ARIC Manuscript Proposal #2705

PC Reviewed: 2/9/15	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title:

The race specific prevalence of atrial fibrillation with 48 hour ambulatory electrocardiography: The ARIC study

b. Abbreviated Title (Length 26 characters):
Race specific prevalence of AF

2. Writing Group:
Writing group members:

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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __LL__ **[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: Final data collection should be complete by March 2016, and data cleaning by May 2016. Manuscript fully drafted and submitted to the ARIC publications committee by June 2016.

4. Rationale:

Atrial fibrillation (AF) is the most common sustained arrhythmia worldwide and it is a known risk factor for stroke[1]. Despite an adverse risk profile for AF and a much higher risk of stroke in African-Americans compared to Whites, a lower prevalence of AF in African-Americans has been reported from multiple sources[2-4]. It has been theorized that this paradox may be due to differential detection of AF by race[5]. Because AF can be paroxysmal and asymptomatic, ambulatory electrocardiography is considered optimal for accurate ascertainment of AF. Most prior studies, however, have defined AF by self-report, hospitalizations, administrative claims data, and/or 12-lead electrocardiograms (ECG), which may miss subclinical and intermittent AF. The National Heart Lung and Blood Institute (NHLBI) has called for advancements in AF epidemiology through increased surveillance of AF in longitudinal studies, especially among non-White ethnic groups.

The putative low prevalence of AF in African Americans is puzzling, and theories regarding the cause of this paradox have been discussed in the literature[5-7]. An important consideration is ascertainment bias, such as through differential access to healthcare and thus to cardiac monitoring for minorities. The study from Kaiser Permanente of a population with HF addresses this concern to some extent since similar outpatient utilization rates were found for African Americans and Whites prior to hospitalization for AF[8]. An alternate interpretation is there is a higher frequency of subclinical AF in African Americans than Whites, even given similar healthcare. As an avenue less explored, ancestry informative markers from a genome wide array suggest that degree of European ancestry among African Americans is predictive of AF[9]. Survival bias must also be considered as a possible interpretation positing that African-Americans may not survive AF as well as Whites. Differential mortality from conditions such as myocardial infarction (MI) that increase risk for AF is yet another plausible interpretation. While higher mortality post-MI in African Americans has been reported, the difference by race is not sufficient to explain the AF paradox[5].

We propose to determine the prevalence of AF in African Americans, including underreported, subclinical and manifest AF, in an informative study nested in the ongoing, bi-ethnic and population-based Atherosclerosis Risk in Communities (ARIC) cohort which uses 48 Holter monitoring for the detection of AF.

5. Main Hypothesis/Study Questions:

Aim 1.0 Estimate the race-specific <u>prevalence</u> of AF in African-Americans and Whites aged 70 years and older.

1.1. Quantify the prevalence of AF (occurrence) in African-Americans and Whites.
1.2. Document type of AF (persistent or intermittent; symptomatic or not), time in AF, and heart rate while in AF in African-Americans and Whites.

Aim 2.0 Calibrate the prevalence of AF by quantifying under-ascertainment in the detection of AF according to length of Holter monitoring.

2.1. Quantify the detection of AF events by 24- hour additional length of Holter monitoring from 48-hour continuous ambulatory monitoring in an informative sample of African American and White cohort members.

2.2. Adjust AF prevalence estimates for under-ascertainment and by length of Holter monitoring.

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: A sample of ARIC participants from 2 ARIC sties (Jackson and Forsyth) were invited to participate in this ancillary study. Only ARIC participants that attended Visit 5, self-reported as Black or White, and had an echocardiography (ECHO) measurement were invited to participate. Participants were sampled for this study as members of an enriched group or from the general cohort. The enriched group consisted of participants at higher risk for AF due to one of the following factors: history of heart failure, low ejection fraction or enlarged left atrial size on ECHO. Participants were invited to attend a one hour clinic visit to review medications, and have anthropometric, and blood pressure measurements, and answer a questionnaire, then begin 48-hours of ambulatory ECG monitoring. The goal was to recruit 1,225 participants with a majority (67%) of African-Americans.

In addition, we recruited 100 volunteers (50 from each study site) to wear the Holter for an additional 48 hours. The target for this volunteer sample was ~50 women and ~60% African Americans (all 50 participants from Jackson would be African American). The repeat visit occured within 6 weeks of the initial visit. The repeated measures were processed at EPICARE using the same method previously described, and with blinding that they are repeats.

Inclusion/exclusion:
Inclusion: All participants that attended the AF study and wore a Holter monitor
Exclusion: Holter recordings with >10% noise, or < 20 hours of Holter recording time

AF variables of interest
Percent of time in atrial fibrillation or atrial flutter on 48-hour Holter
Self-report of AF at the time of the AF clinic visit
Self-report of AV ablation to treat AF at time of the AF clinic visit
Self-report of AF on ARIC AFU questionnaires
AF ICD code at the time of hospitalization per the ARIC study
AF detected from an ECG during ARIC visits 1-5

Covariates
Heart rate while in AF
Race group
Age at the time of Holter measures
Gender
Heart failure

Left atrial size
BMI
Blood pressure
CHD (defined as…)
Valvular disease by Visit 5 ECHO
Left atrial volume index by visit 5 ECHO

Statistical Analysis

AF prevalence (and 95% CI) will be estimated by race using weighted analyses that account for the complex sampling design. The characteristics of AF will be described by race including the frequency that was symptomatic or not, persistent, paroxysmal, and associated with valvular heart disease per Visit 5 ECHOs. For those with paroxysmal AF by monitoring, the distribution (mean, and interquartile range) of: 1) the number of AF episodes, 2) the duration of AF episodes, 3) heart rate during AF episodes will be described, stratified by race. Also, the distribution of heart rate will be described, regardless of AF type, and will include the duration in which heart rate is >100. We will quantify the frequency of AF events detected per incremental 24 hours of monitoring (up to 48 hours). Prevalence estimates previously estimated will be adjusted to reflect the error in monitoring for 48 hours instead of 96 hours.

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)?
First authors from both of the below studies were included.
#798 Soliman EZ et al Incidence of AF in whites and AA: The aRIC study

#780 Alonso, A et al. Ethnic distribution of ECG predictors of AF and its impact on understanding the ethnic distribution of ischemic stroke in the ARIC study

There is only one other manuscript proposal involving the Holter Ancillary study, and the author group is mostly overlapping with the current group.
#2665 Repeatability of ectopic beats from 48 hour ambulatory electrocardiography: The ARIC study

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? __x__ Yes ____ No

11.b. If yes, is the proposal

__x__ A. primarily the result of an ancillary study (list number* 2012.08)
___ 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 for the Use of Linked ARIC CMS Data, approved manuscripts using linked ARIC 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.

References

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