ARIC Manuscript Proposal # 3253

PC Reviewed: 10/9/18       Status: _____       Priority: 2
SC Reviewed: _________       Status: ____       Priority: ____

1.a. Full Title: Using Self-Reported Hearing Quality to Infer About Epidemiological Associations between Functional Outcomes and Objective Hearing Loss in ARIC

b. Abbreviated Title (Length 26 characters): Self-Reported Hearing

2. Writing Group:
   Writing group members: Joshua Betz, Frank Lin, Jennifer A. Deal, Nicholas Reed, others welcome

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

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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).
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3. Timeline:
   Data Management: 1 month
   Analysis: 1 month
   Writing: 1 month
4. Rationale:

Hearing loss is an important public health issue due to its increasing prevalence with age and its independent associations with several health outcomes, including cognition and hospitalizations. Unfortunately, few cohort studies include any measures of hearing, and even fewer include objective hearing measures. Previous studies have reported poor sensitivity and/or specificity of self-reported hearing items, however these studies often included a limited range of responses or used instruments which were designed to measure the psychosocial impact of hearing loss, which may limit their utility.

Using a single self-report of hearing loss could allow for assessment of hearing at scale in clinical and research contexts with minimal burden on patients, researchers, and clinicians. Additionally, qualitative hearing variables can borrow additional information from demographic risk factors for predicting hearing loss, such as age and sex, using regression methods. Under certain assumptions, regression-predicted values of objective hearing loss could enter into other analyses as a covariate that is measured with measurement error. Depending on the type of measurement error assumed, appropriate statistical methods must be used to mitigate potential bias and loss of precision that some types of measurement error can induce.

While measurement error models have been used in other contexts when a reference standard is not feasible in all subjects due to the costs, risks, or burden of measurement, no study has attempted to use self-reported hearing to infer about objective hearing loss using such methods. ARIC contains objective hearing data, measured by the pure tone average in the better hearing ear (bPTA), subjective hearing data, and epidemiological outcomes of interest. Additionally, a single-item subjective hearing item used in ARIC, in combination with age and sex, has been shown to explain 69% of variability in bPTA in a population based study (NHANES cycles 2005-2006 through 2011-2012). We propose to use ARIC data to externally validate the predictions of bPTA, and provide an exemplar of using measurement error models to infer about objective hearing loss from subjective self-report items.

5. Main Hypothesis/Study Questions:

Aim 1: To validate associations between self-reported hearing and pure tone audiometry seen in NHANES, estimating the agreement between better hearing ear pure tone average (bPTA) and prediction model derived from NHANES using the concordance correlation coefficient.

Aim 2: To compare cross-sectional associations between hearing and health outcomes using:
1. Better hearing ear pure tone average (bPTA) as the reference standard
2. Regression-predicted bPTA as a covariate measured with error that is potentially correlated with PTA using models that do not account for measurement error.

Formal hypothesis testing will not be conducted, although we hypothesize that using predicted bPTA may provide estimates that are similar to those obtained using actual bPTA, although efficiency is lost due to Berkson measurement error.

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 observational study of men and women (27% African American) who underwent audiometric hearing testing in visit 6 and underwent cognitive assessment in visit 6. All individuals with audiometric and cognitive data will be included in analyses.

Outcomes: A global cognitive score, as described by Gottesman et al. (ARIC Manuscript Proposal (MP) 1982), will be used as an outcome, along with the Mini Mental State Exam (MMSE). The global cognitive score includes the Delayed Word Recall Test (DWRT), the Digit Symbol Substitution Test (DSST) of the Wechsler Adult Intelligence Scale–Revised, and the Word Fluency Test (WFT).

