ARIC Manuscript Proposal #2432

PC Reviewed: 9/9/14	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Life's Simple 7 (ideal CV risk) and heart failure

b. Abbreviated Title (Length 26 characters): Simple 7 & HF

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

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3. Timeline: start Fall 2014

4. Rationale:

The American Heart Association has recently promoted primary prevention of cardiovascular disease (CVD) by recommending Americans follow "Life's Simple 7." The Simple 7 identify ideal, intermediate and poor levels of CVD risk factors or behaviors (namely, smoking, body mass index, physical activity, diet, total cholesterol, blood pressure, and fasting serum glucose).[1] The Atherosclerosis Risk in Communities (ARIC) Study reported that the number of ideal factors achieved is associated strongly and inversely with subsequent incidence of total CVD and cancer.[2,3] ARIC also previously reported that low cardiovascular risk was associated with reduced heart failure (HF) incidence[4] and that a sizeable portion of HF incidence might be reduced by reducing modifiable risk factors. [5]

Yet, some additional work is possible in this area. The previous ARIC publication on Life's Simple 7 [2] did not specifically look at Life's Simple 7 and HF incidence, nor did it estimate lifetime risk of HF in relation to risk factors. Moreover, no study has examined whether midlife levels of Life's Simple 7 might be related to subsequent cardiac structure

and function in elderly people without a heart failure history. The proposed paper will address these topics.

[Note, Dr. Shah has submitted a somewhat similar (yet unnumbered) proposal to examine adherence to 6 of Life's Simple 7 components over time in relation ARIC visit 5 echo findings. We have determined these proposals are different because the current paper will examine baseline Simple 7 components and will include diet.]

5. Main Hypothesis/Study Questions:

Adherence to Life's Simple 7 at ARIC baseline is associated inversely, in the whole cohort, with (a) HF incidence rates and (b) lifetime HF risk.

Adherence to Life's Simple 7 at ARIC baseline is associated inversely with structural and functional cardiac abnormalities at visit 5, among those with no history of HF.

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).

Hypothesis 1

Design: cohort

Endpoints: time to HF incidence and lifetime risk of HF

Exposure: Components of Life's Simple 7
We will categorize Life's Simple 7 in two ways for analysis. Firstly, we will count the number of ideal Life's Simple 7 components a participant meets. Secondly, as done in REGARDS (5), we will create a score in which each component was given points of 0, 1, or 2 to represent poor, intermediate, or ideal health categories, respectively, and these were summed to yield a Life's Simple 7 score. This score will be categorized as inadequate (0-4), average (5-9), or optimal (10-14) for cardiovascular health.

Exclusions: prevalent HF or missing HF status at baseline, missing CHD status at baseline, missing Simple 7 data.

Main covariates: age, race, sex, CHD (at baseline and during follow-up)

Analysis: We will calculate incidence rates of HF and 95% confidence intervals using Poisson regression, and calculate hazard ratios (HR) and 95% confidence intervals of incident HF using Cox proportional hazards models. We will compute lifetime risk of HF using a macro from Dr. Donald Lloyd-Jones[6]. It employs a Kaplan Meier analysis that incorporates competing risks, with deaths from other causes as competing events.

One of the assumptions of this competing risk model is that each failure mechanism leading to a particular type of failure (i.e., failure mode) proceeds independently of every other one, at least until a failure occurs.

We will also explore the association of each Simple 7 component with HF incidence, to see which components contribute most to any overall association.

Hypothesis 2

Design: cohort, based on visit 5 attendees

Endpoints: Echocardiographic variables (visit 5 echo) of LV structure (wall thickness, relative wall thickness, systolic and diastolic diameters and volumes), LV systolic function (LVEF, longitudinal strain, circumferential strain, end-systolic elastance), LV diastolic function (E wave, A wave, E wave deceleration time, TDI E', and LAVi), pulmonary artery systolic pressure, RV size and function (fractional area change, tricuspid annular TDI S')

Exposure: Components of Life's Simple 7 at baseline, as defined above

Exclusions: HF or MI present or missing prior to visit 5, missing baseline Simple 7 data.

Main covariates: age, race, sex. Will adjust for visit 5 risk factors in supplemental analyses.

Analysis: We will calculate odds ratios of visit 5 cardiac abnormalities using logistic regression. Sensitivity analyses will incorporate ARIC-type inverse probability weighting to adjust for visit 5 non-response.

REFERENCES

1. Lloyd-Jones DM, Hong Y, Labarthe D, et al., on behalf of the American Heart Association Strategic Planning Task Force and Statistics Committee. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's Strategic Impact Goal through 2020 and beyond. *Circulation.* 2010;121:586-613.

2. Folsom AR, Yatsuya H, Nettleton JA, Lutsey PL, Cushman M, Rosamond WD, for the Atherosclerosis Risk in Communities (ARIC) Study Investigators. Community prevalence of ideal cardiovascular health, by the American Heart Association definition, and relationship with cardiovascular disease incidence. *J Am Coll Cardiol.* 2011;57:1690-1696.

3. Rasmussen-Torvik LJ, Shay CM, Abramson JG, Friedrich CA, Nettleton JA, Prizment AE, Folsom AR. Ideal cardiovascular health is inversely associated with

incident cancer: The Atherosclerosis Risk in Communities Study. *Circulation.* 2013;127:1270-1275.

4. Folsom AR, Yamagishi K, Hozawa A, Chambless LE; Atherosclerosis Risk in Communities Study Investigators. Absolute and attributable risks of heart failure incidence in relation to optimal risk factors. Circ Heart Fail. 2009 Jan;2(1):11-7.

5. Avery CL, Loehr LR, Baggett C, Chang PP, Kucharska-Newton AM, Matsushita K, Rosamond WD, Heiss G. The population burden of heart failure attributable to modifiable risk factors: the ARIC (Atherosclerosis Risk in Communities) study. J Am Coll Cardiol. 2012 Oct 23;60(17):1640-6.

6. Lloyd-Jones DM, Larson MG, Leip EP, Beiser A, D'Agostino RB, Kannel WB, Murabito JM, Vasan RS, Benjamin EJ, Levy D; Framingham Heart Study. Lifetime risk for developing congestive heart failure: the Framingham Heart Study. Circulation.2002 Dec 10;106(24):3068-72.

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.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)?

a) Dr. Shah, a coauthor, has submitted a somewhat similar (yet unnumbered) proposal to examine adherence to 6 of Life's Simple 7 components over time in relation ARIC visit 5 echo findings. We have determined these proposals are different because the current paper will examine baseline Simple 7 components and will include diet.

b) References 4 and 5, above, have some overlap but are already published.

c) Another group pooled ARIC data with other studies to estimate lifetime risk, but not in relation to risk factors: Huffman MD, Berry JD, Ning H, Dyer AR, Garside DB, Cai X, Daviglus ML,Lloyd-Jones DM. Lifetime risk for heart failure among white and black Americans: cardiovascular lifetime risk pooling project. J Am Coll Cardiol. 2013 Apr 9;61(14):1510-7.

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* 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.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.