ARIC Manuscript Proposal #3204

PC Reviewed: 7/10/18 **Status: _____** **Priority: 2**
SC Reviewed: _____ **Status: _____** **Priority: ____**

1.a. Full Title: Association between hearing loss and depression: A cross-sectional analysis from the Atherosclerosis Risk in Communities (ARIC) study

b. Abbreviated Title (Length 26 characters): Hearing loss and depression

2.Writing Group (alphabetical):
Nicole Armstrong, Adele Goman (senior author), Frank Lin, Nick Reed, Aishwarya Shukla (first author) and others.

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

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

4. Rationale:

Depression is one of the most common chronic health conditions in the United States and affects approximately 7 million adults over 65(1). The lifetime risk of major depressive disorder is approximately 17% (2) and nearly 7% of the US population suffered from an episode of major depressive disorder (MDD) in the past year (3). Older adults with depression are at an increased risk for accelerated decline in cognition and functional status (4,5).

Hearing loss is an increasingly common condition among older adults, and two thirds of US adults over 70 have hearing loss significant enough to impair communication (6). A growing body of evidence has shown that age-related hearing loss is associated with negative cognitive (7),

physical (8), and psychosocial (9) health consequences. Previous epidemiological studies have shown an association between hearing loss and increased social isolation and loneliness (10) and decreased emotional vitality (11). However, the association between hearing loss and depression remains unclear in the literature. Patients with hearing loss find it more difficult to communicate with those around them and it is possible that this could lead to increased rates of depression. While some studies have found an association between hearing loss in older adults and depressive symptomatology (12), other epidemiologic studies have found no association after controlling for demographics and cardiovascular disease status (13). Another large epidemiologic study found that although mild hearing loss was significantly associated with depressive symptoms, moderate or severe hearing loss was not (14). Thus, the relationship between hearing loss and depressive symptoms in older adults remains unclear.

Although hearing loss is amenable to treatment, hearing loss treatment remains vastly underutilized and less than 20% of adults with a hearing loss using a hearing aid (15). Notably, although the relationship between hearing loss and depression is not clear in the literature, several studies, including one randomized trial, have demonstrated that use of hearing aids is associated with decreased social isolation and depression in older adults (13, 16-17). Possible reasons for this could be that older patients who are not depressed are more likely to obtain hearing aids than those who are depressed, or that treatment of hearing loss leads to increased social engagement and better communication which in turn decreases depressive symptomatology.

There are few rigorous epidemiological studies examining the association between hearing loss and depression in older adults. Here we propose to assess the cross-sectional relationship between hearing loss and depressive symptoms and secondarily, to determine the impact of hearing aid usage on depressive symptoms among those with hearing loss.

5. Main Hypothesis/Study Questions:

Aim: To quantify the cross-sectional association between hearing loss and depression

Main hypothesis: We hypothesize that compared to persons with no hearing loss, persons who have hearing loss will have a higher odds of depression.

Sub-aim: To determine the impact of hearing aid usage on depression among those with hearing loss.

Sub hypothesis: We hypothesize that persons with hearing loss who use hearing aids will have a lower odds of depression than those who don't use hearing aids.

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 methodological limitations or challenges if present).

Study Design: Cross-sectional analysis within a prospective observational study

Study population: Study population will be from ARIC-5 (2011-2013) and ARIC-6 (2015-2017) cohorts. We will exclude patients for whom a CES-D score would not be calculated or for whom a better ear Pure Tone Average (PTA) could not be calculated.

We will examine descriptive characteristics of those included vs. those excluded from this study to see if our sample is representative of the overall study population.

Exposure: Hearing loss
Pure tone audiometry is the gold standard to determine the softest tones that can be detected for a range of frequencies. A Pure Tone Average (PTA) is calculated using audiometric thresholds at 0.5, 1, 2 and 4 kHz in the better hearing ear, per WHO definition of hearing loss (18). Calculation of a PTA requires a threshold at 0.5, 1, 2, and 4kHz; if any of these values is missing a PTA cannot be calculated.

