ARIC Manuscript Proposal # 3356

PC Reviewed: 2/12/19  Status: _____  Priority: 2
SC Reviewed: _________  Status: _____  Priority: ____

1.a. Full Title: Ideal cardiovascular health and age-related hearing loss in the Atherosclerosis Risk in Communities Study

b. Abbreviated Title (Length 26 characters): Ideal CVD health and ARHL

2. Writing Group: David Couper, Jennifer A. Deal, Frank Lin, Jim Pankow, Nicholas Reed, Matthew Waggenspack

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

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3. Timeline: 6 months

4. Rationale:
About 10% of the population experiences impaired communication attributable to hearing loss, and this rate is 40% in the population older than 65 years. Health-related quality of life is negatively impacted by hearing loss and tinnitus. The United States has identified hearing health of adults as a priority in order to reduce potential negative effects of hearing loss which has been associated with poorer cognition, increased risk of falls, and other negative health outcomes, though their exact relationships remain unclear.

Genetic factors, environmental exposures, physical trauma, and diseases of the ear are all responsible for hearing loss. This study will investigate multiple risk factors that might impact hearing by way of their potential effects on the vasculature of the cochlea. Cochlear functions (maintaining endocochlear potential, ion transport, endolymphatic fluid balance) are reliant on blood supply through capillary networks of the spiral ligament and stria vascularis.

The American Heart Association’s (AHA) “Life’s Simple 7 (LSS)” (physical activity, normal blood cholesterol, healthy diet, normal blood pressure, healthy weight, normal blood glucose, no smoking) are factors that can be used to assess cardiovascular health. These factors can be modified through lifestyle change to attain improved cardiovascular health and reduce risk of cardiovascular disease. Though the relationship of LSS to hearing has not been previously investigated, to our knowledge, some of the components of LSS have been associated with hearing loss in adults. For example, smoking has often been found to have a positive association with hearing loss, though about a third of these studies find no significant association. Non-smokers who live with a smoker have been found to be more likely to have hearing loss than non-smokers in non-smoking households. Diabetes may lead to microvascular changes that have been shown to impair cochlear functions and cause auditory nerve damage, and meta-analysis of studies of diabetes and hearing loss show a 2.1-fold higher prevalence in subjects with diabetes than in those without diabetes, though the included studies often had poorly age or noise-exposure matched controls. Poor CVD health may potentially cause hearing loss by direct mechanisms (e.g. increasing oxidative stress within cochlea or damaging stria vascularis from reduced blood supply) or may hinder the ability of sensory or neural structures to recover from environmental exposures (e.g. noise or ototoxins).

This study will investigate the association of a global measure of ideal cardiovascular health with hearing loss within the ARIC cohort. We will use the AHA’s Life’s Simple 7 as a metric of cardiovascular health. If age-related hearing loss is attributable in part to reduced vascular function, then the Life’s Simple 7 measured in middle age may be able to predict who is able to maintain good hearing into old age. ARIC investigators previously confirmed CVD incidence does show a graded relationship across low, intermediate, and ideal levels of cardiovascular health using the Life’s Simple 7. The current investigation will provide evidence as to whether or not reduced risk of hearing loss is an additional potential health benefit to achieving ideal cardiovascular health.
5. **Main Hypothesis/Study Questions:**

**Primary:**
To quantify the association between cardiovascular health and hearing loss.

We hypothesize that:
Prevalence of hearing loss at visit 6 will have a graded negative relationship among groups who have ideal, intermediate, and poor cardiovascular health at Visit 1, controlling for age, sex, race, socioeconomic status, history of noise exposure, and other potential confounders.

**Secondary:**
If there is a relationship between ideal cardiovascular health and hearing loss, to explore whether ideal cardiovascular health mitigates risk attributable to history of noise exposure.
We hypothesize that:
The association between history of noise exposure and age-related hearing loss will stronger in those with poor CVD health compared to those with ideal CVD health.

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 Population:**
ARIC participants who completed hearing testing at Visit 6 and have physical activity, blood cholesterol, diet, blood pressure, BMI, blood glucose, and smoking status collected at baseline (Visit 1).

**Outcomes:**
Hearing loss as measured by pure tone air-conduction audiometry and categorized by World Health Organization (WHO) definitions. Pure tone audiometry was offered to all ARIC participants at Visit 6 (2016-17). A four-frequency (0.5, 1, 2, and 4 kHz) pure tone average (PTA) will be calculated in the better-hearing ear. A four-frequency average for the worse ear
may be considered in a secondary analysis. WHO hearing loss categorizations are as follows: normal hearing: ≤25 decibels hearing loss (dB HL), mild hearing loss: 26-40 dB HL, moderate hearing loss: 41-60 dB HL, and severe or profound hearing loss: >60 dB HL.

Primary Predictor:
Life’s Simple 7 scored per AHA descriptors (0 = poor, 1 = intermediate, 2=ideal) for 7 categories (physical activity, blood cholesterol, diet, blood pressure, BMI, blood glucose, and smoking status). LSS score ranges from 0-14 with 0 indicating all 7 poor health factors and 14 indicating all 7 ideal health factors. As in several prior ARIC papers, the LSS to be broken into categories (0-4=inadequate; 5-9=average; 10-14=optimal), and also retained as a continuous score in some analyses.

Covariates:
Demographic information collected at baseline including age(years) sex, race, center, and education.

Noise exposure using self-reported measures from Hearing and Noise Exposure form completed at Visit 6. Noise exposure to be categorized using self-report of occupational exposure (10+ hours/week), recreational exposure (10+ hours/week), and firearm use.

Primary Analysis:
Standard logistic regression will be used for analysis of LSS (Visit 1) predictor and binary outcome (normal hearing vs. mild/moderate/severe hearing loss) from Visit 6

Additional analyses:
Ordinal logistic regression will be used to investigate the relationship between LSS (Visit 1) and WHO hearing impairment categories (Visit 6), as defined above. Further analyses may consider change in LSS from Visit 1 to Visit 3 (improved, worsened, or same) as a predictor of hearing loss outcome at Visit 6.

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 3206  Powell et al. Cross-sectional relationship of diabetes mellitus with hearing impairment in older adults
MP 3254  Ting et al. Hypertension and Age-Related Hearing Loss in the Atherosclerosis Risk in Communities Study

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

___ 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.
References: