ARIC Manuscript Proposal #2418

PC Reviewed: 8/12/14 **Status: A** **Priority: 2**
SC Reviewed: _________ **Status: _____** **Priority: ____**

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

b. Abbreviated Title (Length 26 characters): HI PFX

2. Writing Group: (Alphabetical) : Karen Bandeen-Roche, Jennifer A. Deal (first author), Stephen Kritchevsky, Frank R. Lin (senior author), A. Richey Sharrett, Gwen Windham

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

Name: Jennifer A. Deal, Ph.D.
Address: 615 N. Wolfe St., W6509
Baltimore, MD 21205
Phone: 410-502-3115
E-mail: jdeal1@jhu.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, M.D., Ph.D.
Address: Johns Hopkins Center on Aging and Health
2024 E. Monument Street
Baltimore, MD 21205
flin1@jhmi.edu

3. Timeline:
Manuscript will be completed in 6 months.

4. Rationale:
Prevention of disability is a public health priority for an aging society. Self-report is important for disability measurement in older adults, as psychosocial factors are conceptualized as integral to the disablement process.[1] Performance-based measures of physical function are standardized tasks with pre-determined performance criteria that offer an objective alternative to self-report. The Short Physical Performance Battery (SPPB) is a performance-based measure of lower extremity function based on the ability and time to complete three tasks: chair stands, balance and 4-meter walk.[2] The SPPB and its components predict mortality[2], falls,[3] hospitalization[4] and incident disability.[2,5,6]

Hearing impairment (HI) is highly prevalent and increases with advancing age, approximately doubling with every increasing decade of life; an estimated 2 out of 3 adults aged 70 or older have hearing impairment.[7]

Observed associations between HI and physical function outcomes in older adults could be explained through reduced auditory awareness of the environment,[8] concomitant vestibular dysfunction,[9,10] or from a common underlying pathology, such as vascular disease or inflammation. Alternatively, it has also been proposed hearing impairment may be causally associated with functional (both cognitive and physical) decline through mechanisms including (1) an increase in cognitive load, (2) changes in brain structure, and (3) mediation through social isolation and loneliness.[11,12]

Prior studies have reported an association between HI and lower extremity function,[8,11] disability[13] and falls in older adults.[14,15] In cross-sectional analysis of 1,180 participants in the National Health and Nutrition Survey (NHANES), each 25 decibel (dB) increase in hearing loss was associated with 2.0 times the odds (95% confidence interval (CI): 1.2, 3.3) of a **usual gait speed** < 1 meters/second (m/s) and with a difference in usual gait speed of -0.053 (95% CI: -0.090, -0.018) m/s.[11] In an age-adjusted longitudinal analysis of 434 women aged 63-76 years, the odds ratio of self-reported incident major **difficulties walking 2 kilometers** during 3 years of follow-up comparing women with audiometric hearing impairment to women with no HI was 2.04 (95% CI; 0.96-4.33).[8] In 2,461 men and women from the Alameda County Study who were aged 50-102 years at baseline, self-reported difficulty hearing and understanding words was associated with an increased odds of self-reported incident **Activities of Daily Living (ADL)**[16] disability, **Instrumental Activities of Daily Living (IADL)**[17] disability, and **physical performance disability** after one year of follow-up.[13] In the NHANES, each 10 dB increase in hearing loss was associated with 1.4 times the odds (95% CI: 1.2, 1.7) of a self-reported **falls** in the preceding 12 months, after adjustment for demographic and cardiovascular factors.[14] Compared to women with hearing measured in the best quartile (pure tone average <11.5 dB), the age-adjusted incidence rate of **falls** for women with hearing impairment (>27 dB) was 3.4 (95% CI: 1.0, 11.4) during 12 months of follow-up in 423 women aged 63-76 years enrolled in the Finnish Twins Study.[15]

Although HI is potentially amenable to rehabilitative interventions and devices, these interventions remain underutilized. Of an estimated 26.7 million adults aged 50 years or older who have HI, only 3.8 million (14%) use hearing aids. It is estimated that approximately 23 million individuals living in the United States who have HI do *not* use hearing aids.[18]

Here we propose to quantify the association between audiometric hearing impairment and self-reported and performance-based measures of physical function in the Atherosclerosis Risk in Communities (ARIC) Study. To our knowledge, only one other study (under review) has quantified the relationship between hearing impairment and the Short Physical Performance Battery (SPPB).[19]

5. Main Hypothesis/Study Questions:

<u>Aim 1</u>: To test the hypothesis that audiometric hearing impairment is cross-sectionally associated with poorer physical function, objectively measured by performance-based physical activity measures at the time of audiometric hearing assessment.

