1. **Full Title:** Correlates of abdominal aortic diameters among persons without abdominal aortic aneurysms

   b. **Abbreviated Title (Length 26 characters):** Risk factors for aortic size

2. **Writing Group:**
   
   Writing group members: Lu Yao, Aaron Folsom, Weihong Tang, others TBA welcome

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

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3. **Timeline:** Finish by May 2016

4. **Rationale:**

   Abdominal aortic aneurysm (AAA), typically defined by an aortic diameter of 3.0 cm and larger, is a highly-fatal vascular disease common in elderly persons. The primary risk associated with AAA is rupture, and the risk of rupture increases with the size of AAAs. For example, annual risk for rupture is nearly 0% for AAAs between 3.0 and 3.9 cm in diameter, 1% for those between 4.0 and 4.9 cm in diameter, and reaches up to 11% for those between 5.0 and 6.0 cm in diameter.
Most AAAs are asymptomatic. Nonetheless, considering that the estimated mean growth rate of AAA is reported as 0.22 to 0.57 cm per year, once an asymptomatic AAA occurs it has a high likelihood of becoming symptomatic within a few years. Several studies have examined risk factors for symptomatic AAAs, and they include advanced age, male sex, cigarette smoking, hypertension, etc. However, little is known about the determinants for asymptomatic AAAs. Over the last 30 years, AAA incidence has substantially increased in the US and in the European countries, although recent evidence suggests that AAA may be declining as smoking rates fall. Examining risk factors for asymptomatic AAAs or even larger aortic diameters in the normal range is a public health priority for AAA prevention.

Asymptomatic AAAs have been identified through visit 5 ultrasound screening among over 5,900 participants. ARIC offers a nice opportunity to examine the correlates of abdominal aortic diameters, among people without AAA, in this biracial community-based cohort.

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

We will examine levels of cardiovascular risk factors from visit 1 to visit 5 in relation to abdominal aortic diameters at visit 5, among participants without AAA.

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:**

A longitudinal analysis examining levels of risk factors from visit 1 to visit 5 in relation to abdominal aortic diameters at visit 5

**Exclusions:**

We will exclude participants who did not attend the visit 5 abdominal ultrasound exam, those with clinical AAAs prior to visit 5, and those with an aortic diameter ≥3.0 cm in the visit 5 abdominal ultrasound exam.

**Outcome:**

Infrarenal abdominal aortic maximum diameter was measured in a screening abdominal ultrasound in the fifth ARIC examination (2011-2013). Of the 10,036 ARIC participants still alive through August 2013, 6,538 (65%) had a home or clinic ARIC exam and, of these, 5,912 (59%) undertook abdominal ultrasonography and had usable images.

**Risk factors:**

Sex, race, educational level, age, height, smoking status and pack-years, alcohol consumption, blood pressure, blood pressure meds, hypertension, total, LDL, and HDL cholesterols, lipid-lowering meds, glucose/diabetes, carotid intima-media thickness,
carotid distensibility, peripheral artery disease, circulating novel CVD biomarkers at all available exams. In addition, we will consider the correlation between Framingham and ARIC global CVD scores, and use the scores as predictors of aortic diameter. Continuous risk factors will be categorized into quintiles.

Data Analysis:

Generalized linear regression analysis will be performed to examine the relationship of risk factor categories with infrarenal abdominal aortic maximum diameter (in continuous). We will use inverse probability of attrition weighting, as previously described in a study using ultrasound AAA data, to adjust for the potential selection bias caused by differential participation in the 2011 to 2013 examination. The weights will be calculated based on the product of the probability of being alive at visit 5 and the probability of having an abdominal ultrasound conditional on being alive given a variety of covariates measured at baseline and during follow-up. Regression coefficients as well as 95% CI in the regression analysis will be obtained from inverse probability of attrition–weighted general estimating equation models. Basic models will be adjusted for baseline age, gender, race, and ARIC center. Advanced models will include other risk factors as additional covariates. In secondary analysis, multivariate logistic regression models will be used to compare the highest quintile of the study outcome vs. the others.

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 __X__ 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.cscce.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)
2216 Carotid atherosclerosis and abdominal aortic aneurysm (Yao)

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/](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