

ARIC Manuscript Proposal # 2966

PC Reviewed: 04/11/17
SC Reviewed: _____

Status: _____
Status: _____

Priority: 2
Priority: _____

1. a. Full Title:

The American Heart Association's Life Simple 7 and Risk of Atrial Fibrillation: The Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters):

LS7 & AF in ARIC

2. Writing Group:

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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. PKG [**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:

March 2017 – Submit proposal

April-May-June 2017 – Complete primary data analysis

June 2017 – Submit as abstract to AHA Scientific Sessions

July-August-September 2017 – Additional data analysis/Manuscript preparation

October-November 2017 – Submit manuscript for P&P review

4. Rationale:

Atrial Fibrillation (AF) is the most commonly presenting cardiac arrhythmia in clinical practice, affecting over 2 million people in the United States alone, with a prevalence that is expected to more than double by 2050.¹ AF consumes a substantial amount of healthcare expenditures and is a major source of cardiovascular morbidity and mortality.²⁻⁵ Annual costs for AF treatment are estimated in excess of US\$6 billion.⁵

In 2010, the American Heart Association Strategic Planning Task Force and Statistics Committee identified metrics of ideal cardiovascular health known as Life's Simple 7 (LS7), including 7 modifiable health behaviors and biological factors (nonsmoking, body mass index <25 kg/m², physical activity, ideal diet, untreated total cholesterol <200 mg/dL, untreated blood pressure <120/<80 mm Hg, and fasting blood glucose <100 mg/dL), to target for the primary prevention of cardiovascular disease (CVD).⁶ Attainment of ideal cardiovascular health has been associated with a reduced incidence of CVD.⁷⁻¹⁰

While AF and CVD share common risk factors and poor control of individual LS7 metrics have been associated with a higher risk of atrial fibrillation¹¹⁻¹⁸, the association of the combination of these LS7 metrics with incident AF has not been reported. Therefore, the purpose of this study is to examine the association between LS7 and incident AF in the Atherosclerosis Risk in Communities (ARIC) study, a large biracial prospective cohort study of men and women.

5. Main Hypothesis/Study Questions:

- 1) Higher LS7 scores will be associated with a lower incidence of atrial fibrillation in a cohort of middle-aged adults at baseline.
- 2) Achievement of more LS7 metrics will both be associated with a lower incidence of atrial fibrillation in a cohort of middle-aged adults at baseline.

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).

Data:

Study participants

Eligible participants will be from the ARIC cohort (n=15,792) with baseline examination data on all Life's Simple 7 characteristics—food frequency questionnaire¹⁹, physical activity, body mass index, smoking, total cholesterol, seated blood pressure after a 5-minute rest, and fasting glucose.

Life's Simple 7

LS7 components were defined as published by the AHA.⁶ Definitions for components will be in accordance with prior published work in ARIC and shown in Table (below).²⁰ An overall LS7 score ranging from 0 to 14 will be calculated as the sum of the LS7 component scores. This score will be classified as inadequate (0–4), average (5–9), or optimum (10–14) cardiovascular health.

Component	Ideal	Intermediate	Poor
Smoking	Never or former >1 year	Former <1 year	Current
Physical activity	≥150 min/wk moderate or ≥75 min/wk vigorous or ≥150 min/wk mod + vig	1-149 min/wk moderate or 1-74 min/wk vigorous or 1-149 min/wk mod + vig	No physical activity
Body mass index	<25 kg/m ²	25-29.9 kg/m ²	≥30 kg/m ²
Healthy diet†	4-5 components	2-3 components	0-1 component
Blood pressure	<120/80 mmHg without medication	SBP 120-139 mmHg or DBP 80-89 mmHg or Treated to <120/80 mmHg	SBP≥140mmHg or DBP≥90mmHg
Total cholesterol	<200 mg/dl, without medication	200-239 mg/dl or Treated to <200 mg/dl	≥240mg/dl
Blood glucose	<100 mg/dl, without medication	100-125 mg/dl or Treated to <100 mg/dl	≥126mg/dl

†Responses to the Block FFQ were used for the 'healthy diet score' that is based on how many components of the 5 diet goals are met. Fruits and vegetables ≥ 4.5 cups/day; Fish 3.5 ounces ≥ 2 servings/week; Sodium <1500 mg/day; Sweets/sugar-sweetened beverages ≤ 450 kcal/week; Whole grains (1.1g of fiber in 10 gms of carbohydrates), 1-oz equivalent servings ≥ 3 services/day.

Atrial Fibrillation

Incident AF will be defined as in previous ARIC analyses.²¹ Study participants underwent ECG recordings at baseline and at each follow-up exam. All ECG recordings automatically coded as AF were visually re-checked by a trained cardiologist to confirm the diagnosis. A trained abstractor obtained and recorded all ICD-9 hospital discharge diagnoses from each participant's hospitalizations reported in the annual follow-up interview. AF will be defined as the presence of ICD-9 code 427.31 or 427.32 in the discharge codes. AF hospitalization diagnoses occurring simultaneously with heart revascularization surgery or other cardiac surgery involving heart valves or septa, without evidence of AF in subsequent hospitalizations or study exams will be excluded. ARIC participants will be also labeled as AF cases if the underlying cause of death was AF. The incidence date of AF will be defined as the date for the first ECG showing AF or the first hospital discharge with an AF diagnosis. Follow-up will be available through the end of 2013.

Other Variables of Interest

Demographic - Age, Race, Sex, Education, Clinic site

Comorbidities - Coronary heart disease, Heart failure, Stroke, ECG-based left ventricular hypertrophy²²

Others – Alcohol consumption

Exclusion criteria

Individuals without complete baseline LS7 data, with poor quality baseline ECG data, with baseline AF, or without follow-up AF data will be excluded.

Analysis plan:

Eligible participants not meeting any of the exclusion criteria above will be part of the study analysis.

1) Comparison of baseline characteristics

Participants will be compared according to (1) development of AF and (2) LS7 categories—inadequate, average, or optimum.

The distribution of the LS7 components, number of ideal health factors, and overall LS7 score will be compared by race and sex.

2) Associations of LS7 with incident AF

Hazard ratios (HRs) for incident AF will be calculated (1) for each individual LS7 component (referent category=poor), (2) across overall LS7 categories (optimum or average versus inadequate), and (3) number of ideal LS7 components (referent category=0 ideal factors). HRs for incident AF will also be calculated for per a 1-point higher overall LS7 score and per increase in ideal component.

3) Subgroup analysis

Since the LS7 was designed for the setting of primary cardiovascular disease prevention, we will repeat the analysis described in #2 excluding individuals with baseline clinical cardiovascular disease (coronary heart disease, stroke, and heart failure) to see if associations differ. Model 2 (described below) in this analysis will only be adjusted for left ventricular hypertrophy and alcohol consumption.

Multivariable cox proportional hazards ratios will be used to compute HRs and 95% confidence intervals (CI) for the abovementioned associations between LS7 and incident AF, overall and stratified by race and sex. Multivariable models will be adjusted for as follows: Model 1 adjusted for age, sex, race, education, and clinic site; Model 2 will include covariates in Model 1 with the addition of alcohol consumption, coronary heart disease, congestive heart failure, left ventricular hypertrophy, and stroke. We will evaluate the effect modification by race and sex using a stratification technique and comparing models with and without interaction terms

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

The author identifies no significantly related manuscript proposals. Co-authors with extensive ARIC experience for prior proposals related atrial fibrillation have been contacted to collaborate.

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

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 shows you which journals automatically upload articles to Pubmed central.

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