> *We hypothesize that, compared to persons with no hearing impairment, persons with hearing impairment score lower on a test of lower extremity function, the Short Physical*

Performance Battery, and perform more poorly in each of its components, including time to walk 4 meters, balance, and time to complete 5 chair stands.

We hypothesize that greater HI is <u>not</u> associated with poorer grip strength, a measure of upper extremity function.

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).

<u>Study design</u>: Cross-sectional analysis within a prospective observational study of 307 men and women who underwent audiometric hearing testing (Washington County site only) in 2013 as a pilot study. Of the 307, 6 declined participation, 46 did not complete the otoscopic exam (45 due to impacted cerumen in one or both ears), and 2 are of nonwhite race, resulting in an analytic sample of 253. Objective measurements of physical function were collected in 2013 as part of Visit 5. Self-reported mobility dependence was collected as part of the semi-annual telephone call in 2013-14.

<u>Outcomes</u>:

<u>I.</u> <u>Objective physical performance measures</u>

Primary cross-sectional outcomes will include total **Short Physical Performance Battery (SPPB)** score and **grip strength**. In secondary analysis, we will estimate the association between hearing impairment categories and components of the SPPB, including chair stand speed, balance, and 4-m walking speed.

The **Short Physical Performance Battery (SPPB)** is a series of physical performance tests designed to assess lower extremity function in older adults.[2]

1. <u>Total Score</u>. The SPPB ranges in score from 0-12; higher scores indicate better function. The total score is the sum of 3 component scores: chair stands, balance and 4-meter walk; each component score ranges from 0-4.
2. <u>Components</u>
    a) *Chair stands*. Participants were asked to fold arms over chest, and rise to standing from a seated position in a chair. If able to complete one chair stand, participants were then timed as they completed five chair stands in a row, as quickly as possible without stopping, keeping arms folded over chest. Participants were assigned a score ranging from 0-4 based on the ability and time to complete the 5 chair stands (see Table). For our secondary analysis, we will calculate the speed (chair stands/second) in completing the 5 chairs stands by dividing 5 by the time to completion of the task.
    b) *Balance*. Each participant was assigned a score of 0-4 for standing static balance based on his/her ability to balance for 10 seconds with feet side-by-side, in semi-tandem, and in full tandem position (see Table, Figure 1). Because the majority (N=187, 62%) of participants in the hearing pilot study were able to complete the most difficult task (tandem balance for 10 seconds), for our secondary analysis we will create a binary outcome variable: not able to complete first attempted 10 second tandem balance versus able to complete.

c) *4-meter walk*. Participants were asked to complete a 4 meter walk at their normal pace in two trials. Participants were encouraged to complete each walk without a walking aid (e.g., walker, cane) if possible, but allowed to use a walking aid if they chose to do so. Scores of 0-4 were assigned based on distribution of time to complete the walk (see Table). For our secondary analysis, we will calculate the 4-meter walking speed (in meters/second) by dividing 4 by the average (of the 2 trials) time to complete the task in seconds.

Figure 1. Static balance positions

Table. Scoring for SBBP Components (from National Institute of Aging Protocol)[2]

SPPB Component	Cutoff	Score Assigned
Time to complete 5 chair stands (seconds)	Unable	0
	≥ 16.7 s	1
	13.7-16.6 s	2
	11.2-13.6 s	3
	<11.2 s	4
Standing static balance	Side-by-side <10s	0
	Side-by-side 10s & semi-tandem <10s	1
	Semi-tandem 10s, Full tandem ≤ 2s	2
	Semi-tandem 10s; Full tandem 3-9s	3
	Full tandem for 10s	4
Time to walk 4meters	Unable	0
	<0.44 m/s	1
	0.44-0.60 m/s	2
	0.61-0.77 m/s	3
	>0.77m/s	4

A flow diagram of test administration for each SPPB component and number from the hearing pilot study who completed each stage of testing is presented in **Supplemental Figure 1**.