Exposure: All exposures are measured in visit 6. Hearing loss is measured using (1) better-hearing ear speech-frequency pure tone average (bPTA) measured via pure tone air conduction audiometry, and (2) regression-predicted bPTA is defined using a pre-specified linear regression model involving age, sex, and self-reported hearing status. Pure tone audiometry is the gold standard test to determine the faintest tones that a person can detect for a range of pitches. Here, bPTA will be calculated using the average of audiometric thresholds at 0.5, 1, 2, and 4 kHz in accordance with the World Health Organization definition of hearing loss. Self-reported hearing status asks the participant to qualitatively describe their hearing without a hearing aid. Possible responses include: Excellent, Good, A little trouble, Moderate hearing trouble, A lot of trouble, and Deaf.

Covariates: Models will be adjusted for age (years), sex, race-field center, education (basic: ≤ 11 years, intermediate: 12-16 years, or advanced: ≥17 years), cigarette smoking status (current, former, or never), and cardiovascular comorbidities as determined by standardized algorithms (hypertension: diastolic blood pressure ≥ 90 mmHg, systolic blood pressure ≥140 mmHg, or use of hypertensive medications; diabetes: fasting blood glucose level ≥ 126 mg/dL, or the participant self-reported a diagnosis of diabetes or of medication use for diabetes.

Statistical Analysis:

For aim 1, the concordance correlation coefficient will be used to measure the agreement between the measured bPTA and regression-predicted bPTA. A confidence interval will be provided to quantify uncertainty in this estimate due to sampling variability.

For aim 2, the analysis is cross-sectional in nature, and multiple regression will be used to quantify the association between cognitive outcomes in Year 6 and audiometric hearing loss in year 6, adjusting for potential confounding variables. Two separate multiple regression models will be fitted for each cognitive outcome: one using measured bPTA, and the other using regression-predicted bPTA. Model assumptions will be evaluated using residual diagnostic plots, and confidence intervals will be provided. Non-linear relationships may be addressed using cubic splines, and heteroscedasticity may be addressed using robust standard errors.

Methodological limitations:
NHANES is a nationally representative survey sample, and as such, estimated relationships may not hold in more selected study samples. In such cases, this may illustrate the shortcomings of inferring PTA in selected samples from a model based on a nationally representative sample.

Methods to account for classical measurement error in analyses of data from complex survey designs may be limited. As such, an initial approach may ignore classical measurement error in self-reported hearing. A sensitivity analysis to this assumption may be conducted under varying assumptions about the reliability of the item.

Cognition is measured in visits 2, 4, 5 and 6, and hearing is measured in visit 6. Individuals in the analytic cohort represent those individuals who survived until visit 6 and were able to complete both audiometric testing and the neuropsychological battery. We will compare baseline (Visit 1) characteristics between those included in the analytic cohort and those excluded from the analytic cohort to describe potentially important differences between these subgroups.

7.a. Will the data be used for non-CVD analysis in this manuscript? ___X__ Yes  ____ 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? ___X__ 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/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)?

While other authors have published on measurement error in ARIC (e.g. MP1122, MP1967, MP243B), these proposals largely focus on classical measurement error, where measurements are subject to situational and/or technical variability. In classical measurement error, observed measurements are assumed to be a combination of the true value of the measurement with either additive or multiplicative error that is assumed to be independent from the true exposure. Failure
to account for classical measurement error can induce regression dilution, introducing bias and reducing precision in estimation.

This proposal takes a Berkson error approach, which is useful when exposure is aggregated (i.e. individuals are assigned an average exposure based on shared characteristics). In this framework, the true exposure is assumed to be a combination of the observed value of the exposure with either additive or multiplicative error that is assumed to be independent from the observed exposure. While aggregated exposures themselves could be viewed as being measured with classical measurement error (i.e. self-reported hearing in our model is measured with classical error), the focus of this proposal is illustrating the potential utility of the Berkson error model, which we believe will predominate in this situation.

Since the goal is to explore the utility of such models in epidemiological research, we will be using cognitive function as an outcome: we are collaborating with members of the study team of proposal MS2327, which measured associations between hearing and cognitive outcomes at visit 5 in individuals with audiometry measured at visit 5.

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 http://www.cscce.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.cscce.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:


