ARIC Manuscript Proposal #4283

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

1.a. Full Title: Effect of best-practices hearing intervention on health-related quality of life: Findings from the ACHIEVE Study

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

2. Writing Group:
Writing group members:

Frank Lin (senior author), James Pike, Sheila Burgard, Theresa Chisolm (first author), David Couper, Jennifer A. Deal, Adele M. Goman, Nancy W. Glynn, Theresa Gmelin, Lisa Gravens-Mueller, Kathleen Hayden, Alison Huang, Christine M. Mitchell, Thomas Mosley, Jim Pankow, Nick Reed, Victoria Sanchez, Jennifer Schrack, Josef Coresh for the ACHIEVE Collaborative Research Group

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __THC___ **[please confirm with your initials electronically or in writing]**

First author:
Address: Theresa H. Chisolm
University of South Florida, Office of the Provost,
4202 E. Fowler Ave, CGS 401
Tampa, FL 33620
Phone: 813-974-2281 Fax:
E-mail: chisolm@usf.edu

ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).
Name: Josef Coresh
Address: 2024 E. Monument Street

Phone: Fax:
E-mail: coresh@jhu.edu

3. Timeline:

Proposal timeline	June-July 2023	July-Aug 2023	August-Sept 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 in older adults. The prevalence of hearing loss among older adults is high and is independently associated with many negative outcomes including reductions in communication functioning (Dalton et al., 2003), social functioning (Mick et al., 204: Pronk et al., 2011; Shukla et al., 2020) increases in loneliness (Huang et al., 2021; Shukla et al., 2020), reduction in physical activity and function (Choi, Betz, Deal, et al., 2016; Martinez-Amezcua, Kuo, et al., 2021; Martinez-Amezcua, Suen, et al., 2021), and poorer health-related quality of life (HRQoL; Dalton et al, 2003; Tseng et al, 2018). While the results of a systematic review highlighted observed associations between worse objective (pure tone average, [PTA]) and self-assessment of hearing as measured through the Hearing Handicap Inventory for the Elderly [HHIE-S, (Newman & Weinstein, 1988)] and HRQoL, a recent systematic review by Ferguson et al (2017) identified only two previous studies examining the effects of hearing intervention on HRQoL as measured through a generic instrument. McArdle et al (2005) reported a significant benefit of hearing aids compared to the unaided/ placebo condition using the World Health Organization Disability Assessment Schedule (WHO-DAS II) (SMD -0.44, 95% confidence interval (CI) -0.65 to -0.24; 380 participants), and Mulrow et al (1990) found no significant effect of hearing aids using the Self-Evaluation of Life Function (SELF) (SMD -0.26, 95% CI -0.55 to 0.03; 188 participants). Heterogeneity was low and the reviewers concluded that the quality of the evidence for a positive effect of hearing aid use on HRQoL was moderate due to high risk of bias. The association between objectively and subjectively measured hearing loss and reductions in self-perceived HRQoL was demonstrated in the baseline data obtained from the participants in the ACHIEVE trial (Huang et al., submitted) thus providing a unique opportunity to investigate whether or not best-practices hearing loss treatment improves HRQoL in a large sample of well-described older adults. We will evaluate the effect of hearing intervention compared to a control invention on HRQoL as measured by the RAND Short Form 36 Health Survey [RAND-36, (Hays & Morales, 2001].

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 HRQoL in 70-84 year-old well-functioning and cognitively-normal adults with-hearing loss.

Main Hypotheses:

Hearing intervention (versus successful aging health education control) improves HRQoL 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) 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 variables for this manuscript are the RAND 36 Health Survey (RAND-36) (Hays & Morales, 2001) physical health component and mental health component subscale scores. The RAND-36 is a validated measure that includes 36 questions across eight domains of health: physical functioning, physical role limitations, emotional role limitations, energy/fatigue, emotional well-being, social functioning, pain, general health. RAND-36 was collected at baseline and at 6, 12, 24, and 36 months after. Although all data points will be used during analyses, main outcome will assess the change in RAND-36 score from baseline to Year 3.

For items that asked about physical health, participants were instructed to consider hearing as part of their physical health. Domain scores range from 0 to 100 with higher scores indicating better health-related quality of life. Two subscales (physical health component summary score (PCS) and mental health component summary score (MCS) were calculated using the RAND-36 summary component scoring algorithm (Taft et al., 2001), with a normative mean of 50 and standard deviation of 10 (range 0 to 100).

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), type of recruitment (ARIC vs de novo), center, race, age (years), sex (male/female), and education (less than high school/ high school or equivalent/ greater than high school). Other covariates at baseline may include, marital status (currently married, not currently married, living alone), income (<$25k, $25k-$50k, $50k-$100k, >$100k), depression (based on self-report and/or medication use, or CES-D scale), cognition, and chronic condition count (among hypertension, cholesterol, stroke or TIA, osteoporosis, arthritis, asthma, COPD, or renal disease).

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 investigators 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. Assigned biostatistician, Emmanuel E. Garcia Morales, PhD. will responsible for the analysis of this manuscript.

Change in SF-36, PCS, and MCS scores from baseline to Year 3 will be analyzed utilizing linear mixed effects models measuring 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. Stratified analyses by recruitment status (ARIC vs de novo) will also be performed for main outcomes.

A two-level mixed effects model with a random intercept, time slope for each participant, and an unstructured covariance matrix will be used to estimate intervention effects to account for the correlation among repeated measures. The model will adjust for co-randomized spouse or cohabitating partner. Main model will be adjusted in terms 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 (from recruitment time or by calendar time). 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, age, sex, education, income, marital status, depression, cognition, and chronic condition count.

Missing data among ACHIEVE participants will be addressed either (1) by utilizing multiple imputation by chained equations (MICE), or (2) by implementing an inverse probability weighting (IPW) approach. For MICE, the number of imputations needed to generate valid parameter estimates will be determined by a two-stage analysis. Statistical approach to deal with missing data will be determined based on the missingness patterns of the outcome being evaluated.

Exploratory analyses will look at the change over time separately for the 8 eight domains of health: physical functioning, physical role limitations, emotional role limitations, energy/fatigue, emotional well-being, social functioning, pain, and general health. Other analyses might also include per-protocol analyses excluding non-compliant participants assigned to the hearing 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).

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)?

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.

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