ARIC Manuscript Proposal # 1898

PC Reviewed: 2/14/12	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Life's Simple 7's of neurocognitive health

b. Abbreviated Title (Length 26 characters): **Neurocognition Simple 7s**

2. Writing Group:

Writing group members: Thomas Mosley, Alvaro Alonso, Martha Daviglus, Gerardo Heiss, David Knopman, Wassim Tarraf

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

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3. Timeline: Draft manuscript by March 2012; analyses completed and integrated into the manuscript by May 2012 with a submission by fall 2012.

4. Rationale: CVD risk factors and healthy behaviors have also been associated cognitive function and dementing conditions, suggesting common or overlapping etiologic pathways and opportunities for modifying risk. This may be particularly important among ethnic/racial minorities with excess CVD risk. The American Heart Association recently established year 2020 national goals [Life's Simple 7s; (LS7s)] for CVD health promotion and disease reduction. While previous *ARIC* studies have examined several important risk factors associated with cognitive change,[1-4] the proposed paper systematically examines AHA 2020 goals to address the question: *If LS7 goals are*

good for the heart, are they also good for brain function over time? The extent to which cognitive function and dysfunction are attributable to LS7s factors has not been examined systematically, particularly in ethnic/racial groups with excess risk for CVD. The proposed study will use *ARIC* data to examine the relationship between cognitive function and LS7s overall scores and components.

This proposed manuscript builds upon *ARIC* work examining the prevalence of cardiovascular health and incident CVD events (Folsom et al., *JACC*, 2011). Furthermore, it would compliment and inform a similar project underway examining cognitive function and LS7s among Latinos in the Hispanic Community Health Study/Study of Latinos (*SoL*). These studies will serve as a foundation for future work on identifying modifiable risks for dementing conditions. A central aim of this work is to provide communities and participants *actionable information* for promoting health for a major public health problem with unknown cures.

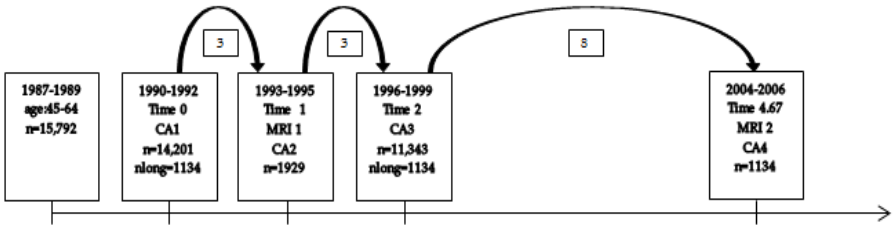
5. Main Hypothesis/Study Questions:

Aim 1: To examine the relationship between neurocognitive functioning and LS7 among Black and White adults.
H_1: Higher neurocognitive performance will be associated with optimal and favorable overall LS7s scores.
$H_{1.1}$: Sustained neurocognitive performance will be associated with more favorable LS7s.

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).

The study will focus on a subset of ARIC participants (n=1,134) with cognitive assessments completed at four time points (Figure 1).

Figure 1. Timeline for ARIC visits including conducted assessments and number of participants



Main outcomes. Three cognitive measures are proposed as the primary outcomes: (1) the Delayed Word Recall Test (DWR); (2) Digit Symbol Substitution Test (DSS); and (3) Word Fluency Test (WF).

Main predictors. To operationalize *Life's Simple Seven* (LS7) factors, we propose following ARIC definitions used by Folsom et al (2010).[2] These main predictors are assessed during all ARIC visits starting at baseline (1987-1989) and include diet, physical activity, smoking status, BMI level, total cholesterol level, fasting glucose levels, and blood pressure. Following AHA guidelines, all indicators will be classified into 3 categories: ideal, intermediate, or poor. Baseline dietary practices would be evaluated using, the modified, 66-item Harvard food frequency questionnaire. Physical activity will be assessed using items from the Baecke questionnaire to quantify sports and walking behaviors in the previous year. Self-reported values would be converted into minutes/week of moderate or vigorous exercise. Smoking status will be based on self-reports (current, former, or never smokers) derived from questionnaires. Body mass index (kg/m^2) would be calculated from weight in a scrub suit and standing height. Fasting plasma total cholesterol measured by enzymatic methods would be used. Serum glucose measured by a hexokinase/glucose-6-phosphate dehydrogenase method will be used. Finally, sitting blood pressure, measured three times using a random-zero sphygmomanometer after a 5-min rest will be evaluated. The average values of the last 2 measurements will be calculated and used. Following AHA guidelines for metabolic criteria, medication use including antihypertensive, cholesterol-lowering, and glucose lowering prescriptions will be accounted for using self-reported use within the past 2 weeks of interview or direct accounts taken from respondents' prescription bottles. A composite LS7 scale (range 0-14) will calculated by summing respondents scores on each of the LS7 indicators (0=Poor, 1=Intermediate, and 2=ideal).

Covariates. Time will be coded as years since baseline in the mixture models, or as visit timing in the longitudinal growth curve model. Time invariant covariates will include age at baseline, sex (male, female), race (African American, non-Latino White), and education level.

Methods. First, descriptive statistics for the cognitive tests (CA1, see Figure 1), LS7 indicators (1987-1989), and covariates of interest will be provided. Average change for both cognitive test scores and LS7s will also be assessed. Second, bivariate associations between each of the cognitive test scores and LS7s will be tested. Additionally, unadjusted associations between cognitive test scores change and LS7s will be examined. Third, we will use linear regression models to test the cross-sectional association between each cognitive test score and LS7s, at baseline, controlling for the specified covariates. Finally, to examine change in

cognitive functioning, linear random-effects models assuming unstructured variance-covariance structures will be used to test the relationship between cognitive change and LS7s controlling for our model covariates using Stata's (11.2) mixed modeling functionalities.

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 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 _X 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.cscc.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)?

1. Knopman D, Boland LL, Mosley T, Howard, G., Liao, D., Szklo, M., McGovern, P., & Folsom, A. R. Cardiovascular risk factors and cognitive decline in middle-aged adults. *Neurology*. 9 2001;56(1):42-48.

2. Knopman DS, Mosley TH, Catellier DJ, Coker LH. Fourteen-year longitudinal study of vascular risk factors, APOE genotype, and cognition: The ARIC MRI Study. *Alzheimer's & dementia: the journal of the Alzheimer's Association.* 2009;5(3):207-214.

3. Folsom AR, Yatsuya H, Nettleton JA, Lutsey PL, Cushman M, Rosamond WD. Community Prevalence of Ideal Cardiovascular Health, by the American Heart Association Definition, and Relationship With Cardiovascular Disease Incidence. *Journal of the American College of Cardiology*. 2011;57(16):1690-1696.

4. Ohira T, Shahar E, Chambless LE, Rosamond WD, Mosley TH, Folsom AR. Risk Factors for Ischemic Stroke Subtypes. *Stroke.* October 1, 2006 2006;37(10):2493-2498.

5. Bezzera, DC, Sharrett, AR et al. Risk factors for lacune subtypes in the Atherosclerosis Risk in Communities (ARIC) Study. *Neurology*, 2012: 102-108.

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

___ A. primarily the result of an ancillary study (list number* _____)

XX B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* ___1991.01_____* ancillary studies are listed by number at http://www.cscc.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.cscc.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.