ARIC Manuscript Proposal #2736

PC Reviewed: 4/12/16       Status: A       Priority: 2
SC Reviewed: _________    Status: _____    Priority: ____

1.a. **Full Title:** Comparing Brain Imaging Findings Among American Indians in the Strong Heart Stroke Study to Whites and Blacks in the Cardiovascular Health Study and the Atherosclerosis Risk In Communities Study

b. **Abbreviated Title (Length 26 characters):** Comparing Brain Imaging

2. **Writing Group:**
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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __PJ__ [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:** Analyses and manuscript preparation are expected to be completed within six months of receipt of data, and submitted for publication shortly after.

4. **Rationale:**

American Indians experience a disproportionately high incidence of vascular disease affecting the brain relative to other racial and ethnic groups. The Strong Heart Study (SHS), a longitudinal study of cardiovascular disease in 4,549 American Indians, estimated that they have an alarming incidence of stroke, twice that of the general U.S. population adjusted for age and sex.\(^1\) Moreover, American Indians experience high levels of key risk vascular risk factors, such as hypertension, diabetes mellitus, hypercholesterolemia, and obesity.\(^2-5\)

The Strong Heart Stroke Study examined 1,033 American Indians aged 65 to 80 years in 2010-13 to characterize the prevalence and correlates of MRI-defined findings reflecting vascular disease of the brain. To understand how the American Indian participants of SHSS compare with other racial groups, we are proposing to compare demographic and medical characteristics of SHSS participants with those of participants in the Cardiovascular Health Study (CHS), a longitudinal cohort study of risk factors for cardiovascular disease among community dwelling whites and blacks aged 65+, and the Atherosclerosis Risk In Communities (ARIC) study, a longitudinal cohort study of white and black adults aged 45-64 at baseline from four communities in the US. CHS participants underwent MRI examinations in 1991-94 and again in 1997-99; ARIC participants underwent MRI examinations in 1993-95, in 2004-06, and again in 2011-13. Similar imaging protocols were used in all three studies, which facilitates comparisons of infarcts and 10-point grades for white matter, sulci, and ventricles. We will also compare the relative strength of association of these MRI findings with cognitive impairment, motor deficits, and depressive symptoms where available between white and blacks in CHS and ARIC and American Indians in SHSS.

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

1. To assess how SHSS American Indian participants differ from CHS and ARIC white and black participants who received MRIs, we will compare the demographic, medical history, and cerebrovascular disease risk profiles among those who received MRI scans in SHSS, CHS, and ARIC. We hypothesize that the SHSS study population will have a higher prevalence of cerebrovascular risk factors than the white and black study populations in CHS and ARIC who received MRIs.

2. In the context of differences observed in (1), we will compare MRI findings (number of infarcts, sulcal grade, ventricular grade, white matter grade, site of scan) among whites and blacks in CHS and ARIC to those in SHSS. We hypothesize that American Indians, relative to CHS and ARIC whites and blacks, will have a higher prevalence of these MRI findings adjusted for age and sex, and that these differences will attenuate after further adjustment for demographic and risk factor characteristic differences observed in (1).

3. We will compare the strength of association of these MRI findings with cognitive impairment, motor deficits, and depressive symptoms between SHSS American Indian participants and CHS and ARIC white and black participants.
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).

We will include all SHSS, CHS (1991-94, 1997-99), and ARIC (1993-95, 2004-06, 2011-13) participants with data for the following variables:

Age, sex, study site, education, race, number of infarcts, sulcal grade, ventricular grade, white matter grade, site of scan, neurocognitive test scores (e.g., Modified Mini Mental State Examination, Digit Symbol Test Score), physical performance scores, and cardiovascular risk factors (smoking, hypertension, diabetes, cholesterol, history of stroke, history of heart attack).

A. We will compare demographic and risk factor characteristics of the CHS and ARIC white and black participants and the SHSS American Indian participants who received brain imaging. We will use standard descriptive statistics such as Pearson’s chi-square test, Student’s t-tests or other non-parametric tests, if necessary. Age, sex, and education-adjusted differences will be assessed using regression models, with race (white, black, American Indian) included as a dummy variable. For primary analyses, we will use data from CHS years 1994-94 and ARIC years 1993-95; in an effort to account for differential survival biases, comparisons of SHSS to CHS years 1997-99 and ARIC years 2004-06 and 2011-13 will be included as a sensitivity analysis.

B. We will calculate age and sex-specific prevalence of MRI findings (number of infarcts, sulcal grade, ventricular grade, white matter grade, site of scan) among CHS and ARIC whites and blacks and SHSS American Indians, and will assess the differences between these groups using linear (for continuous outcomes) and logistic (for binary outcomes) regression models, which will include adjustment for age and sex, and further adjustment for demographic and risk factor characteristics differences observed in (A) that are also associated with the outcome of interest. We will use a step-up Benjamini Hochberg method to account for multiple comparisons.

C. We will use regression models adjusted for age, sex, and confounding demographic and risk factor characteristics, to assess whether MRI-defined abnormalities are associated with cognitive, physical, and depression scores. We will assess whether the strength any associations differ between CHS and ARIC whites and blacks and SHSS American Indians using adjusted linear regression models that incorporate interaction terms of study/race and MRI-defined abnormalities. We will use a step-up Benjamini Hochberg method to account for multiple comparisons.

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 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.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)?

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 )

___  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.cscce.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.cscce.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, approved manuscripts using 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  ___X___ No.