ARIC Manuscript Proposal #H3556

PC Reviewed: 1/14/20	**Status: _____**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: The Aging and Cognitive Health Evaluation in Elders (ACHIEVE) trial: Recruitment and baseline data of a randomized trial of hearing treatment for reducing cognitive decline

b. Abbreviated Title (Length 26 characters): Baseline ACHIEVE

2. Writing Group:

Writing group members: (Alphabetical)

Michelle Arnold
Joshua Betz
Sheila Burgard
David Couper
Terry Chisolm
Joe Coresh (Second Senior Author)
Jennifer Deal
Josh Evans
Nancy Glynn
Adele Goman
Kathleen M Hayden
Frank Lin (Senior Author)
Lisa Miller
Melissa Minotti
Tom Mosley
Stacee Naylor
Tiffany Owens
Jim Pankow
Nicholas Reed (First Author)
A. Richey Sharrett
Vicky Sanchez
Jennifer Schrack

Other ACHIEVE investigators may be added as named authors as the manuscript progresses

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

First author: **Nicholas S. Reed**

Address: Cochlear Center for Hearing and Public Health

Johns Hopkins Bloomberg School of Public Health
2024 East Monument Street, Suite 2-700, Baltimore, MD, 21205

Phone: 410-502-4332 Fax: N/A
E-mail: nreed9@jhmi.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: **Frank R. Lin**
Address: Cochlear Center for Hearing and Public Health
Johns Hopkins Bloomberg School of Public Health
2024 East Monument Street, Suite 2-700, Baltimore, MD, 21205

Phone: 410-502-0150 Fax: N/A
E-mail: flin1@jhmi.edu

3. Timeline: Manuscript submission 3-6 months following approval

4. Rationale:

Novel approaches to reduce the risk of age-related cognitive decline are needed. Hearing loss is highly common and prevalence increases with age such that it affects nearly two-thirds of adults aged 70 years and older.[1] Recent epidemiologic observational studies have independently associated hearing loss with numerous negative health outcomes including poor physical function[2], accelerated cognitive decline,[3] and incident dementia.[4]

The mechanistic pathways through which hearing loss may contribute to poorer outcomes includes increased cognitive load due to degraded auditory signal processing in the cochlea, changes to brain structure and function, social isolation due to communication difficulties, and loss of environmental sound cues.[5] These pathways may be amenable to hearing loss treatment via amplification (i.e. hearing aids) and rehabilitative communication counseling. Indeed, observational data has generally suggested positive effects on cognition and quality of life; however, results are limited by confounding given the strong association between hearing aid use and socioeconomic variables, which are protective of cognitive decline.[6] To date, there have been no large, well-characterized randomized control trials of the impact of hearing loss treatment on cognitive decline among older adults.

The Aging and Cognitive Health Evaluation in Elders (ACHIEVE) trial is a large multicenter randomized trial designed to determine efficacy of hearing treatment in delaying cognitive decline in older adults. Cognitively intact (based on Mini Mental Status Exam [MMSE] score) participants aged 70-84 years with mild to moderate hearing loss (based on World Health Organization [WHO] criteria) were randomized 1:1 to a best-practice hearing intervention with a licensed audiologist or health education control. The primary outcome is change from baseline to year 3 in a global cognitive function factor score that is derived from a test battery of multiple domains. Secondary outcomes include loneliness, social network, health-related quality of life, hospitalization, falls, physical function, physical activity, and auditory-specific (i.e., speech understanding) outcomes. Uniquely embedded within the Atherosclerosis Risk in Communities

(ARIC) study, the ACHIEVE trial includes both well-characterized ARIC participants and de novo recruited participants. Initial estimated sample size of 850 provided 90% power to detect standardized effect size of 0.26 for difference between intervention and control groups in mean change from baseline in global cognitive factor score. The study design and pilot results have been described in full elsewhere.[7,8]

This manuscript will describe the recruitment process and results as well as report on baseline measures of the ACHIEVE trial.

5. Main Hypothesis/Study Questions:
The paper has the following aims:

1) Describe the process and results of screening and recruitment across the four study sites as well as covariates associated with recruitment outcomes (e.g., enrollment, refusal, etc) stratified by prior ARIC and de novo participants.
2) Report baseline measures (sociodemographic, health-related measures, baseline cognitive and audiometric measures) of the study cohort to demonstrate the results of randomization.

