ARIC Manuscript Proposal # 1793

PC Reviewed: 5/10/11	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1. **a. Full Title**: Socioeconomic status and the incidence of atrial fibrillation in whites and African Americans: the ARIC study.

b. Abbreviated Title (Length 26 characters): SES and AF in ARIC

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

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3. **Timeline**:

Data analysis: 1-2 months from manuscript approval date.
First draft of the manuscript: 3-4 months from the manuscript approval date.

4. Rationale:

Atrial fibrillation (AF) is becoming an increasing concern within the United States. With the current U.S. estimate at over two million individuals, AF is predicted to double its current prevalence by 2050.[1] In addition to being the most frequent cardiac arrhythmia observed in clinics, AF has been associated with increased risk of cardiovascular disease (CVD), heart failure, stroke, and overall mortality,[2] and those with AF are nine times more likely to die within the first four months after the AF event than those without AF.[3] Various studies have examined potential risk factors of AF to gain a better understanding of its predictors. Some of the known AF risk factors are age, gender, white race, cigarette smoking, hypertension, obesity, diabetes, heart failure, coronary heart disease (CHD), left ventricular hypertrophy, metabolic syndrome, and inflammatory biomarkers.[2,4-8]

AF and other CVDs share many common risk factors.[2] However, while lower socioeconomic status (SES) has been associated with a higher risk of CVD overall,[9] we observe that the association of SES and AF has not been investigated to date. Accordingly, this analysis of the ARIC study would be the first to prospectively explore SES and the incidence of AF over time to determine if the same inverse association exists between SES and AF risk.

In addition, the race-specific associations between SES and AF risk can be analyzed within the biracial ARIC population. Because many of the studies examining risk factors for AF were based on predominately white populations,[6] it is important to determine if the SES-AF association is the same or different between African-Americans and whites. Overall, the incidence of AF is lower in African-Americans[1,10] even though they have higher stroke rates and a higher prevalence of risk factors for AF and stroke.[11] Lower diagnosis of AF cases in African-Americans due to poorer access to healthcare and lower overall SES have been hypothesized as potential explanations for the lower AF incidence in African-Americans. However, if lower SES is associated with higher AF risk in both whites and African-Americans along with the racial difference in AF risk being observed within levels of SES, we could assume that lower SES in African-Americans may not explain the observed racial difference in AF incidence between whites and African-Americans.

5. Main Hypothesis/Study Questions:

Aim #1: To determine if SES is associated with the incidence of AF in the ARIC study.

Aim #2: To determine if race (white vs. African-American) modifies the association between SES and AF.

We hypothesize that individuals with lower SES will have an increased risk for AF. In addition, we hypothesize that the SES-AF association will be present and of a similar magnitude in white and African-American individuals.

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 follow-up data analysis will be conducted utilizing longitudinal data from the ARIC cohort, using visit 1 as baseline.

Inclusion/exclusion criteria:
We will exclude individuals with prevalent AF or atrial flutter at baseline based on electrocardiogram (ECG), missing baseline ECG data, missing SES variables at visit 1 and other covariates, with a race other than white or African-American, and non-whites from the Minnesota and Washington County sites.

Variables of interest:

Main outcome of interest: Atrial fibrillation incidence
The time to incident AF cases from baseline through December 31, 2007, will be the main outcome variable. Incident AF cases were ascertained from three sources: ECGs completed during the study exams, ICD-9 codes of 427.31 or 427.32 from hospital discharges, and death certificates that include AF as a cause of death (ICD-9 code 427.3 or ICD-10 code I48). AF incidence date will be defined as the date of the first ECG showing AF, the first hospital discharge date for an AF or atrial flutter diagnosis, or date when death occurred due to AF, whichever occurred first.[4,7]

Main independent variable of interest: Socioeconomic status
In the ARIC study, SES was assessed at baseline through education level and family income. Each variable will be modeled separately to assess the association between SES and AF. The six categories for education level are 8th grade completed or less, some high school, high school degree, vocational school, college, and graduate/professional school. Total family income is categorized into eight groups: under $5000, $5000-$7999, $8000-$11,999, $12,000-$15,999, $16,000-$24,999, $25,000-$34,999, $35,000-$49,999, and over $50,000. Due to the number of categories for each variable, the analysis may

involve combining some categories with smaller count totals together, but this collapsing of categories will depend on the variable's overall distribution.