3. Rescaling of the SPPB score

Possible SPPB scores range from 0-12 and observed SPPB scores in this sample show a ceiling effect (see Figure 2). In order to better discriminate physical function in this high-functioning population, we will repeat analyses, rescaling each SPPB component according to previously published guidelines developed in the Health Aging and Body Composition (Health ABC) study.[20] Rescaled scores will be calculated as follows:

- Chair stands: observed time to complete 5 chair stands for an individual / maximal time to complete 5 chair stands; scores range from 0-1

- Balance: sum of the time the participant was able to hold each balance position; scores range from 0-30 (up to 10 s for each position: side by side, semi-tandem, full tandem)
- 4-meter walk: observed time to walk 4 meters/ maximal time to walk 4 meters; scores range from 0-1

Scores will be standardized (so that each task contributes equally to the total scores) and summed to create a rescaled total SPPB score

B. **Grip Strength.** Grip strength was measured with a hand held dynamometer. After one practice trial, participants were asked to complete two trials, squeezing as hard as possible, with a 15-20 second rest between trials. In keeping with current ARIC Physical Function workgroup recommendations, we will use the average of the 2 grip strength trials in the analysis.

II. Self-reported mobility dependence

Self-reported dependence with heavy housework, walking up and down stairs, and walking ½ mile was collected as part of the annual telephone follow-up calls (forms D, F-K) from 1993-2006 (mean follow-up time 12.6 ± 0.4 years) and as part of the semi-annual telephone follow-up call in 2013-14.

Next, I would like to find out whether you can do some physical activities without help. By 'without help', I mean without the assistance of another person. These questions refer to the last 4 weeks.

Are you able to do heavy work around the house, like shoveling snow or washing windows, walls or floors, without help?

Are you able to walk up and down stairs to the second floor without help?

Are you able to walk ½ mile without help? That's about 8 ordinary blocks.

We propose to quantify the cross-sectional association between hearing impairment and self-reported mobility dependence assessed by the semi-annual follow-up call in 2013-14. In addition to testing whether each type of dependence, we will create a composite outcome: time to incident dependence for any of the 3 measures.

Exposure: Pure tone air conduction audiometry was conducted at Visit 5 in a sound-treated booth within a quiet room. Pure tone audiometry is the gold-standard test to determine the faintest tones that a person can detect for a range of pitches. We will calculate a speech frequency Pure Tone Average (PTA) using audiometric thresholds at 0.5, 1, 2, and 4 kHz in the better-hearing ear in accordance with the World Health Organization definition of hearing loss.[21] The primary analysis will categorize hearing impairment using a clinically defined ordinal variable for hearing impairment: no HI: <25 dB, mild HI: 26-40 dB, moderate/severe HI: >40db. Additionally, we will utilize PTA as a continuous variable to determine if there is a linear relationship with functional performance overall, and within the clinically defined categories defined above.

Additional independent variables:
Demographic information was collected at Visit 1, including age (years), sex, and education (highest grade or year of school completed). Education will be categorized according to standardized ARIC algorithms as basic (≤ 11 years), intermediate (12-16 years), or advanced (≥ 17 years). Audiometric testing was limited to Washington County, Maryland. Because of the

small number of non-white participants (N=1 Asian and N=1 Black), the analysis will be restricted to participants self-reporting white race.

Self-reported information on current and past cigarette smoking status was collected at each study visit and recorded as never, former or current according to a standardized algorithm. Quantity of lifetime tobacco use (cumulative cigarette-years) among ever smokers was calculated at Visit 1 and 2 according to standardized algorithms. Body mass index (kg/m^2) was calculated at each study visit and will be categorized according to clinical cutpoints: normal weight ($<25\ kg/m^2$), overweight ($25\text{-}30\ kg/m^2$) and obese ($>30\ kg/m^2$).

Disease covariates were collected at each study visit, and adjudicated according to standardized algorithms. Hypertension will be considered present based on a diastolic blood pressure ≥ 90 mmHg, systolic blood pressure ≥140 mmHg, or use of hypertensive medications. Diabetes will be considered present if fasting blood glucose level was ≥ 126 mg/dL, nonfasting level ≥ 200 mg/dL, or the participant self-reported a diagnosis of diabetes or of medication use for diabetes.

The Mini-Mental State Exam[22], a measure of global cognitive function that was designed as a brief clinical screening tool for dementia, was administered to the entire ARIC cohort at Visits 2, 4 and 5.

Depressive symptoms were measured at Visit 2 using 7 items that relate to depression from the 21-item Maastricht Questionnaire for vital exhaustion.[23] Responses to these items (0=no, 1=don't know and 2=yes) were summed to yield a possible score ranging from 0-14, with higher scores indicating higher depressive symptoms. Depressive symptomatology in 2013 was measured using the 11-item Center for Epidemiologic Studies Depression Scale (CES-D);[24] possible scores ranged from 0-22, with higher scores indicating greater depressive symptomatology.

