ARIC Manuscript Proposal #2367

PC Reviewed: 5/13/14	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Prevalence, Incidence, and Lifetime Risk for Abdominal Aortic Aneurysm

b. Abbreviated Title (Length 26 characters): Aortic Aneurysm Risk

2. Writing Group:

Writing group members: Weihong Tang, Alvaro Alonso, Pam Lutsey, Frank Lederle, Lu Yao, Weihua Guan, Lindsay Bengtson, Aaron Folsom; others welcome

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

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3. Timeline: Finish by mid 2014

4. Rationale:

Abdominal aortic aneurysms (AAA) are an important manifestation of vascular disease in older age. Traditional atherosclerotic disease risk factors, particularly age, male sex, smoking and hypertension, contribute to the etiology of AAA. Rupture of an AAA is a

life threatening condition, and a lot of research has been put into clinical guidelines for screening and revascularization of AAAs.

The annual incidence rate of AAA in adults of 25 to 75+ years is estimated to be 0.4%, higher in men than women, and increases rapidly after age 60.[1-3, 4] African Americans seem to have a lower AAA prevalence rate[5] and death rate than whites.[6] The incidence and mortality of AAA has been increasing in Western countries in the past decades.[6-11] However, a few newly published studies suggest a pattern of decreasing prevalence,[12] mortality,[13] ruptured and emergency AAA admissions[13] in Sweden, England, and Wales, while a steady rate of nonruptured AAA admission was still observed.[13] This decline was suspected to be caused by declined smoking rate.[11] A decreasing mortality rate of AAA has also been observed in the US since 1990s[11] but there is no recent data available on incidence and prevalence of hospital and asymptomatic AAAs.

Dr. Tang's ancillary study has identified hospitalized AAAs through ARIC and CMS, outpatient AAAs through CMS, and silent/asymptomatic AAAs through visit 5 ultrasound screening. A total of 637 AAAs have been identified in the ARIC cohort. ARIC offers a nice opportunity to examine the prevalence, incidence, and lifetime risk of AAA in this biracial community-based cohort.

5. Main Hypothesis/Study Questions:

-Data on prevalence, incidence, and lifetime risk of hospital and asymptomatic AAAs from ARIC will provide useful information on the changing epidemiology of AAA in the general population in US.

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 from visit 1 through the 2011 event follow-up for ARIC hospitalized AAAs, CMS through 2011 for CMS hospitalized and outpatient AAAs, and the abdominal aortic ultrasound exam at Visit 5. We will also describe the design of ARIC AAA study in this manuscript.

Outcome: clinical/hospital AAAs, outpatient AAAs, and ultrasound AAAs as defined below.

1. Hospital AAAs ascertained through hospital discharge diagnoses and death certificates from Visit 1 to 2011 events follow-up. Hospital AAAs were defined using the definite ICD diagnostic codes 441.3, 441.4, 441.02, 38.44 and 39.71, and mortality code I71.02, I71.3, I71.4, 441.3 and 441.4. Other diagnostic codes that indicate probable diagnosis of AAA will be investigated case-by-case to clarify or rule out AAA diagnosis. The CMS data will be used to identify additional hospital and outpatient AAAs.

Identification of outpatient AAAs from the CMS data requires two claims that were at least seven days apart.

2. Asymptomatic AAAs ascertained based on the Visit 5 abdominal aortic ultrasound exam. We will use a widely used definition for asymptomatic AAA, which is infrarenal abdominal aortic diameter ≥ 30 mm.

Overlap between the hospital and asymptomatic ultrasound AAAs: we expect a small overlap between the two groups because 1) a majority of clinical AAAs had symptoms, surgical repair or rupture, 2) clinical AAAs who had a history of rupture or surgical repair have been excluded from the abdominal ultrasound exam.

Exposures: Incidence and prevalence of AAA, age, gender, race, and smoking.

Data Analysis:
Incidence of hospital and outpatient AAAs will be calculated in the whole ARIC and by race, age group, gender, and smoking status/duration/amount at baseline. Time trend in age-standardized rate will be calculated and also stratified by race, gender, and smoking status/duration/amount at baseline. To look at time trends, we will consider calculating age-specific rates at different time periods (by 5 years), similar to the method used in the atrial fibrillation time trend study in ARIC.[14]

Prevalence of asymptomatic AAA will be calculated based on the V5 abdominal aortic ultrasound exam. The prevalence will be stratified by small (diameter: 3.0cm-5.0cm) and big AAA (diameter ≥ 5.0 cm) as well as by race, age group, gender, and smoking status/duration/amount at the V5 exam.

The prevalence of all AAAs, including hospital and asymptomatic AAA, will be calculated in the whole ARIC for the whole duration of follow-up and by race, age group, gender, and smoking status/duration/amount at baseline.

