To: ARIC Publications Committee

Re: Manuscript Proposal for Peripheral Aneurysms

Date: 08/10/2018

Dear Publications Committee members,

Please review the attached manuscript proposal regarding the study of peripheral aneurysms in the ARIC study. The proposal is entitled “Burden and outcomes associated with peripheral aneurysm disease”. My co-authors on this proposal is Dr. Weihong Tang from the University of Minnesota. She has reviewed and approved this proposal. I have also invited Dr. Aaron Folsom to participate, but he has been out of the office. All other ARIC investigators are welcome to participate.

I look forward to hearing back from the committee.

Best regards,

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1.a. Full Title: Burden and outcomes associated with peripheral aneurysm disease

b. Abbreviated Title (Length 26 characters):

2. Writing Group:
   Writing group members: Corey Kalbaugh (UNC); others welcome

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __CK___ [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).
   Name: Weihong Tang
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3. Timeline: Submit to AHA in October 2018; Present in March 2019 and submit manuscript at time of presentation

4. Rationale: While the incidence of abdominal aortic aneurysms is well-documented¹, data are scarce on the burden of peripheral artery aneurysm disease. Existing literature is primarily
from the 1990s when Lawrence et al (1995) found hospitalized incidence of femoral, popliteal and popliteal artery aneurysms of 7 per 100,000. More recent publications rely on small case series. The disease may be more common now and updating the epidemiology of this disease is warranted and appropriate. Additionally, management of the disease has changed over time with the increase in the use of endovascular techniques. The impact of these changes in management on outcomes is unknown, particularly if femoral and iliac aneurysms are included.

5. Main Hypothesis/Study Questions:
Overall Aim: To estimate prevalence and incidence of peripheral aneurysm disease in the inpatient and outpatient setting among participants in the Atherosclerosis Risk in Communities (ARIC) Study cohort. Also interested in outcomes of limb loss and mortality.

1. Data on the prevalence and incidence of peripheral aneurysm disease will provide useful information on the changing epidemiology of the disease.
2. Rates of limb loss and mortality will be high.

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).

Design: Prospective cohort data from visit 1 through 2013 event follow-up for ARIC hospitalized peripheral aneurysms, CMS claims for years 1991-2013 (or latest data available) for hospitalized and peripheral aneurysms linked with ARIC cohort participant data. Annual peripheral aneurysm period prevalence and incidence will be estimated.

Inclusion/Exclusion: Medicare beneficiaries can opt to have additional coverage of their health care services provided by managed care programs, such as Medicare Advantage. Insurance agencies offering managed care programs are not required to submit claims for individual services and, consequently, information on health care utilization by beneficiaries in these programs is incomplete. Thus, we will only include CMS Medicare data available for all fee-for-service CMS Medicare beneficiaries ages 65 years and older residing in the four geographically defined areas of the ARIC Study.

Variables of interest: age, gender, and race.

Outcomes: ICD-9-CM and CPT-4 codes will be examined to determine peripheral aneurysm events of additional lower extremity procedures and limb loss. Beneficiaries’ death dates will be obtained from the Master Beneficiary Summary File.

Hospitalized peripheral aneurysms ascertained though ICD diagnostic codes 442.2, 442.3, I72.3, I72.4. CMS data will be used to identify additional hospital and outpatient peripheral aneurysms.
Amputation will be defined by ICD codes 84.10, 84.12, 84.13, 84.14, 84.15, 84.16, 84.17, 84.18, 84.3, 84.91 and CPT-4 codes 27295, 27590, 27591, 27592, 27594, 27596, 27598, 27599, 27880, 27881, 27882, 27888, 27889, 28800, 28805, 28810, 28820, 28825

**Data Analysis:** Direct standardization will be used to estimate age-standardized overall and annual prevalence of PAD with 95% confidence intervals (CI) for each year of analysis. Direct standardization will be used to estimate age-standardized overall and annual incidence of PAD (per 1000 person-years) with 95% CI for each available year. Prevalence estimates will be age-standardized to reflect the age, race, and sex distribution of the 2005 Medicare population ages 65 years and older. Age categories for standardization of prevalence estimates include 65-69, 70-74, 75-79, and ≥ 80 years of age. Incidence estimates will be age-standardized to reflect the age, race, and sex distribution of the 2005 Medicare population ages 67 years and older given a two-year look back period for excluding prevalence cases. Estimates will be calculated overall, by health care setting (inpatient versus outpatient setting) and by age, race, sex, and race/sex subgroups. Age categories for incidence estimate standardization include 67-69, 70-74, 75-79, and ≥ 80 years of age. All analyses will be performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

**Limitations:** As this study will be based on inpatient and outpatient care among CMS Medicare enrollees in FFS programs, our estimates will not be generalizable to Medicare beneficiaries enrolled in Medicare Advantage, who have been reported to be healthier than those in FFS8. Our estimates will reflect cohort survivors and we will not attempt to quantify peripheral aneurysm prior to enrollment in fee-for-service in 2003. Administrative claims data reflect billing practices and, therefore, diagnostic coding found in claims data is not always accurate in relation to documented diagnoses or procedures. Codes selected will not be independently validated, which could lead to misclassification of disease occurrence. Upcoding might increase billing by as much as 15% ⁹ and illness severity is not readily obtainable from claims data.

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 website at:  http://www.cscc.unc.edu/aric/mantrack/maintain/search/dtSearch.html

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)? 2260 (Kalbaugh10), 2296 (Kalbaugh11), 2367 (Tang1)

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 https://www2.cscc.unc.edu/aric/approved-ancillary-studies

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.