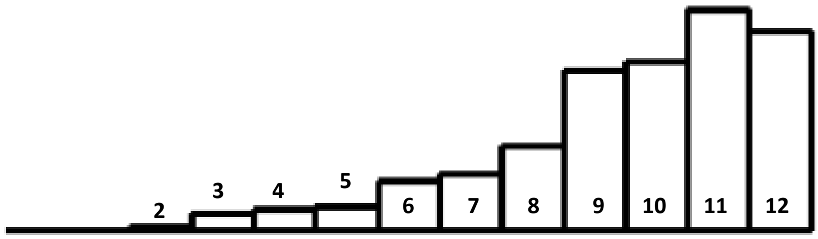
Self-reported hearing aid use and duration of use was collected at Visit 5. Hearing aid use will be defined self-reported hearing aid use in either ear during the previous month based on the following two questions:

> "*Do you currently use a hearing aid in your right (left) ear*?"
> If Yes, "*Averaged over the past month, about how many hours per day have you worn your hearing aid in the right (left) ear*?"

Statistical analysis:

Multivariable linear regression will be used to estimate the average difference in performance at Visit 5 comparing persons with hearing impairment to persons without hearing impairment for our two primary outcomes of interest: SPPB score and grip strength. Because of the ceiling effect with the SPPB (maximum score=12), tobit regression will be utilized for this outcome. Tobit regression uses maximum likelihood estimation to estimate the linear association between an exposure and a latent outcome when censoring is present in the observed outcome variable (see Figure 2). We conceptualize the SPPB as measuring a latent variable of lower extremity function, denoted here as SPPB*. The observed SPPB scores are censored at 12 (the highest possible score, a function of the test). Although some participants would truly score a 12 on the SPPB*, other participants would score higher. Because tobit model estimates will be biased in the presence of heteroskedastic errors, we will carefully evaluate this assumption. If heteroskedasticity is violated, we will model the SPPB using quantiles.

Figure 2. Distribution of Observed SPPB Scores, N=250



Multivariable logistic regression will be used to estimate the log odds of self-reported mobility dependence associated with hearing impairment.

Model building: We will employ a three-step model building process for adjustment. Model 1 will incorporate demographic covariates, including age, sex and education. Based on previous analyses, we will include both a linear term and a quadratic spline for age, in order to allow for the non-linear association of age with functional performance. Model 2 will include those covariates in Model 1, as well as additional risk factors for physical function decline, including smoking status, body mass index (BMI), and prevalent diabetes and hypertension. As depression could be a possible mediator of the relationship between HI and cognitive performance, Model 3 will further adjust for depressive symptoms.

Hearing aid use: In order to quantify the estimated effect of hearing aid use on the outcome among those with hearing impairment, we will repeat analyses restricting to participants with moderate/severe hearing impairment (N=85), including hearing aid use as a covariate. Of the 85 participants with moderate/severe hearing impairment, 42 (49%) reported wearing a hearing aid. Only 9 other participants self-reported hearing aid use: 3 with no hearing impairment and 6 with mild hearing impairment.

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Association of hearing impairment with declines in physical functioning and the risk of disability in older adults. .
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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? N/A
____ 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"? N/A
____ 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/search.php

__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 2327. Deal et al. Hearing impairment and cognitive performance in the Atherosclerosis Risk in Communities Neurocognitive Study (ARIC NCS): cross-sectional and longitudinal results
MP1697. Kucharska-Newton et al. Functional status and cardiovascular disease
MP2254. Windham et al. Relationship of Adiposity Trajectories to Later Life Physical Function and Strength
MP2289. Demerath et al. Age at Menopause and Physical Function in Older Women: The ARIC Study
MP2303. Godino et al. Diabetes, hyperglycemia, and the burden of frailty syndrome in the Atherosclerosis Risk in Communities Study
MP2304. Godino et al. Diabetes, hyperglycemia, and the burden of functional disability in the Atherosclerosis Risk in Communities Study
MP2311. Palta et al. Individual and contextual socioeconomic profile and physical function in late life: the Atherosclerosis Risk in Communities (ARIC) Study
MP2312. Matsushita et al. Ankle-brachial index and physical function and activity in older individuals: the Atherosclerosis Risk in Communities (ARIC) Study
MP2383. Windham et al. Relationship of Life's Simple 7 Score in Midlife to Late Life Physical Function

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? ____Yes __ X __ No

11.b. If yes, is the proposal N/A

___ 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)* 1999.01)

*ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

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.

Supplemental Figure 1. Flow diagram of test administration for each SPPB component