For primary analysis we will define hearing function categorically using the WHO criteria for PTA (18) as normal (<25dB) or hearing loss [mild (≥25 to40dB), moderate or greater (≥40dB)]. We will also conduct secondary analysis using PTA as a continuous variable to determine whether there is a linear relationship with depressive symptomatology.

Outcome: Depressive symptoms
Depressive symptomology is measured in the ARIC cohort using an 11-item Center for Epidemiologic Studies Depression (CES-D) that is scored from 0-22, with higher scores indicating greater depressive symptoms. A CES-D score of 9 or greater can identify individuals with increased risk for clinical depression (19).

If more than three items on the CES-D is missing, a score is not calculated. If one to three items are missing, scores on the completed items are summed and the total is divided by the number of items answered and multiplied by 11.

For primary analysis, we will evaluate CES-D as a dichotomized variable with a score of 9 or greater considered "positive" for depression. For secondary analysis we will define CES-D scores continuously to determine if there is a linear relationship with hearing loss.

Sub-aim: Hearing aid use
Our sub-aim will be to determine the impact of hearing aid usage on depressive symptoms among those with hearing loss. Hearing aid use will be defined in the primary analysis as self-reported hearing aid use in either ear using the following question:
"Do you currently use a hearing aid in your right (left) ear?"

For secondary analysis, we will consider a definition of hearing aid usage as wearing a hearing aid a minimum of 5 hours per week to allow for comparison with other studies in the literature (13). We will determine duration of hearing aid usage using the following question:
"Averaged over the past month, about how many hours per day have you worn your hearing aid in the right (left) ear?"

Covariates:
Demographic data including: age (years), sex (male, female) race (black, white, other), educational level (highest grade or year of school completed; education will be categorized consistent with standardized ARIC algorithm as basic [<11 years], intermediate [12-16 years] or advanced [>17 years]).

Other vascular risk factors and chronic medical conditions: smoking status (never, former, current smokier), BMI (categorized as normal [<25], overweight [25-30], obese [>30]), hypertension (systolic BP >140mmHg or diastolic BP >90mmHg; or use of antihypertensive medication), diabetes (fasting blood glucose >126mg/dl, non-fasting blood glucose >200 mg/dl, or use of diabetes medication), history of myocardial infarction, history of transient ischemic attack (TIA) or stroke.

Statistical analysis:
Baseline characteristics of participants will be compared using one-way analysis of variance or Fisher Exact test.

Aim 1: To quantify the cross-sectional association between hearing loss and depression.

Primary analysis: We will examine the relationship between hearing loss (mild/moderate or greater versus normal hearing) and depression (CES-D score >9) using multivariate logistic regression. We will perform the following:
Unadjusted analysis
Model 1: Adjusted for demographic variables (age, sex, education, race/field center)
Model 2: Adjusted for model 1 + vascular risk factors and chronic medical conditions (smoking status, BMI, hypertension, diabetes, history of MI, history of TIA or stroke)

We will also examine the relationship continuously using linear regression models to examine the association of hearing loss (per 10dB increase) on depressive symptomatology.

Odds ratios overestimate risk ratios if the prevalence of disease is above 10%. If the prevalence of depressive symptomology in our study population is above 10%, we will consider using a long-linear regression model to obtain prevalence ratios.

Sub-aim: To determine the impact of hearing aid usage on depression among those with hearing loss.

In order to determine the impact of hearing aid usage on depressive symptomatology amongst those with hearing loss, we will repeat analyses restricting to patients with mild or moderate or greater hearing loss and include hearing aid use as a covariate.

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
N/A

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)?

2418: Deal et al, Hearing Impairment and Physical Function in the Atherosclerosis Risk in Communities (ARIC) Hearing Pilot Study
3156: Guo et al, Visual Function, Retinal Pathology, and Associations with Quality of Life in a Bi-community Population 75 Years and Older: The Eye Determinants of Cognition 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* _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 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.

13. Per Data Use Agreement Addendum, approved manuscripts using CMS data shall be submitted by the Coordinating Center to CMS for informational purposes prior to publication. Approved manuscripts should be sent to Pingping Wu at CC, at pingping_wu@unc.edu. I will be using CMS data in my manuscript ___ Yes _X__ No.

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