ARIC Manuscript Proposal #2459

PC Reviewed: 11/11/14	Status: <u>A</u>	Priority: <u>2</u>
SC Reviewed:	Status:	Priority:

1.

a. Full Title: The Association Between Alcohol Consumption and Incident Atrial Fibrillation: The Atherosclerosis Risk in Communities (ARIC) Study.

b. Abbreviated Title (Length 26 characters): Alcohol & Atrial Fibrillation

2. Writing Group:

Writing group members: Shalini Dixit, Alvaro Alonso, Elsayed Soliman, Lin Y. Chen, Gregory M. Marcus

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

Dr. Marcus has this data available from previously approved manuscript proposals and grant funding. Shalini Dixit, the first author, is a medical student at UCSF on a yearlong pre-doctoral clinical and translational research grant, simultaneously taking classes in epidemiology and biostatistics. As such, she should have sufficient time and support from Dr. Marcus and the biostatistics department at UCSF to complete this project within six months from its approval. In addition, we already have certification from the UCSF Committee on Human Research to perform this study, as they do not require specific approval to analyze de-identified data.

4. Rationale:

Atrial fibrillation (AF) affects millions of Americans and is growing in incidence and prevalence.¹ It is one of the most common causes of stroke and nearly doubles mortality.^{2,3} Though the cause of AF remains largely unknown, several risk factors have been established including age, male sex, hypertension, heart failure, diabetes, and obesity.⁴ Episodic heavy alcohol consumption, or binge drinking, has long been posited as a trigger for AF. In recent years, researchers have also begun to investigate the effects of chronic alcohol consumption on AF risk. Several studies have found an association between heavy alcohol consumption, usually defined as >3 drinks/day, and incident AF.^{5,6} Though the data on moderate alcohol consumption is less conclusive, a previous meta-analysis determined that there is a linear relationship between alcohol consumption and AF, reporting an 8% increase in risk associated with each 10g/day of alcohol intake.⁷ Thus, lowering alcohol intake could be a potentially effective strategy for preventing AF.

Interestingly, an analysis of the Cardiovascular Health Study (CHS), a populationbased cohort of elderly women and men, published in 2007 had largely negative findings regarding alcohol and AF.⁸ The authors found that current moderate alcohol consumption was not associated with risk of AF but that former drinking identified individuals at higher risk of AF. Possible explanations for this paradox include that past drinkers drank more alcohol or that they had other comorbidities which led them to quit. Nonetheless, this begets the question of how past drinking affects AF risk as compared to current alcohol consumption.

While studies on alcohol and AF have been performed in several major cohorts and trials, including the Framingham Study, the Women's Health Study, and CHS, the data from ARIC on this important matter has yet to be reported. The senior author on this project (and mentor of the first author) currently has an R01 grant from the NIAAA to explore the mechanisms underlying the potential relationship between alcohol and AF, and these data would complement that ongoing effort. Using data from ARIC, we would be able to examine the relationship between alcohol and AF in a large, population-based cohort with previously validated AF ascertainment, thereby adding to the growing body of knowledge on chronic alcohol consumption and AF. Furthermore, in the spirit of searching for modifiable risk factors for AF, we could begin to answer the question of whether one can reduce one's risk of AF by quitting drinking given the specific data available in ARIC.

5. Main Study Questions:

- 1) Does chronic moderate alcohol consumption increase the risk of incident AF?
- 2) Do past drinkers have an increased risk of incident AF?
 o Related sub-questions:
 - Is this risk affected by the length of time for which they drank?
 - Is this risk affected by the length of time for which they have abstained?
- 3) Does type of alcohol consumed influence the risk of incident AF in current and past drinkers?

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).

This will be a secondary data analysis of existing ARIC data. We will use the alcohol information from the baseline dietary intake form (form DTIA), and the specific variables of interest include DTIA91-DTIA100C. These variables contain information on current alcohol consumption, including frequency, amount, and type of alcohol, and information on past consumption, including frequency, amount, type of alcohol, years of drinking, and years of abstaining. In addition, we will use the derived variable ETHANL03, a measure of usual ethanol intake in grams per week for current drinkers. Our main outcome variable will be incident AF, defined as cases of AF occurring in participants without prevalent AF. Prevalent AF was determined by baseline ECG at visit 1. Cases of incident AF were obtained from ECGs during study exams, hospital discharge diagnoses, and death certificates.

In our analysis, we will first exclude those participants with prevalent AF. Then, using Cox proportional hazards, we will perform analyses to determine if current alcohol consumption and past consumption are associated with incident AF. For both, we will also investigate whether the type of alcoholic beverage consumed (wine, beer, or hard liquor) is associated with incident AF. If past alcohol use is predictive of AF, we will examine whether the number of years of drinking, the amount of alcohol consumed, and the number of years of abstaining are associated with incident AF in former drinkers. This too will be done using Cox proportional hazards. In the analysis, we plan to adjust for the following possible confounders all obtained from visit 1: age, gender, race, clinic site, education, smoking status (current, past, never), body mass index, systolic and diastolic blood pressure, use of antihypertensive medication, physical activity, diabetes mellitus, congestive heart failure, and coronary heart disease. Finally, if we find an association between alcohol use and incident AF, we will examine whether this relationship is mediated by incident heart failure.

- 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)?

- Alcohol consumption and the incidence of hypertension: The Atherosclerosis Risk in Communities Study.
- Relationship of alcohol consumption and type of alcoholic beverage consumed with plasma lipid levels: differences between Whites and African Americans of the ARIC study.
- Alcohol consumption with age: a cross-sectional and longitudinal study of the Atherosclerosis Risk in Communities (ARIC) study, 1987-1995.

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 <u>http://www.cscc.unc.edu/aric/forms/</u>

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://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.

1. Naccarelli GV, Varker H, Lin J, Schulman KL. Increasing prevalence of atrial fibrillation and flutter in the United States. The American journal of cardiology 2009;104:1534-9.

2. Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Circulation 2006;114:e257-354.

3. Chugh SS, Blackshear JL, Shen WK, Hammill SC, Gersh BJ. Epidemiology and natural history of atrial fibrillation: clinical implications. Journal of the American College of Cardiology 2001;37:371-8.

4. Andrade J, Khairy P, Dobrev D, Nattel S. The clinical profile and pathophysiology of atrial fibrillation: relationships among clinical features, epidemiology, and mechanisms. Circulation research 2014;114:1453-68.

5. Djousse L, Levy D, Benjamin EJ, et al. Long-term alcohol consumption and the risk of atrial fibrillation in the Framingham Study. The American journal of cardiology 2004;93:710-3.

6. Conen D, Tedrow UB, Cook NR, Moorthy MV, Buring JE, Albert CM. Alcohol consumption and risk of incident atrial fibrillation in women. JAMA : the journal of the American Medical Association 2008;300:2489-96.

7. Kodama S, Saito K, Tanaka S, et al. Alcohol consumption and risk of atrial fibrillation: a meta-analysis. Journal of the American College of Cardiology 2011;57:427-36.

8. Mukamal KJ, Psaty BM, Rautaharju PM, et al. Alcohol consumption and risk and prognosis of atrial fibrillation among older adults: the Cardiovascular Health Study. American heart journal 2007;153:260-6.