

## ARIC Manuscript Proposal #2483

PC Reviewed: 12/9/14  
SC Reviewed: \_\_\_\_\_

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

Priority: 2  
Priority: \_\_\_\_\_

**1.a. Full Title:** Brain Health in African-Americans: The ARIC experience

**b. Abbreviated Title (Length 26 characters):**

**2. Writing Group:**

Writing group members: Rebecca Gottesman, Myriam Fornage, David Knopman, Tom Mosley

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. RG [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:** To be submitted for a special issue (solicited review) in December 2014, in *Current Alzheimer Research*: “Impact of racial differences on brain health among the oldest old”.

**4. Rationale:**

Disparities in stroke rates and stroke-related mortality are commonly reported in the so-called “stroke belt”,<sup>1,2</sup> with higher rates among African-American individuals than among

Caucasians. Beyond clinical stroke, African-Americans appear to be at increased risk for adverse subclinical brain changes and related sequelae, including cognitive impairment and dementia.<sup>3</sup> Possible explanations for the excess burden of negative neurologic outcomes in African-Americans include: 1) higher prevalence of vascular risk factors, including hypertension,<sup>4</sup> diabetes,<sup>5</sup> and smoking; 2) earlier onset of risk and greater severity, or more poorly controlled<sup>6</sup> risk factors; 3) greater sensitivity to risk factors (i.e., greater target organ damage at comparable levels of risk factor severity), or 4) differences in the social and environmental context. However, the precise cause of excess risk in African-Americans remains to be determined.

In this report, we will review findings from the Atherosclerosis Risk in Communities (ARIC) study, with over 25 years of long-term follow-up on clinical and subclinical brain outcomes in a large cohort of African-American and Caucasian men and women. We will summarize findings related to stroke, subclinical cerebrovascular disease (silent infarcts, leukoaraiosis), brain atrophy, cognitive decline and dementia, with particular emphasis on disparities by race. We will provide evidence that observed differences by race may be due to differences in risk factor presence, severity, and control. In addition, we will review genetic differences in or explanations for some of these observed associations by race, and will discuss plans to evaluate unanswered questions regarding race-specific disparities in brain health.

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

Invited review paper without any new analysis. We will summarize the ARIC experience regarding stroke, brain small vessel disease (subclinical infarcts, white matter hyperintensities), cognitive decline and dementia. We will focus on possible explanations for race-based differences on the basis of differences in vascular risk factor prevalence. We will also discuss data on the possibility of genetic differences by race explaining some of the observed differences in brain aging.

#### **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).**

**7.a. Will the data be used for non-CVD analysis in this manuscript?** \_\_\_ Yes  
\_\_\_X\_\_\_ No (non-CVD but no new analyses planned)

**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?** \_\_\_X\_\_\_ 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 (again, no new analyses but will be discussed from prior papers)

**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)?**

Yatsuya H, Folsom AR, Yamagishi K, North KE, Brancati FL, Stevens J. Race- and Sex-specific associations of obesity measures with ischemic stroke incidence in the Atherosclerosis Risk in Communities (ARIC) Study. *Stroke*. 2010;41(4):417-425.

Huxley RR, Bell EJ, Lutsey PL, et al. A comparative analysis of risk factors for stroke in blacks and whites: the Atherosclerosis Risk in Communities study. *Ethn. Health*. 2014;19(6):601-616.

Schneider ALC, Sharrett AR, Gottesman RF, et al. Normative data for eight common neuropsychological tests for blacks and whites from the Atherosclerosis Risk in Communities (ARIC) Study. *Alzheimer's Disease and Associated Disorders*. 2014;In press.

Hutchinson RG, Watson RL, Davis CE, et al. Racial differences in risk factors for atherosclerosis. The ARIC Study. Atherosclerosis Risk in Communities. *Angiology*. 1997;48(4):279-290.

**11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?**

Yes  No

(Again, no new analyses, but discusses papers using ARIC ancillary study data)

**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 <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.