severe hearing handicap (26-40), or dichotomized into no hearing handicap (range: 0-8) and any hearing handicap (range: 10-40) per instrument criteria(Ventry & Weinstein, 1983).

Exposure Variables

Intervention group (hearing intervention vs. successful aging education) assigned at baseline randomization

Other Variables

The primary analysis may include adjustments for the baseline hearing loss (PTA continuous), ARIC vs de novo status, center-race, age (years), sex (male/female), education (less than high school/ high school or equivalent/ greater than high school), depression (self-reported or based on CES-D scores), marital status (currently married, not currently married, living alone), cognition, and chronic condition count (among hypertension, cholesteronl, stroke or TIA, osteoporosis, arthritis, asthma, COPD, or renal disease)

For secondary analyses restricted to study participants assigned to the HI group, we would like to review elements of the intervention as a possible predictor variables. Hearing intervention elements include but are not limited to: hearing aid technology level (50, 70, 90), fitting prescription (real-ear, SII) usage of hearing intervention (datalogging, self-report), additional assistive devices, and patient-centered hearing goal improvements.

Analytic Plan

A statistical analysis plan (SAP) for the primary analysis of the ACHIEVE Study was previously developed by the CC in conjunction with ACHIEVE invesigators and was approved by the NIA and ACHIEVE DSMB in June 2022. The analysis requested with this proposal is considered secondary to the primary for the study, but the analytic process is similar and is briefly summarized below. The Data Coordinating Center and assigned biostatisitician, Emmanuel E Garcia Morales, PhD., will responsible for the analysis of this manuscript.

Change in HHIE scores over time will be analyzed utilizing mixed effects models (linear for continuous HHIE score and logistic mixed effect model for binary outcome) that specify time in years from the baseline as the time scale under the intention-to-treat principle. An interaction term between time and the exposure (assigned to HI group versus SA control group) will be used to test if the rate of change in the outcome is associated with the exposure. Additional analyses will include estimating the main model stratified by source of recruitment (ARIC vs de novo).

A three-level mixed effects model with a random intercept and time slope for each participant, a random intercept for each individual or cohabitating pair, and an unstructed covariance matrix will be used to estimate intervention effects to account for the correlation among repeated measures as well as the correlation between spouses or cohabitating partners. Main model will be adjusted in terms of number of random effects and structure of variance-covariance matrix in case convergence of the model is not achieved.

Continuous time in years from the baseline will be the time scale. If a linear trend appears reasonable, we will fit a model with a linear slope. If a nonlinear trend is observed, the model will be adapted to include time splines. Model fit will be assessed with residual plots and other statistics (Akaike Information Criterion, Bayesian Information Criterion, etc.). The primary analysis may include adjustments for the baseline hearing loss, ARIC vs de novo status, center-race, age, sex, education, depression, marital status, cognition, and count of chronic conditions/

Missing data among ACHIEVE participants will be addressed by using multiple imputation by chained equations (MICE) or by implementing inverse attrition probability weighting (IPAW). For MICE the number of imputations needed to generate valid parameter estimates will be determined by a two-stage analysis. The empirical strategy selected to address missing data will be determined based on the missingness patterns of the outcome being evaluated.

Secondary analyses include estimating the main model stratified by sex and race and might also include per-protocol analyses excluding non-compliant participants assigned to the intervention group. To reduce potential bias observed in the per-protocol analyses(Little & Rubin, 2000), we might also perform a complier average causal effect (CACE) analysis using group original assignment as an instrumental variable for intervention compliance (Hernán & Robins, 2017). Exploratory analyses restricted to participants assigned to the HI group will look at the association between intervention elements and change in main outcomes overtime.

7.a. Will the data be used for non-ARIC analysis or by a for-profit organization in this manuscript? ____ Yes _X___ No

b. If Yes, is the author aware that the current derived consent file ICTDER05 must be used to exclude persons with a value RES_OTH and/or RES_DNA = "ARIC only" and/or "Not for Profit" ? ____ Yes ____ No
(The file ICTDER has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? ____ Yes _X___ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the current derived consent file ICTDER05 must be used to exclude those with value RES_DNA = "No use/storage DNA"? ____ Yes ____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/aric/mantrack/maintain/search/dtSearch.html

___X___ Yes _____ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

Main results of the ACHIEVE trial. No proposal approved at the time of this proposal submission.

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? _X_ Yes ____ No

11.b. If yes, is the proposal

_X_ A. primarily the result of an ancillary study (list number* _2016.03_)

___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

*ancillary studies are listed by number https://sites.cscc.unc.edu/aric/approved-ancillary-studies

12a. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PubMed Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

References

Hernán, M. A., & Robins, J. M. (2017). Per-protocol analyses of pragmatic trials. *N Engl J Med*, *377*(14), 1391-1398.

Little, R. J., & Rubin, D. B. (2000). Causal effects in clinical and epidemiological studies via potential outcomes: concepts and analytical approaches. *Annual review of public health*, *21*(1), 121-145.

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