ARIC Manuscript Proposal # 3198

PC Reviewed: 7/10/18	**Status: _____**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Life's Simple 7 and Pulse Wave Velocity

b. Abbreviated Title (Length 26 characters): Life's Simple 7 and PWV

2. Writing Group:

Writing group members: Abayomi Oyenuga, Aaron Folsom, Susan Cheng, Hirofumi Tanaka, Lynne Wagenknecht, Michelle Meyer

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: Complete before Fall 2018

4. Rationale:

The American Heart Association has 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 HF incidence. [2,3]

A higher level of pulse wave velocity (PWV) is a non-invasive marker of greater arterial stiffness. PWV is associated positively and independently with risk of incident CVD. [4,5] ARIC obtained PWV measures at Visit 5 (V5) via the Omron Healthcare VP-1000 Plus, and showed that several individual risk factors are associated with PWV in the expected direction. [6-8]

A cross-sectional study from Framingham showed that greater adherence to Life's Simple 7 is associated with better arterial health (based on central PWV and BP). [9]] Similarly, two other studies showed greater adherence to Life's Simple 7 or cumulative exposure to Life's Simple 7 was associated with better brachial-ankle PWV (baPWV), a mix measure representing both central and peripheral arterial stiffness. [10,11] To our knowledge, there are no prospective studies associating Life's Simple 7 and central PWV, nor any studies specifically in blacks.

5. Main Hypothesis/Study Questions:

Adherence to Life's Simple 7 at ARIC baseline is associated inversely with pulse wave velocity at ARIC visit 5. This is true in both whites and blacks.

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: cohort

Endpoints: carotid-femoral PWV (continuous and categorical using a predefined cutpoint). We will explore pressure pulsatility (via central pulse pressure) as a secondary outcome.

Exposure: V1 Life's Simple 7 components
We will categorize Life's Simple 7 at baseline in two ways for analysis. Firstly, we will count the number of ideal Life's Simple 7 components a participant meets. Secondly, 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 poor (0-4), average (5-9), or ideal (10-14) for cardiovascular health.

Baseline exclusions: prevalent or missing CVD, missing Simple 7 data, self-identified as Asian from any site and blacks from Minnesota and Maryland sites.

V5 exclusions: missing PWV data or factors affecting the validity of PWV: BMI ≥ 40 kg/m^2 at Visit 5, major arrhythmias (Minnesota code 8-1-3, 8-3-1, and 8-3-2 from Visit 5 ECG), Minnesota code 8-1-2 from Visit 5 ECG with low quality PWV waveforms, aortic aneurysms/abdominal aorta diameter $\geq$5 cm by ultrasound at Visit 5, self-reported history of aortic or peripheral revascularization or aortic graft at Visit 5, echocardiographic evidence of aortic stenosis at Visit 5, and moderate or greater aortic regurgitation at Visit 5.
For some models, also exclude incident CVD before V5.

Main covariates: age, race, sex, and V5 heart rate

Analysis: We will use linear models for V5 PWV as a continuous outcome or logistic regression for PWV as a categorical variable, with the exposure modeled in the categories described above. The main models will adjust just for V5 age, sex, race and V5 heart rate, since other risk factors are part of Life's Simple 7. We will test for interactions of PWV with age, sex, and race, but we will still show findings stratified further by race and sex for interest's sake.

In a sub-analysis, we will exclude people who developed CVD before V5 to see to what extent the association is independent of developing CVD and V5 CVD medications. In another sub-analysis, we will adjust for mean arterial pressure instead of heart rate and then will repeat the analysis after removing baseline blood pressure from the Life's Simple 7 score as it could be redundant with V5 mean arterial pressure.

REFERENCES

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7.a. Will the data be used for non-CVD analysis in this manuscript? ____ Yes _xx___ 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 __xx__ 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

___xx___ 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)?

References 6-8 listed above

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? _xx___ Yes ____ No

11.b. If yes, is the proposal

_xx__ A. primarily the result of an ancillary study (_____2015.23_____)

___ 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/