

21 July 2016

Dear Dr. Josef Coresh and ARIC Committee:

We revised MS2782, 'Educational Attainment and Lifetime Risk of Cardiovascular Disease: the Atherosclerosis Risk in Communities Study'.

Revised points are,

1. We added Gerardo Heiss as a coauthor.
2. Since Gerardo Heiss suggested we should also investigate the lifetime risk of cardiovascular disease according to parental educational attainment, we added it in the last sentence of 'Statistical analysis' section.

We do not think there is much overlap of topics with the proposal, MS2798. It is looking at risk prediction and we are looking at lifetime risk. The analytic techniques and purposes are different.

We look forward to hearing from you at your earliest convenience.

Yours sincerely,

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ARIC Manuscript Proposal #

PC Reviewed: ___/___/16 **Status:** _____ **Priority:** _____
SC Reviewed: _____ **Status:** _____ **Priority:** _____

1.a. Full Title: Educational Attainment and Lifetime Risk of Cardiovascular Disease: the Atherosclerosis Risk in Communities Study

b. Abbreviated Title (Length 26 characters): Education & lifetime risk

2. Writing Group:

Writing group members: Yasuhiko Kubota, Gerardo Heiss, Richard F. Maclehose, Nicholas S. Roetker, Aaron Folsom, others welcome

Commented [久保田1]: We added Gerardo Heiss as a new coauthor.

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]

First author: Yasuhiko Kubota

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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:

Inequalities in cardiovascular disease (CVD) are due in part to inequalities in socioeconomic status such as education, occupation, and income, and present a major and persistent public health challenge across industrialized nations (1). Particularly educational inequalities may be one of the most important contributing socioeconomic

factors. Education can help create healthier people and communities by leading them to healthy behaviors (not smoking, physical activity, healthy diet, etc.), occupations with better conditions including higher income, and effective health care (2–6). Since education is an exposure starting in childhood, educational inequalities may increase the risk of CVD at young ages, and thus accelerate premature death. Therefore, interventions to address educational inequalities at the community level may have a great impact on the prevention of CVD (7).

One way that may encourage such interventions may be to provide more information on the lifetime risk of CVD according to educational attainment. Lifetime risk estimates, which provide an absolute risk assessment, assist the general people, clinicians and policy-makers to understand the burden of CVD in a population (8), and thus can be expected to increase public awareness of to what extent educational inequalities can contribute to the increase in CVD risk, as shown in the case of the lifetime risk of breast cancer (9). However, to the best of our knowledge, there has been no study so far estimating lifetime risks for CVD according to educational attainment.

We aim to estimate the lifetime risk of CVD (coronary heart disease, heart failure and stroke) according to educational attainment. Since gender or race may affect education levels or CVD risk, we will also estimate not only overall but also sex or race-specific lifetime risks.

5. Main Hypothesis/Study Questions:

To estimate individual lifetime risks of incident CVD (coronary heart disease, stroke, and heart failure by level of educational attainment.

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

Inclusion/exclusion criteria

Inclusion: participants who provided information on educational attainment at visit 1.

Exclusion: those who had prevalent CVD at visit 1.

Main exposure

Educational attainment: grade school, high school without graduation, high school with graduation, vocational school, some college, and graduate/professional school

Statistical analysis

First, we will compare the prevalences of CVD risk factors (smoking, physical activity, healthy diet score, hypertension, diabetes, hypercholesterolemia and income) according

to educational attainment (Table 1). Next, we will compute lifetime risk of CVD using a macro from Dr. Donald Lloyd-Jones (10) (Figure 1). It employs a Kaplan Meier analysis that incorporates competing risks, with deaths from other causes as competing events. Remaining conditional lifetime risk at age 45 years will be calculated. We will also conduct sex or race-specific analyses (Figure 2). Lastly, we will also calculate the lifetime risk of CVD according to income and parental educational attainment (Figure 3) and joint associations of educational attainment and each of them with lifetime risk of CVD (Figure 4). We will use data on parental educational attainment obtained at visit 4. For parental educational attainment, baseline will be at visit 4

Commented [久保田2]: Following a new coauthor, Gerardo Heiss's suggestion, we added the analyses of lifetime risk of CVD according to parental educational attainment.

Commented [久保田3]:

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 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>

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)?

Multiple ARIC papers on individual outcomes. For example:

#2432: Life's Simple 7 (ideal CV risk) and heart failure

#926: Individual and Area-Level Lifecourse Socioeconomic Status and Subclinical Atherosclerosis: The Atherosclerosis Risk in Communities (ARIC) Study

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* **2006.16**)
 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 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. I will be using CMS data in my manuscript Yes No.

References:

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