ARIC Manuscript Proposal #3553

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

1.a. Full Title: The Association Between Hearing Impairment and Physical Function in the Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters): Hearing and physical function

2. Writing Group:

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

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3. Timeline: Analyses and manuscript to be completed within 1 year

4. Rationale:

Physical functioning is necessary for independent living(1,2). With aging, the capacity to perform physical tasks (e.g., walking, lifting objects, etc.) decline gradually(3). In the United Sates in 2016, 22.5% of adults over the age of 65 years have some form of walking disability(4) Additionally, aging is also strongly associated with multiple sensory impairments including hearing loss(5). Per nationally representative measures, two-thirds of adults over 65 years have a hearing loss. However, there is a paucity of work characterizing the association of hearing loss and physical function with objective measures in a well-defined cohort.

In recent years, due to its high prevalence (~66% of those aged>65 years (5)) hearing loss has been identified as a target for interventions for healthy aging. Previous work has identified hearing loss as a risk factor for functional decline including accelerated declines in gait speed (6) and self-reported measures of physical limitations (7). Notably, in ARIC, the association between hearing loss and physical function was explored by Deal. et al. in the "hearing pilot study" in 2016, they examined 250 individuals and found that participants with hearing impairment had a lower short physical performance battery score (-0.77), indicating poorer physical function, and were slower to complete chair stands when compared to individuals with normal hearing. However, regarding walking speed and balance, no differences were found between individuals with or without hearing impairment (8). There are several mechanisms that may explain an association between hearing loss and physical function:

First, in a direct pathway, reduced perception from environmental auditory cues leads to difficulty in moving and walking. Such auditory cues help with spatial localization and standing balance, both necessary to perform physical tasks (9). Second, in a pathway mediated by increased cognitive demands, individuals with hearing loss allocate more cognitive resources to understand sounds, resulting in reduced cognitive resources for movement (9). Third, in a pathway mediated by reduction in physical activity, hearing loss leads to social isolation(10) and reduced life-space mobility(11), both of which may contribute to lower levels of physical activity. In the long term this mechanism may result in physical deconditioning and reduced physical function(12).

However, there are some confounding variables that might partially explain this association. Since the hearing and vestibular systems are located in the same organ, it is possible that exposures that damage the inner ear lead to dysfunction in both systems, explaining an association between hearing loss and poor balance. Other potential confounders include age, sex, race, cardiovascular disease and risk factors, and socioeconomic status(5).

With our proposed manuscript, we aim to extend the previous investigation done by Deal, et al., by incorporating/updating using data from Visits 6 and 7. Additionally, we aim to look at the change over time in physical function measures by hearing status at Visit 6.

5. Main Hypothesis/Study Questions:

Determine the association between peripheral hearing impairment measured at visit 6 (2016-2017) and physical functioning (cross-sectional associations where hearing and physical function were measured at the same visit [6]) and changes in physical functioning from visit 6 to visit 7 (2016-2019) in older adults (where hearing is measured at visit 6 and treated as a fixed variable and the change in physical function is calculated by subtracting the SPPB score (total and for each component) at visit 7 from the SPPB score at visit 6).

- *For our cross-sectional analysis, we hypothesize that participants with hearing impairment at visit 6, compared to normal hearing, are more likely to have poorer physical function*
- *For our longitudinal analysis we hypothesize that participants with hearing impairment, compared to normal hearing, will have greater reductions in objective measures of physical function from visit 6 to visit 7 (from 5 to 7 in the subsample that participated in the pilot study).*

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: Cross-sectional and longitudinal analyses using Visit 6 hearing status and measures of physical function and their change from Visit 6 to Visit 7. In a secondary analysis, we will also use hearing data from Visit 5 in a subset of participants that were included in a pilot study. For these participants, we will use their hearing data at visit 5 and treat it as a fixed variable. The change in physical function for this group will be calculated by subtracting the SPPB score (total and for each component) at visit 7 from the SPPB score at visit 5.

Study Population: Our study sample originates from the full cohort of 15,792 participants and incorporates data from Visit 1 through Visit 7. Audiometry was completed in a subset of 250 participants from the Washington County, MD study site at Visit 5 and offered to all participants who attended Visit 6 (2016-2017). In Visits 6 and 7, physical function of 3,628 participants was assessed using the short physical performance battery and endurance performance (the ability to exert which is necessary for completing some tasks with an aerobic burden such as walking longer distances) was measured using the 2-minute walk test where the distance completed, walking as fast as possible, is recorded.

