ARIC Manuscript Proposal #2640

PC Reviewed: 10/13/15  Status: A  Priority: 2
SC Reviewed: _________  Status: _____  Priority: ____

1a. Full Title: Disparities in cholesterol treatment and control by race, gender, and socioeconomic status among older patients with established atherosclerosis.

b. Abbreviated Title (Length 26 characters): Cholesterol control in older patients with atherosclerotic CVD.

2. Writing Group:
   Writing group members: Sruthi Valluri, Sally Stearns, Michael Miedema, Alvaro Alonso [others welcome]

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

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3. Timeline:
Analysis will begin after approval of the manuscript, and will take 2-3 months. We anticipate a first draft of the manuscript within 6-8 months after approval.

4. **Rationale:**

Hypercholesterolemia is a significant risk factor for primary and secondary cardiovascular disease (CVD) events.\textsuperscript{1,2} In patients with established atherosclerosis, management and control of cholesterol levels is essential as it can reduce recurrent CVD events and CVD mortality.\textsuperscript{3,4} This is especially true among older adults who are at even greater risk for both CVD morbidity and mortality.\textsuperscript{5}

Despite clinical recommendations for aggressive management of dyslipidemia, cholesterol management is not consistent across patient populations. African-Americans are less likely to have cholesterol screening, use cholesterol-lowering medications, and achieve target cholesterol levels.\textsuperscript{6-8} Studies on gender differences in use of cholesterol-lowering medication have shown mixed results,\textsuperscript{6,9} but evidence suggests that women are less likely than men to achieve cholesterol control.\textsuperscript{10} Treatment rates among patients with established CVD are also low.\textsuperscript{8,11-13}

Although inconsistencies in cholesterol management exist, patterns of cholesterol management among older patients with a history of atherosclerosis have not been studied. Previous studies have not been specific to older populations with established atherosclerotic CVD,\textsuperscript{7,8} or refer to study populations that may not be representative of the general population.\textsuperscript{14} Furthermore, while objective socioeconomic status (SES) has been explored, the interaction between subjective SES and CVD risk factor control has not been fully addressed, especially among patients with established CVD.\textsuperscript{15,16,17, 18}

Our analysis will address these issues and explore the effect of race, gender, and objective and subjective SES on cholesterol treatment and control in older patients with established atherosclerosis. Analysis of the ARIC study would allow for examination of a large cohort of older individuals with both African-American and white subgroups. The analysis would pertain to data collected in recent years.

5. **Main Hypothesis/Study Questions:**

The primary aim of this analysis is to determine the association of race, gender, and objective and subjective SES with the treatment and control of hypercholesterolemia among older individuals with established atherosclerosis. We hypothesize that African-American individuals and women will be less likely to exhibit cholesterol control. We also hypothesize that higher objective and subjective socioeconomic status will be associated with greater cholesterol control.

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 cross-sectional analysis will be conducted using Visit 5 data (2011-2013) from the ARIC cohort.

Inclusion/exclusion criteria:
Analysis will include individuals 65 years or older with a history of atherosclerosis. Established atherosclerosis will be defined according to the ACC/AHA definition of atherosclerotic CVD (ASCVD): a history of coronary heart disease (CHD), cerebral vascular accident (CVA), peripheral vascular disease (PVD), myocardial infarction (MI), or stable or unstable angina. We will exclude participants who were nonwhite or nonblack or were missing measurements for cholesterol levels or other covariates at Visit 5.

Variables of interest:
Main outcome of interest: Cholesterol treatment and control
Cholesterol treatment will be defined as self-reported use of statins, niacin, bile acid resins, fibric acid derivatives, or cholesterol absorption inhibitors at Visit 5. Cholesterol control will be defined according to Adult Treatment Panel (ATP)-III guidelines for low density lipoprotein (LDL) goals (Table 1).