Lifetime risk of AAA: We will use a modified technique of survival analysis,[15-17] similar to what was used for atrial fibrillation lifetime risk calculation in the Framingham Heart Study.[18] Each subject was followed up from entry through the last examination until the occurrence of a first AAA event, death free of AAA, attainment of the oldest age in ARIC, or last ARIC examination or medical contact at which the subject was known to be free of AAA. Age specific hazards, incidence rates, cumulative incidence, and survival probabilities will be calculated as in a Kaplan-Meier analysis. In lifetime risk estimation, the multiple decrement life-table approach treats death as a true competing event, and the decedent's risk for subsequent events is set to zero. The lifetime risk calculation will be repeated for different groups defined by race, gender, age, and smoking status.

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 ICTDER03 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

8.c. If yes, is the author aware that the participants with RES_DNA = 'not for profit' restriction must be excluded if the data are used by a for profit group?
____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)?

1505 Risk Factors for Abdominal Aortic Aneurysm (Tang)
1505A Hemostatic Factors and Aortic Aneurysm Incidence (Folsom)

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

11.b. If yes, is the proposal
__X__ A. primarily the result of an ancillary study (AS 2009.18: "Identifying Genetic and Epidemiological Risk Factors for Abdominal Aortic Aneurysm", R01HL103695, PI Weihong Tang**)**
___ 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/

12. 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.

References:

1. Forsdahl SH, Singh K, Solberg S, et al. Risk factors for abdominal aortic aneurysms: a 7-year prospective study: the Tromso Study, 1994-2001. *Circulation.* Apr 28 2009;119(16):2202-2208.

2. Lederle FA, Johnson GR, Wilson SE, et al. Yield of repeated screening for abdominal aortic aneurysm after a 4-year interval. Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators. *Arch Intern Med.* Apr 24 2000;160(8):1117-1121.

3. Vardulaki KA, Prevost TC, Walker NM, et al. Incidence among men of asymptomatic abdominal aortic aneurysms: estimates from 500 screen detected cases. *J Med Screen.* 1999;6(1):50-54.

4. Singh K, Bonaa KH, Jacobsen BK, et al. Prevalence of and risk factors for abdominal aortic aneurysms in a population-based study : The Tromso Study. *Am J Epidemiol.* Aug 1 2001;154(3):236-244.

5. Lederle FA, Johnson GR, Wilson SE, et al. Prevalence and associations of abdominal aortic aneurysm detected through screening. Aneurysm Detection and Management (ADAM) Veterans Affairs Cooperative Study Group. *Ann Intern Med.* Mar 15 1997;126(6):441-449.

6. Gillum RF. Epidemiology of aortic aneurysm in the United States. *J Clin Epidemiol.* Nov 1995;48(11):1289-1298.

7. Best VA, Price JF, Fowkes FG. Persistent increase in the incidence of abdominal aortic aneurysm in Scotland, 1981-2000. *Br J Surg.* Dec 2003;90(12):1510-1515.

8. Melton LJ, 3rd, Bickerstaff LK, Hollier LH, et al. Changing incidence of abdominal aortic aneurysms: a population-based study. *Am J Epidemiol.* Sep 1984;120(3):379-386.

9. Fowkes FG, Ruckley CV, Powel JT, et al. Screening for abdominal aortic aneurysms. *Bmj.* Oct 24 1992;305(6860):1013.

10. Fowkes FG, Macintyre CC, Ruckley CV. Increasing incidence of aortic aneurysms in England and Wales. *Bmj.* Jan 7 1989;298(6665):33-35.

11. Lederle FA. The rise and fall of abdominal aortic aneurysm. *Circulation.* Sep 6 2011;124(10):1097-1099.

12. Svensjo S, Bjorck M, Gurtelschmid M, et al. Low prevalence of abdominal aortic aneurysm among 65-year-old Swedish men indicates a change in the epidemiology of the disease. *Circulation.* Sep 6 2011;124(10):1118-1123.

13. Choke E, Vijaynagar B, Thompson J, et al. Changing epidemiology of abdominal aortic aneurysms in England and Wales: older and more benign? *Circulation.* Apr 3 2012;125(13):1617-1625.

14. Alonso A, Agarwal SK, Soliman EZ, et al. Incidence of atrial fibrillation in whites and African-Americans: the Atherosclerosis Risk in Communities (ARIC) study. *Am Heart J.* Jul 2009;158(1):111-117.

15. Beiser A, D'Agostino RB, Sr., Seshadri S, et al. Computing estimates of incidence, including lifetime risk: Alzheimer's disease in the Framingham Study. The Practical Incidence Estimators (PIE) macro. *Stat Med.* Jun 15-30 2000;19(11-12):1495-1522.

16. Lloyd-Jones DM, Larson MG, Beiser A, et al. Lifetime risk of developing coronary heart disease. *Lancet.* Jan 9 1999;353(9147):89-92.

17. Vasan RS, Beiser A, Seshadri S, et al. Residual lifetime risk for developing hypertension in middle-aged women and men: The Framingham Heart Study. *Jama.* Feb 27 2002;287(8):1003-1010.

18. Lloyd-Jones DM, Wang TJ, Leip EP, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. *Circulation.* Aug 31 2004;110(9):1042-1046.