Outcome: Our primary outcome of interest is physical function ascertained in ARIC participants who attended clinic visits 6-7 (2016-19), in a subsample (n~250 participants) we will also use data from visit 5 . We will look at two performance-based measures of physical function and endurance: the short physical performance battery, and the two-minute walk. Additionally, we will look at changes in these measures from Visit 6 to Visit 7 (Visit 5 to Visit 7 in the subsample). For the short physical performance battery, we will use the composite score (range 0-12), the score for each test (balance [0-4], gait speed [0-4], and chair stands [0-4]), and the raw measurements (time to complete) for gait speed and chair stands. The composite score will be further categorized into high (10-12), intermediate (7-9), and low (≤6) function(1). Meters walked during the two-minute walk test will be used as a continuous variable. The change in the continuous measures will be calculated by subtracting the score in Visit 7 from the score in Visit 6. In the general population, the SPPB scores tend to cluster in the higher end (the majority of individuals have scores from 10-12, also called ceiling effect(8)). However, it is possible that in this cohort of older adults we encounter lower scores at baseline (visit 5 for the subsample and 6 for the main analysis), thus, possible floor effects will be examined. If we encounter low average SPPB scores at the baseline visit, we will conduct an analysis in which individuals with lower scores (≤6 as defined above) will be excluded as they may drive to that floor effect, precluding us from finding significant changes between visits.

Exposure: Pure tone audiometry was completed in a sound-proof booth using insert earphones (EARTone 3a; 3M) and the Interacoustics AD629 audiometer (Interacoustics A/S, Assens, Denmark). Air conduction was completed at standard octaves from 500-8000 Hz. A four-frequency pure-tone average (PTA) in the better ear was calculated (the hearing sensitivity or threshold is measured at each one of the four sound frequencies [500,1000,2000,8000 Hz] for each ear, an average of those sensitivities is calculated). Hearing impairment will be categorized along WHO standards: Normal hearing, PTA ≤25 dB; mild loss, 26-40 dB; moderate loss, 41-60 dB; severe or greater loss, >60 dB in the better hearing ear(13). We will also investigate the association treating PTA as continuous. Moreover, we will look at asymmetrical hearing, which might be particularly relevant for physical functioning, which we will define, according to the American academy of otolaryngology, head, and neck surgery (AAO-HNS) as ≥15 dB difference in PTA between ears(14).

Additional Independent Variables: Basic demographic information was collected at Visit 1, including birthdate for calculating age at study visit, sex, education, and race-study site. We will assess smoking status, diabetes, hypertension, and body mass index covariates as visit 6 status.

Statistical Analysis: We will explore differences in demographic and clinical characteristics by hearing status using chi square and t-tests as appropriate. The mean differences in gait speed, time to complete the chair stands, and meters walk in two minutes between hearing loss groups and by 10 dB greater hearing loss, will be calculated using linear regression models, crude and progressively adjusted for covariates.

For the cross-sectional analysis, the odds of being in a lower category of function (high, intermediate, low) will be calculated by using ordinal logistic models, crude and adjusted for covariates. Alternatively, tobit regression models can be used to evaluate a linear relationship between hearing loss and short physical performance score, given the possible ceiling effect of the short physical performance battery (the previous examination in ARIC by Deal et al., found the median SPPB to be 10 for those with hearing loss and 11 for those without(8)). Finally, depending on the distribution of the data, the short physical performance battery can be dichotomized into low (≤6: for the composite score; ≤2: for each component) and normal (7-12: for the composite score; 3-4 for each component)(15). If the last approach is used, logistic regression models can be used to estimate the odds of having a low score by hearing status.

The change in physical outcomes will be modeled using linear regression models, where the difference between Visit 7 and 6 will be the outcome. For the secondary analysis, in which there are 3 time-points we will use multilevel regression models, with random intercept and slope, adding an interaction term with time and hearing groups to assess if the change over time differs by hearing status.

7.a. Will the data be used for non-CVD analysis in this manuscript? _ _ Yes _ X _ No

b. If Yes, is the author aware that the file ICTDER03 must be used to exclude persons with a value RES_OTH = "CVD Research" for non-DNA analysis, and for DNA analysis RES_DNA = "CVD Research" would be used? _ _ Yes ____ No
(This 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 file ICTDER03 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)?

MP#2418 Deal et al. Hearing impairment and physical function in the Atherosclerosis Risk in Communities (ARIC) Hearing Pilot Study

MP#3284 Shukla et al. Association between hearing loss and frailty: a cross-sectional analysis from the Atherosclerosis Risk in Communities (ARIC) study

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?

11.b. If yes, is the proposal
___ A. primarily the result of an ancillary study (list number* _________)
___ 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 at https://www2.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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