Table 1. ATP-III Guidelines for LDL Cholesterol Goals, 2004 update

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Definition</th>
<th>LDL Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>CHD or CHD Risk Equivalents (10-year risk &gt;20%)</td>
<td>&lt;100 mg/dL; optimal goal &lt;70 mg/dL</td>
</tr>
<tr>
<td>Moderately high risk</td>
<td>2+ Risk Factors (10-year risk ≤ 20%)</td>
<td>&lt;130 mg/dL</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>≥ 2 Risk Factors (10-year risk &lt;10%)</td>
<td>&lt;130 mg/dL</td>
</tr>
<tr>
<td>Low risk</td>
<td>0-1 Risk Factors</td>
<td>&lt;160 mg/dL</td>
</tr>
</tbody>
</table>

For patients in Group 1 of the risk categories, primary analysis will be conducted on the LDL goal of <100 mg/dL; a secondary analysis will be conducted with the suggested optimal goal of LDL < 70 mg/dL. CHD risk equivalents will be defined as clinical or symptomatic CHD, PVD, or abdominal aortic aneurysm. Risk factors include cigarette smoking, hypertension (defined as a systolic blood pressure greater or equal to 140/90 mmHg or self-reported use of anti-hypertensive medications), low high density lipoprotein (HDL) cholesterol (less than 40 mg/dL), or family history of
premature CHD (CHD in first degree relative younger than 55 years if male and younger than 65 years if female). Ten-year Framingham risk scores will be calculated for participants without CHD or CHD risk equivalents but with more than two risk factors other than LDL.

**Main independent variables of interest: Race, gender, and objective and subjective socioeconomic status**

Race will be defined as white or black, with exclusion of participants who were nonwhite or nonblack. Socioeconomic status (SES) will be assessed in two ways: objectively and subjectively. Objective SES was determined using self-reported total household income and number of individuals supported by the income, and education. Subjective SES was determined using the MacArthur Scale of Subjective Social Status. Participants were first shown a 10-rung ladder and asked to rank themselves relative to others in the United States in terms of income, education, and occupation status. Participants were then shown a second 10-rung ladder and asked to rank themselves relative to others in their community, with “community” defined as “whatever way is most meaningful to [the participant].”

**Covariates:**
Other covariates to be included in the analysis are study site, age, CVD risk factors (Body Mass Index [BMI], hypertension, diabetes, current smoking, and family history of heart attack), and access to health care.

**Statistical analysis:**
We will perform preliminary descriptive statistics to analyze the behavior of the variables, and test for multicolinearity between variables using nonparametric methods (i.e., Kendall Tau and Spearman correlation). We will use multivariable logistic regression to assess the association of race, gender, and objective and subjective SES with our two outcomes of interest, which will be analyzed separately: cholesterol treatment and control (treated as dichotomous outcomes). Subjective SES will be modeled as a continuous variable. Separate models for treatment and control will be fit, and all demographic and SES variables will be analyzed simultaneously in the model. Additional analysis will be conducted to explore interactions between the independent variables. Specifically, we will explore whether the association of objective and subjective SES varies between races and genders. Analysis will be adjusted for the covariates listed above. We expect a sample size of approximately 1500. The association between the independent and dependent variables will be assessed using odds ratios and 95% confidence intervals.

**Strengths and limitations**
There are several strengths to the proposed study. The analysis will be conducted on a large sample size of older adults with both white and black subgroups. Furthermore, in contrast to existing literature addressing similar questions, the data is recent (2011-2013). However, there are limitations worth noting. First, although the Forsyth, North Carolina, site provides variation in race, the African-American
population in the ARIC dataset is largely limited to the Jackson, Mississippi site. It might therefore be difficult to separate race from geographic site in our analysis. Second, our analysis will not reflect the most recent guidelines for cholesterol management. In 2013, the ACC/AHA released new guidelines with a much lower risk threshold (7.5% 10-year risk for atherosclerotic CVD) to initiate statin therapy. The new threshold of is aggressive and creates a near-universal recommendation for statin use in older adults. At the time of Visit 5 data collection, participants were being treated according to ATP-III guidelines, which will guide our definition for cholesterol treatment and control. In addition, our analysis will not account for changes in access to health care 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 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)?
    MS 2178 – Prevalence and control of hypertension and hyperlipidemia and use of preventive CV meds in a US cohort
    MS 2043 – Medication adherence, health literacy, and subjective and objective SES
    MS 490 – Lipid lowering medication use patterns (Visit 1 – 4), SES, race, gender
11a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? 
   ____ Yes   ___X__ No

11b. 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.cscs.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.cscs.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


13. Pearson TA, Laurora I, Chu H, Kafonek S. The lipid treatment assessment project (L-TAP): a multicenter survey to evaluate the percentages of dyslipidemic


