ARIC Manuscript Proposal #2697

PC Reviewed: 1/12/16	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Socioeconomic status and incidence of lower-extremity peripheral artery disease: Atherosclerosis Risk in Communities Study

b. Abbreviated Title (Length 26 characters): SES and PAD

2. Writing Group:

Writing group members:

Priya Vart, Josef Coresh, Lucia Kwak, Shoshana Ballew, Gerardo Heiss, Kunihiro Matsushita

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

First author: Priya Vart
Address: 2024 E. Monument Street, Baltimore, MD, 21205

Phone: (410) 955-0495 Fax: (410) 955-0476
E-mail: pvart1@jhu.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: Josef Coresh
Address: 2024 E. Monument Street, Baltimore, MD, 21205

Phone: 410-955-0495 Fax: 410 955-0476
E-mail: coresh@jhu.edu

3. Timeline:

Since data for this project are already available, we anticipate to complete the project in approximately 6 months.

4. Rationale:

The association between socioeconomic status (SES) and cardiovascular disease is well established. Studies has consistently reported increased risk of coronary heart disease, stroke, heart failure and cardiovascular mortality in individuals of low SES.[1-4] However, fewer studies have examined the relationship between SES and lower-extremity peripheral artery disease (PAD). PAD is associated with increased mortality risk and reduced quality of life.[5-6]

Existing studies of the association between SES and PAD has been inconsistent. A number of studies has shown association between SES and high prevalence of PAD but some did not find such association.[7-11] It should be noted that none of these studies has prospectively examined the association between SES and PAD. Consequently, it is not well established whether or not low SES is associated with risk of PAD. Moreover, the potential role of cardiovascular disease risk factors in the association between SES and PAD is unclear. Identification of socioeconomic disparities in PAD might be helpful in directing resources to reduce or eliminate risk of PAD in disadvantageous groups and thereby help in achieving the American Heart Association 2020 Impact Goal of improving cardiovascular health of all Americans by 20%.[12]

In a large longitudinal study, therefore, we aim to examine the association between SES and PAD. We will examine the association of individual and area based SES assessed in middle age of participants with incidence of PAD. We also aim to understand factors that might account for an association between SES and PAD.

5. Main Hypothesis/Study Questions:

Study question 1: Whether, if at all, low SES is associated with incidence of PAD?
Study question 2: If association exists, whether established cardiovascular disease risk factors explain the association between SES and PAD?

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: We intend to use prospective data (visit 1 to 5) to explore those study questions.

Inclusion/exclusion: Participants with no clinical history of PAD at baseline will be included. Participants with missing information on SES measures (household income, educational attainment and area deprivation index), PAD and missing information on covariates of interest (i.e. total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes, body mass index, physical activity index (sport), alcohol use, tobacco use) at visit 1 (1987-1989) will be excluded.

Exposure: SES

SES will be defined using household income, educational attainment and area deprivation index of participants. We aim to use SES measures separately. Using a composite SES measure (from individual SES measures) might provide more comprehensive SES

assessment but it gives little information about potential pathways that link low SES to a health outcome.[13]

Outcome: Incident PAD

Given the uniform data availability over follow-up visits, we will primarily define PAD using hospital records. In line with previous literatures,[14,15] we will use following ICD codes for identification of PAD: 440.20 (atherosclerosis of native arteries of the extremities, unspecified); 440.21 (atherosclerosis of native arteries of the extremities with intermittent claudication); 440.22 (atherosclerosis of native arteries of the extremities with rest pain); 440.23 (atherosclerosis of native arteries of the extremities with ulceration); 440.24 (atherosclerosis of native arteries of the extremities with gangrene); 440.29 (other atherosclerosis of native arteries of the extremities); 440.3 (atherosclerosis of bypass graft of the extremities); 440.8 (atherosclerosis of other specified arteries); 443.9 (peripheral vascular disease, unspecified); 38.18, 39.25, 39.29, 39.50 (leg artery revascularization).

In additional analyses, cases with 440.22, 440.23, 440.24 or those with PAD codes plus codes for amputation, ulcer, or gangrene will be considered as critical limb ischemia (CLI) and we will repeat analysis for CLI. We will also repeat our analysis for self-report of a PAD diagnosis assessed at a clinic visit or during an annual telephone call.

Summary of data analysis:

For prospective association between SES household income and educational attainment and PAD, survival analyses will be conducted using Cox proportional hazard models. For association between area of residence and PAD, multi-level analysis will be performed. To assess the association between SES and PAD, we will adjust for demographic factors (i.e. age, gender and race-center). To assess whether established cardiovascular disease risk factors explain the association between SES and PAD, in case association between SES and PAD is significant, we will additionally adjust for major cardiovascular disease risk factors (i.e. total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes, body mass index, physical activity index (sport), alcohol use, tobacco use). Moreover, to estimate the attribution of aforementioned cardiovascular disease risk factors to the SES-PAD association, we will add cardiovascular disease risk factors individually and then together to the base model (adjusted for demographic factors) and estimate the reduction in regression coefficient of the SES-PAD association. Percentage reduction in regression coefficient will be estimated by using formula: ((β base model - β model (after adding one risk factor or all risk factors together))/β base model)*100.

For historical reasons African-Americans have poor educational attainment and less economic opportunities and consequently, disproportionately high number of African-Americans belong to low SES. Therefore, we will test the interaction between SES and race, and will stratify these analyses by race.

Anticipated methodological limitations or challenges:

PAD is often identified in the outpatient setting. Thereby, ascertaining PAD from hospital discharge records might result in missing a number of PAD events. Because access to care is associated with SES, ascertaining PAD from hospital discharge records might

influence the association between SES and PAD. Moreover, self-reported PAD and lower extremity revascularization are often misreported.

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)?

MP#926. Individual and Area-Level Lifecourse Socioeconomic Status and Subclinical Atherosclerosis: The Atherosclerosis Risk in Communities (ARIC) Study
The **MP#926** will be most related to current proposal. It examined association between cumulative SES, involving retrospective assessment of SES, and PAD at visit 2. It did not prospectively investigate the association between SES and PAD. Moreover, the results from that proposal are already published (Ann Epidemiol. 2007;17:296-303.) and thus the current proposal will not interfere with that proposal. The key authors of that proposal are requested to be part of current proposal as well.

MP #2260 The burden of peripheral artery disease: linkage of Medicare claims with the ARIC study

MP #180 Neighborhood socioeconomic characteristics and cardiovascular disease.

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 http://www.cscc.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.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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