ARIC Manuscript Proposal #3468

PC Reviewed: 9/10/19	**Status: _____**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Temporal trends in the incidence of atrial fibrillation (AF) in the Atherosclerosis Risk in Communities (ARIC) Cohort

b. Abbreviated Title (Length 26 characters):

2. Writing Group:

Writing group members: Kunali Parimal Ghelani, Lin Yee Chen, Faye L. Norby, Elsayed Z. Soliman, Silvia Koton, Alvaro Alonso

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. _KG_ **[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:

The draft will be ready for submission in late fall 2019. Analysis will be started immediately.

4. Rationale:

Atrial fibrillation (AF) is one of the most commonly encountered cardiac arrythmias. It is characterized by tachyarrhythmia occurring due to abnormal electrical activity causing the atria of the heart to fibrillate.[1] AF is associated with 1.5 to 2-fold increase in mortality and cardiovascular morbidity (stroke, heart failure, etc).[2,3] The lifetime risk of developing AF for men and women 40 years or older is approximately 1 in 4 (25%) and is associated with advancing age.[4] Due to the growing elderly population the number of cases of AF is likely to increase 2.5 times by 2050 in the US.[5] AF is predicted to affect 17.9 million people in Europe by 2060.[6] The burden of AF varies regionally with low-middle income countries experiencing lower prevalence compared to high-income countries.[1] AF is more common in men than in women across all age groups (1.1% vs 0.8%; $p<0.001$) with a higher prevalence in whites than in blacks (2.2% vs 1.5%; $p<0.001$) despite the higher burden of AF risk factors in African-Americans.[5,7]

The burden of AF has increased over time. This increasing prevalence can be attributed to enhanced detection, rising incidence, improved survival in patients following AF and increased survival of patients with cardiovascular diseases predisposing to AF.[8] Some studies, conducted in mostly white populations, suggest incidence of AF has increased over time which is in contrast to a study of Medicare insured population that reported the incidence rates of AF being fairly stable from 1993 to 2007 in beneficiaries 65 years or older .[9] For example, the Framingham study reported the age-adjusted incidence increased from 3.7 to 13.4 per 1000 person-years in men and from 2.5 to 8.6 per 1000 person-years in women between 1958 and 2007.[10] Similarly a study in Olmsted County, Minnesota, consisting predominantly of a white population, reported that sex and age-adjusted AF incidence increased from 3.0 in 1980 to 3.7 per 1000 person-years in 2000.[11]Whether these results can be generalized to other communities and other racial and ethnic groups is an open question.

The rising trends in the incidence of AF, thus, are incompletely understood and studied. The population diversity, the sample size, and long follow-up of the ARIC cohort provide a unique opportunity to understand the racial and sex-specific differences in the incidence of AF over time. The results obtained from this study will provide insights into the future burden of AF in the general population.

5. Main Hypothesis/Study Questions:

Our overall aim is to examine trends in the incidence of AF over time, overall and by sex and race among the ARIC study participants. Specifically, we will:

- Evaluate temporal trends in the incidence of AF in the ARIC cohort.
- Determine if there are any sex and race differences in the trends of AF.

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:
This is a Prospective Cohort Study.

Inclusion/ Exclusion:
Inclusion:
ARIC participants who are free of AF at the time of study enrollment in the 4 US communities mostly whites from suburbs of Minneapolis, Minnesota, and Washington County, Maryland; African-Americans from Jackson, Mississippi; and whites and African-Americans from Forsyth County, North Carolina).

Exclusion:
- Individuals with race other than white or black, and non-whites from the Minnesota and Maryland sites.
- Prevalent cases of AF on ECG at study baseline or missing ECG
- Transient AF occurring due to operative cardiac procedures

Dependent Variable: Incident cases of AF through the end of 2017

Independent Variables: Age, Sex, Race, Calendar year.

AF ascertainment: New incident cases of AF were diagnosed based on study electrocardiogram, hospital discharge records and death certificates. AF was defined as date of first ECG showing AF or ICD-9 / ICD-10 on hospital discharge summary records or death due to AF.[12]

Analysis: Analysis will be conducted using SAS 9.4 statistical software for the data collected. We will compute person-years of follow-up in 5-year age groups and 5-year periods. The incidence rate ratios and the corresponding 95% CI by age, sex, race and period will be computed using Poisson regression models. Age-specific incidence rates by calendar year will be used to present temporal trends of AF. We will also report incidence rates by center and race.

Limitations: Since the ascertainment of AF cases is based primarily on hospital discharge codes, one major limitation is under-ascertainment of AF cases that did not require hospitalization. Also, with the diagnosis being based on study ECG and hospital discharge records, it is not possible to differentiate between paroxysmal AF and persistent AF. Since most of the black participants come from the Jackson site, it will not be possible to perfectly disentangle race differences from differences in location.

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)?
MS 1351 (Alonso): Incidence of atrial fibrillation in a biracial cohort. This proposal reported race-specific rates of AF with follow-up through 2004. The current proposal extends the follow-up through 2017, allowing estimation of temporal trends.

MS 2030 (Koton): Trends in stroke incidence and mortality. This paper reports trends in stroke incidence. Our current proposal uses similar methodology. Dr. Koton has been invited as a coauthor.

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.

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