

## ARIC Manuscript Proposal #2973

PC Reviewed: 5/9/17

Status: \_\_\_\_\_

Priority: 2

SC Reviewed: \_\_\_\_\_

Status: \_\_\_\_\_

Priority: \_\_\_\_\_

**1.a. Full Title:** Prospective Study of Lipoprotein(a) and Abdominal Aortic Aneurysm Risk: the Atherosclerosis Risk in Communities Study

**b. Abbreviated Title (Length 26 characters):** Lp(a) and AAA

### 2. Writing Group:

Writing group members: Yasuhiko Kubota, Weihong Tang, Christie Ballantyne, Aaron Folsom

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. YK [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).

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### 3. Timeline:

Data analysis: 1-2 months from manuscript approval date.

First draft of the manuscript: 2-3 months from manuscript approval date.

### 4. Rationale:

Abdominal aortic aneurysm (AAA) is a common disease in Western populations (1). With aging societies, the incidence of AAA is increasing (2). Although AAA is usually asymptomatic, ruptured AAA is usually fatal (3). Thus, it is very important to identify populations at high risk of AAA to prevent AAA events.

Lipoprotein(a), consisting of an low-density lipoprotein-like lipoprotein and apolipoprotein(a), has been reported to be a risk factor for several cardiovascular diseases, including coronary heart disease (4) and stroke (5). Several case-control studies have suggested that lipoprotein(a) is also associated with the presence of AAA (6, 7). However, to the best of our knowledge, there is no prospective study investigating the association between lipoprotein(a) and AAA risk in general populations.

The Atherosclerosis Risk in Communities Study (ARIC) has hospitalized AAA data through 2011. Therefore, we sought to prospectively test the hypothesis that lipoprotein(a) is positively associated with the risk of AAA, independent of other AAA risk factors including other lipid profiles, in a population-based study in the U.S.

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

To test the hypothesis that lipoprotein(a) is positively associated with the risk of AAA, independent of other AAA risk factors.

#### **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 design.

##### Inclusions

Participants with plasma lipoprotein(a) measurements at visit 1.

##### Exclusions

Those at visit 1 who had prior AAA surgery or aortic angioplasty; were using lipid medication; or were not white or black.

##### Main exposure

Plasma lipoprotein(a) level.

##### Statistical analysis

We will present the prevalences of potential AAA risk factors at visit 1 (age, sex, race, smoking status, pack-years of smoking, height, hypertension, diabetes mellitus, HDL-C, LDL-C, triglycerides, hormone replacement therapy use) according to quintiles of plasma lipoprotein(a) level. Then, we will examine the association between quintiles of plasma lipoprotein(a) level and AAA risk using Cox proportional hazard models adjusting for potential AAA risk factors. We will also draw a cubic spline graph to investigate the dose-response relation in detail. Because of differences in lipoprotein(a) concentrations between blacks and whites, we will also do a race-specific supplementary analysis.

#### **7.a. Will the data be used for non-CVD analysis in this manuscript?**

Yes  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.csc.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 (PMID: 27834688)
- #2633: Associations between Novel Biomarkers and Risk of Abdominal Aortic Aneurysm (PMID: 26085454)
- #1610: Associations between lipoprotein(a) levels and cardiovascular outcomes in African Americans: The Atherosclerosis Risk In Communities (ARIC) Study. (PMID: 22128224)
- #1090: Risk Factors for Ischemic Stroke Subtypes. The Atherosclerosis Risk in Communities (ARIC) Study (PMID: 16675734)

**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 (list number\* 2009.18)**  
\_\_\_ **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.csc.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.csc.unc.edu/aric/index.php>, under Publications, Policies & Forms. [http://publicaccess.nih.gov/submit\\_process\\_journals.htm](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](mailto:pingping_wu@unc.edu). I will be using CMS data in my manuscript \_\_\_\_ Yes \_\_\_\_ No.

#### **References:**

1. U.S. Preventive Services Task Force. Screening for abdominal aortic aneurysm: recommendation statement. *Ann Intern Med.* 2005 Feb 1;142(3):198-202.
2. Li X, Zhao G, Zhang J, Duan Z, Xin S. Prevalence and trends of the abdominal aortic aneurysms epidemic in general population--a meta-analysis. *PLoS One.* 2013 Dec 2;8(12):e81260. doi: 10.1371/journal.pone.0081260.
3. Ashton HA, Buxton MJ, Day NE, Kim LG, Marteau TM, Scott RA, Thompson SG, Walker NM; Multicentre Aneurysm Screening Study Group. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. *Lancet.* 2002 Nov 16;360(9345):1531-9.
4. Danesh J, Collins R, Peto R. Lipoprotein(a) and coronary heart disease. Meta-analysis of prospective studies. *Circulation.* 2000 Sep 5;102(10):1082-5.
5. Smolders B, Lemmens R, Thijs V. Lipoprotein (a) and stroke: a meta-analysis of observational studies. *Stroke.* 2007 Jun;38(6):1959-66.
6. Takagi H, Manabe H, Kawai N, Goto SN, Umemoto T. Circulating lipoprotein(a) concentrations and abdominal aortic aneurysm presence. *Interact Cardiovasc Thorac Surg.* 2009 Sep;9(3):467-70. doi: 10.1510/icvts.2009.208843.
7. Kotani K, Sahebkar A, Serban MC, Ursoniu S, Mikhailidis DP, Mariscalco G, Jones SR, Martin S, Blaha MJ, Toth PP, Rizzo M, Kostner K, Rysz J, Banach M; Lipid and Blood Pressure Meta-analysis Collaboration (LBPMC) Group. Lipoprotein(a) Levels in Patients With Abdominal Aortic Aneurysm. *Angiology.* 2017 Feb;68(2):99-108. doi: 10.1177/0003319716637792. 8-2477.