ARIC Manuscript Proposal #2993

PC Reviewed: 06/06/17	**Status: _____**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Lifetime risk of atrial fibrillation by race and socioeconomic status in the ARIC cohort

b. Abbreviated Title (Length 26 characters): Lifetime risk of AF

2. Writing Group:

Writing group members: Liping Mou, Wesley T. O'Neal, Lin Yee Chen, Elsayed Soliman, Faye Norby, Tené Lewis, Alvaro Alonso

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

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3. Timeline:

Analysis is to be started immediately. We expect a manuscript draft to be prepared in the summer of 2017.

4. Rationale:

Atrial Fibrillation (AF) is the most common clinically relevant heart arrhythmia. It is estimated that in the U.S. 2.7 – 6.1 million people live with AF, and the number is expected to increase as the population ages.[1] The incidence rate of AF is 6.7 and 4.0 per 1,000 persons per year in white men and women, respectively.[2] Although the incidence rate of AF in African-American populations is lower than that in white populations, 1 out of 9 African-Americans will still develop AF before the age of 80.[3] Risk factors for AF include, among others, high blood pressure, obesity, diabetes, smoking, and heavy drinking.[4]

Socioeconomic and racial health disparities exist in the U.S, [5] which influence health outcomes, including the management and care of cardiovascular diseases [5] and diabetes.[6] A previous analysis of the ARIC cohort showed that lower income in the overall population and lower education level among women is associated with increased risk of AF.[7]

Lifetime risk is a measurement of the absolute risk of developing a disease of interest before death which accounts for the competing risk of death. Estimates of the lifetime risk of developing AF can be used as an easy way to communicate future risk to individuals. [8] A prior analysis of the Framingham Heart Study reported that in the US white population 1 out of 4 individuals aged 40 and older would develop AF during their lifetime.[9]

To date, there are no publications on the lifetime risks for development of AF by race and socioeconomic status (SES). To address this gap, we propose to assess whether there are any differences in lifetime risks of AF between whites and African Americans overall and by income and education levels. Low income and less education are indicators of low SES. The findings from our study may provide helpful information about the overall burden of AF in the population and among more vulnerable populations.

5. Main Hypothesis/Study Questions:

We will address the following specific aims:

1) To estimate the lifetime risk of AF in African Americans and whites
2) To determine the lifetime risk of AF by education level and income separately among African Americans and whites

We hypothesize that the lifetime risk of AF will be lower in African Americans compared to whites. We also hypothesize that lifetime risk will be higher among those reporting lower income and lower educational attainment both among African Americans and whites.

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).

1) Study design
   Prospective cohort study
2) Study population
   Among the initial 15,792 ARIC participants, the following will be excluded: 48 of non-white or non-African-Americans; 55 of African-Americans in the study centers of MN and MD due to small numbers; 37 with AF or atrial flutter diagnosed by ECG at the baseline visit; 225 whose ECG is missing or unreadable at the baseline visit; 27 whose information on total family income is missing; 924 whose information of total family income is missing. Visit 1 will be used as baseline.
3) Dependent variable

Lifetime risk of AF in African-Americans and whites

4) Independent variables
   Total family income categorized as < $25,000/year, $25,000 – 50,000/year, and > $50000/year (assessed at baseline)
   Educational level categorized as ≤ high school, ≥ graduated from high school to < college, and ≥ graduated from college (assessed at baseline)
   Age and sex
   High blood pressure, myocardial infarction, coronary heart disease, and diabetes
5) AF ascertainment
   As previously described.[3] Briefly, we will ascertain AF from 3 sources: ECGs conducted at ARIC visits, hospitalization discharge codes (ICD-9-CM 427.3x in the absence of procedure codes for open cardiac surgery), and death certificates (ICD-9 427.3 or ICD-10 I48). Events ascertained through 2014 are available for the analysis.
6) Statistical analysis
   All statistical analysis will be conducted with the use of SAS 9.4 statistical software. A modified technique of survival analysis will be applied to calculate lifetime risk.[10] In brief, after preparing data for analysis, a SAS macro will be used for the computation of the unadjusted cumulative incidence and the cumulative incidence adjusted for competing risk (death). We will also calculate age-, sex- and race-specific incidence of AF. Each participant will be followed up from baseline to the time of the first AF event, death, loss to follow-up, or the end of 2014 (whichever occurs first). The lifetime risk will be calculated only up to the age of 90 years because few ARIC participants are older than that age at the end of 2014.
7) Limitations
   - The information on education and total family income was collected only at baseline and, therefore, we will group participants in the analysis based on baseline information. In the Social Ecology of Health Model, SES is not easily modifiable. Although individual SES could be persistent, it could change. Therefore, we will take caution in the interpretation of our findings.
   - Information on education and total family income was self-reported in a questionnaire. Participants may have provided incorrect information, leading to misclassification (likely nondifferential regarding the outcome). Information bias may exist.

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/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)?
MS # 1351 Atrial fibrillation incidence in African-Americans and whites (Alonso). This paper reported incidence of AF by 2004 and cumulative risk of AF by age 80. The current proposal extends the previous analysis with 10 more years of follow-up and more than 1000 additional AF events.
MS #1793 SES and AF in ARIC (Misialek). This analysis reported the association between SES at baseline and incidence of AF, but did not specifically calculate lifetime risks.

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.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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