Covariates
From visit 1, other measured covariates to be included in this analysis are age, gender, study site, race, body mass index, smoking status, drinking status, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes mellitus, and a history of stroke, heart failure, or CHD.

Statistical analysis:
Cox proportional hazards models will be used to determine the association between SES (education and income as separate models) and incident AF. The following models will be used to analyze the association between SES and AF risk:

- Model 1: adjustment for age, gender, and race
- Model 2: Model 1 + adjustment for study site, diabetes, systolic blood pressure, diastolic blood pressure, use of antihypertensive meds, smoking status, drinking status, body mass index
- Model 3: Model 2 + history of heart failure, CHD, and stroke
- Model 4: Model 3 + incidence of heart failure and CHD as time-dependent covariates

Effect modification will also be evaluated by age, gender, and race conducting stratified analysis and including multiplicative terms between the effect modifier and SES measures in the models.

We expect to include more than 1500 incident events of AF, which will provide sufficient power to study the association of SES with AF risk in the entire sample. However, limited power might exist to study race-specific associations, particularly in African-Americans.

Strengths and limitations:
Strengths of the study include the large sample size and power to measure associations between SES and AF and the sizable sample of African-Americans to evaluate risk factors of interest in relation to AF. However, there are a couple of limitations. Although hospital discharge codes being used for identifying incident AF cases have shown to be valid,[4] there is some likelihood of AF cases being missed in outpatient settings. In addition, there may be some misclassification of the SES exposure if SES levels happened to change over time.

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 ICTDER03 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

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 overlap found. _____ 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)?

No previous manuscript proposals in ARIC have specifically examined the association between socioeconomic status and atrial fibrillation. Other ARIC manuscripts have explored the association between individual SES and CVD.

#385 SES and incidence of CHD
#1333 SES and sudden death

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

b. If yes, is the proposal
_X_ **A. primarily the result of an ancillary study (list number*** 2008.09**,** 2008.12**)**
___ **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/

12. 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.

References:

1. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults. National implications for rhythm management and stroke prevention: the Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) study. *JAMA.* 2001; 285:2370-2375.
2. Benjamin EJ, Levy D, Vaziri SM. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. *JAMA.* 1994; 271(11):840-4.
3. Miyaska Y, Barnes ME, Bailey KR et al. Mortality trends in patients diagnosed with first atrial fibrillation: a 21-year community-based study. *J AM Coll Cardiol.* 2007; 49:986-92.
4. Alonso A, Agarwal SK, Soliman EZ et al. Incidence of atrial fibrillation in whites and African-Americans: the atherosclerosis risk in communities (ARIC) study. *Am Heart J.* 2009; 158:111-117.
5. Wang TJ, Parise H, Levy D, et al. Obesity and the risk of new-onset atrial fibrillation. *JAMA.* 2004; 292(20):2471-7.
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7. Chamberlain AM, Agarwal SK, Ambrose M, et al. Metabolic syndrome and incidence of atrial fibrillation among blacks and whites in the atherosclerosis risk in communities (ARIC) study. *Am Heart J.* 2010; 159:850-856.
8. Aviles RJ, Martin DO, Apperson-Hansen C, et al. Inflammation as a Risk Factor for Atrial Fbirillation. *Circulation.* 2003; 108:3006-3010.
9. Kaplan GA, Keil JE. Socioeconomic factors and cardiovascular disease: a review of the literature. *Circulation*. 1993; 88:1973–1998.
10. Ruo B, Capra AM, Jensvold NG, et al. Racial Variation in the Prevalence of Atrial Fibrillation Among Patients With Heart Failure. *J AM Coll Cardiol.* 2004; 43:429-435.
11. Soliman EZ, Alonso A, Goff DC, Atrial fibrillation and ethnicity: the known, the unknown, and the paradox. *Future Cardiology.* 2009; 5.6:547-557.