

ARIC Manuscript Proposal # 3132

PC Reviewed: 3/20/2018
SC Reviewed: _____

Status: _____
Status: _____

Priority: 2
Priority: _____

1.a. Full Title: Sex and Race Differences in Incident Coronary Heart Disease in the ARIC Cohort 1987-2015

b. Abbreviated Title (Length 26 characters):

Differences in Incident CHD

2. Writing Group:

Writing group members: Duygu Islek, Alvaro Alonso, Wayne Rosamond, Viola Vaccarino, others welcome

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

First author: Duygu Islek

Address: Emory University
Department of Epidemiology
1518 Clifton Road, NE
Atlanta, GA 30322

Phone: 470-439-90-53

E-mail: dislek@emory.edu

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).

Name: **Alvaro Alonso**

Address: Emory University
Department of Epidemiology
1518 Clifton Road, NE
Atlanta, GA 30322

Phone: 404-727-8714

E-mail: alvaro.alonso@emory.edu

3. Timeline:

The analysis is estimated to be completed in 8 months and we are considering 2 manuscripts (one focusing on sex differences and one focusing on race differences of incident fatal, nonfatal and total CHD in the cohort data), which will be submitted at the end of one year (November 2018). Depending on the results, we may aggregate the analyses by race and by gender in one manuscript.

4. Rationale:

A previous analysis in the ARIC cohort reported no difference between fatal, nonfatal and total CHD incidence among black vs white women when adjusted for age and other co-variables (Colantonio et al. *Circulation*. 2017;136:152–166). Similarly, there was no difference in incident nonfatal and total CHD events comparing black vs white men. However, black men showed higher incidence of fatal CHD compared to white men. In the same analysis, case fatality was also higher for black men vs white men while there was not a difference between black vs white women.

These inconsistent published results regarding black-white differences in incidence and mortality of CHD in the ARIC study could be explained by a higher rate of out-of-hospital CHD deaths in blacks, especially black men (a large proportion of CHD deaths occur before hospital admission). This question has been rarely examined in the published literature, and was not addressed in the Colantonio et al. paper, which used the ARIC public use dataset. Another limitation of the Colantonio et al. paper is that the follow-up ended in 2001 so the analysis would need to be updated (currently, ARIC has follow up through the end of 2015).

Blacks compared to whites, particularly women, are reported to have higher in-hospital mortality for myocardial infarction (MI) (Vaccarino et al, *N Engl J Med* 2005;353:671-82). Also, in the ARIC study blacks were previously reported to have a lower rate of clinically documented MI than whites (Zhang et al *Circulation*. 2016;133(22):2041) which may be a consequence of more out-of-hospital cardiac events among blacks. Annual out-of-hospital death rates due to CHD were higher in blacks compared to rates in whites and higher in men compared to rates in women after adjustment for age in ARIC Surveillance data (Rosamond et al. ARIC Surveillance Committee Report, Community trends in the incidence of MI, mortality due to CHD, and case fatality for ARIC communities for event years 2005-2013). A previous paper has also examined the differences in stroke incidence in the ARIC cohort and the black versus white age-adjusted rate ratio for ischemic stroke was reported as 2.4 (95%CI, 1.85-3.15). This remained significant in seven different level of models adjusted for potential confounders (Rosamond et al. *Stroke*. 1999;30:736-743).

Considering the inconsistent published results on racial differences in CHD incidence, exploring differences in out-of-hospital deaths as part of our analysis of CHD incidence data, as well as case fatality, would help better understand CHD incidence and mortality differences according to race, and sex.

We believe that the proposed analysis will provide a more complete picture of differences in incident CHD by race and sex. In addition, analysis of ARIC cohort data will allow us to examine the impact of socioeconomic status (SES) and cardiovascular risk factors on the outcome differences we may observe by race and sex.

5. Main Hypothesis/Study Questions:

Hypothesis 1- 'Blacks have a higher incidence of CHD and MI case fatality than whites. This difference is attenuated by adjustment for socioeconomic status and cardiovascular risk factors. The higher CHD incidence among blacks reflects a higher out-of-hospital CHD mortality rate in blacks vs whites.'

Hypothesis 2- 'Men have a higher CHD incidence and higher out-of-hospital CHD mortality than women, but similar or lower MI case fatality than women.'

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).

For this analysis, we will use the most updated ARIC cohort data available. Standardized incidence rates of fatal, nonfatal, and total CHD will be calculated by race and sex, as well as in-hospital and out-of-hospital mortality rates and case fatality rates.

We will exclude patients who are non-white and non-black, as well as non-whites in the Minnesota or Maryland sites. We will also exclude those with baseline history of CHD.

Proportional hazards models will be constructed before and after adjusting for SES (income, education) and CVD risk factors (hypertension, diabetes, body mass index, total cholesterol, and non-HDL cholesterol).

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.csc.unc.edu/ARIC/search.php>

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)?

Wayne D. Rosamond et al 'Twenty-Two-Year Trends in Incidence of Myocardial Infarction, Coronary Heart Disease Mortality, and Case Fatality in 4 US Communities, 1987–2008' DOI: 10.1161/CIRCULATIONAHA.111.047480

Wayne D. Rosamond et al 'Stroke Incidence and Survival Among Middle-Aged Adults 9-Year Follow-Up of the Atherosclerosis Risk in Communities (ARIC) Cohort'. Stroke.1999;30:736-743.

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