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).
This manuscript will describe the protocol and results of screening and recruitment in the ACHIEVE trial and report the results of randomization by describing baseline measures.

Design: Cross-sectional.

Participants: ACHIEVE participants include ARIC participants and de novo recruited participants across four ARIC field sites (Forsyth County, NC, Jackson, MS, Minneapolis, MN, and Washington County, MD).

Inclusion/Exclusions: All participants screened for inclusion and randomized for inclusion in ACHIEVE.

Outcome/Exposure:
Aim 1: Results of telephone and in-person screening visits and randomization across four sites including attendance of screening visit, eligibility, refusal, prior participation in ARIC (v de novo) and randomization. Covariates including but not limited to study site, socioeconomic variables, prior hearing aid usage, presence of spouse/partner, and psychosocial traits will be examined within the more extensively characterized ARIC cohort to identify those associated with recruitment factors (e.g., willingness to participate, enrollment, refusal, etc).
Aim 2: Baseline measures including:

- demographic (e.g., age, race, sex, study site, education, etc.)
- medical history
- audiometric (e.g., pure-tone audiometric results, speech understanding, perceived hearing handicap, etc.)

- proximal outcomes (e.g., loneliness, social network, depression, physical function/performance, falls and mobility, hospitalizations, etc.)
- cognitive measures (individual and global composite scores of delayed word recall, digit symbol substitution, incidental learning, trial making parts A and B, logical memory, digit span backward, Boston naming test, word fluency, and animal naming).

Analysis and potential challenges: We will present descriptive statistics of the variables noted above. Aim 1 analysis and results will be stratified by prior ARIC participants and de novo participants. Further, aim 1 analysis will stratify recruitment by time period (e.g., months, quarters, etc) to examine differences in patterns over time. Notably, aim 2 will present overall descriptive data summary for the entire combined cohort and will not stratify by intervention status. Few challenges are expected.

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)?
#2880 – Deal et al. A Randomized Pilot Trial of Hearing Treatment for Reducing Cognitive Decline: Results from the Aging, Cognition, and Hearing Evaluation in Elders Pilot (ACHIEVE-P) Study

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 ACHIEVE_____)

__ _ 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.

Citations

1 Lin, F. R., Niparko, J. K., & Ferrucci, L. (2011). Hearing loss prevalence in the United States. *Archives of internal medicine*, *171*(20), 1851-1853.

2 Chen, D. S., Betz, J., Yaffe, K., Ayonayon, H. N., Kritchevsky, S., Martin, K. R., ... & Pratt, S. (2014). Association of hearing impairment with declines in physical functioning and the risk of disability in older adults. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, *70*(5), 654-661.

3 Lin, F. R., Yaffe, K., Xia, J., Xue, Q. L., Harris, T. B., Purchase-Helzner, E., ... & Health ABC Study Group, F. (2013). Hearing loss and cognitive decline in older adults. *JAMA internal medicine*, *173*(4), 293-299.

4 Lin, F. R., Metter, E. J., O'Brien, R. J., Resnick, S. M., Zonderman, A. B., & Ferrucci, L. (2011). Hearing loss and incident dementia. *Archives of neurology*, *68*(2), 214-220.

5 Lin, F. R., & Albert, M. (2014). Hearing loss and dementia–who is listening?.

6 Amieva, H., Ouvrard, C., Giulioli, C., Meillon, C., Rullier, L., & Dartigues, J. F. (2015). Self-reported hearing loss, hearing aids, and cognitive decline in elderly adults: A 25-year study. *Journal of the American Geriatrics Society*, *63*(10), 2099-2104.

7 Deal, J. A., Albert, M. S., Arnold, M., Bangdiwala, S. I., Chisolm, T., Davis, S., ... & Mosley, T. (2017). A randomized feasibility pilot trial of hearing treatment for reducing cognitive decline:

results from the Aging and Cognitive Health Evaluation in Elders Pilot Study. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, *3*(3), 410-415.

8 Deal, J. A., Goman, A. M., Albert, M. S., Arnold, M. L., Burgard, S., Chisolm, T., ... & Mosley, T. (2018). Hearing treatment for reducing cognitive decline: Design and methods of the Aging and Cognitive Health Evaluation in Elders randomized controlled trial. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, *4*, 499-507.