ARIC Manuscript Proposal # 3228

PC Reviewed: ___/___/18 **Status: _____** **Priority: ____**
SC Reviewed: _____ **Status: _____** **Priority: ____**

1.a. Full Title: The Association of Life's Simple 7 and Atrial Fibrillation Burden in the Atherosclerosis Risk in Communities (ARIC) study

b. Abbreviated Title (Length 26 characters): LS7 and AF burden

2. Writing Group: Wendy Wang, Faye L. Norby, Mary R. Rooney, Michael Zhang, Alejandra Gutierrez Bernal, Elsayed Z. Soliman, Alvaro Alonso, Samuel C. Dudley, Jr., Pamela L. Lutsey, Lin Yee Chen

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

First author: Wendy Wang
Address: Division of Epidemiology and Community Health
1300 South 2nd St, Suite 300
Minneapolis, MN 55455

Phone: (612) 626-7755
E-mail: wang5694@umn.edu

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).
Name: Lin Yee Chen
Address: University of Minnesota Medical School
Department of Medicine, Cardiovascular Division
420 Delaware St SE, MMC 508
Minneapolis, MN 55455

Phone: (612) 625-4401 Fax: (612) 626-4411
E-mail: chenx484@umn.edu

3. Timeline:
Data analysis to begin immediately; pen draft expected spring/summer 2019.

4. Rationale:

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and remains a public health issue as its prevalence continues to increase.[1] Numerous studies have shed light on the risk factors of AF, but most have merely considered AF as either being present or not. As highlighted in a recently published American Heart Association Scientific Statement, it is important to consider the amount or quantity of AF, i.e., AF burden.[2] A higher burden of AF has been shown to be associated with various adverse outcomes, such as increased risk of ischemic stroke, mortality and lower cognitive function; however, the determinants of AF burden have not been clearly defined.[2,3]

Many lifestyle factors, such as obesity, smoking, and low levels of physical activity, have been linked to increased risk of AF.[4] However, a combination of healthy lifestyle choices and its relationship with AF burden has not been clearly documented. The American Heart Association has a defined set of metrics that promote ideal cardiovascular health known as Life's Simple 7 (LS7), which include 7 modifiable health behaviors and factors (physical activity, total cholesterol, diet, blood pressure, body mass index, fasting blood glucose, and smoking status).[5] It has been shown that an improvement in LS7 risk factors may reduce overall AF incidence,[6,7] but this has not yet been reported with respect to AF burden.

AF burden has previously been difficult to quantify due to short monitoring periods from either ECGs or 24-48 hour Holter monitors. In addition to a short monitoring timeframe, patient compliance with Holter monitors is sometimes reduced due to skin irritations or inconvenience.[8] The Zio Patch is a leadless, ambulatory ECG recording device and is more convenient to wear than a traditional Holter monitor.[9] In addition, because the Zio XT Patch is worn for 2 weeks continuously it has a higher diagnostic yield for arrhythmia events[10] and the longer period of monitoring will provide us with a more accurate AF burden measurement. As knowledge gaps pertaining to AF burden currently exist, the use of Zio XT Patch measurements will allow us to identify the modifiable health behaviors that are associated with AF burden.

5. Main Hypothesis/Study Questions:

(1) To evaluate the association of Life's Simple 7 (LS7) score at visit 3 with AF burden at visit 6
We hypothesize that compared to participants with low LS7 scores, those with optimal LS7 scores at visit 3 will have lower AF burden at visit 6.

(2) To identify which LS7 factors at visit 3 are associated with higher AF burden at visit 6
We hypothesize that higher BMI and SBP and lower physical activity at visit 3 will be associated with higher AF burden at visit 6.

(3) To determine the cross-sectional (visit 6) association of LS7 risk factors obtained in late-life with AF burden. * We hypothesize that compared to participants with low LS7 scores, those with optimal LS7 scores at visit 3 will have lower AF burden at visit 6.

*Diet was not collected at visit 6, therefore aim 3 will focus on only the 6 LS7 factors for which data is available.

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).

Study design

Ho 1 & 2: Prospective cohort from visit 3 to visit 6 (when the Zio XT Patch device was applied).
Ho 3: Cross-sectional at visit 6.

Inclusion/Exclusion:

Participants who wore the Zio XT Patch and had complete data on the LS7 characteristics will be included in this analysis.

Variables

Exposure: LS7 risk factors will be classified as has been done previously in ARIC (see table below).[11] LS7 will be represented in two different ways: each risk factor will be analyzed individually, and also as an overall composite score. A composite score ranging from 0-14 will be created, in which each risk factor is given points of 0, 1, or 2 for poor, intermediate, or ideal, respectively. The score will be categorized as inadequate (0-4), average (5-9), or optimum (10-14) cardiovascular health.[11]

Risk factor	**Ideal**	**Intermediate**	**Poor**
Physical activity	$\geq$ 150 min/week moderate or $\geq$ 75 min/week vigorous or $\geq$ 150 min/week moderate + vigorous	1-149 min/week moderate or 1-75 min/week vigorous or 1-149 min/week moderate + vigorous	None
Total cholesterol	<200 mg/dL, without medication	200-239 mg/dL or treated to <200 mg/dL	$\geq$240 mg/dL
Blood pressure	<120/<80 mmHg, without medication	SBP 120-139 or DBP 80-89 mmHg or treated to <120/<80 mmHg	SBP $\geq$ 140 or DBP $\geq$ 90 mmHg
Body mass index	< 25 kg/m^2	25-29.99 kg/m^2	$\geq$ 30 kg/m^2
Fasting blood glucose	< 100 mg/dL, without medication	100-125 mg/dL or treated to < 100 mg/dL	$\geq$ 126 mg/dL
Smoking status	Never or quit >12 mo	Former $\leq$ 12 mo	Current
Diet[†]	4-5 components	2-3 components	0-1 components

[†]Responses to the Block food frequency questionnaire (FFQ) were used to construct the LS7 healthy diet score based on how many of the following five diet goals are met: > 4.5 cups of fruits and vegetables per day, > 2 servings of at least 3.5 ounces of fish per week, < 1500 mg of sodium per day, < 450 kcal of sugar-sweetened beverages per week, > 3 servings of 1-oz servings of whole grain (1.1 gram of fiber per 10 grams of carbohydrate).

Primary outcome: AF burden classified as: no AF, intermittent (>0-<100% AF) or continuous (100% AF)

Other confounders/covariates: age, sex, race/center, education level, alcohol intake, CHD history, HDL cholesterol, LDL cholesterol, stroke history

Statistical analysis

- Participant characteristics will be described using mean ± SD for continuous variables and proportions for categorical variables, stratified by LS7 classifications.
- Prevalence of AF burden status will be compared across LS7 categories.
- Multinomial logistic regressions will be used to evaluate the relationship between the LS7 composite score with AF burden, as well as for each LS7 risk factor with AF burden individually.
    - Model 1 will be adjusted for age, sex, race/center
    - Model 2 will be adjusted for model 1 plus education, alcohol intake
    - Model 3 will be adjusted for model 2 plus prevalent CHD, HDL cholesterol, LDL cholesterol, prevalent stroke
- Inverse probability weighting will be used to account for attrition due to death or visit 6 non-attendance.
- Interactions by age (median split), race and sex will be evaluated by including cross-product terms in the models.

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/mantrack/maintain/search/dtSearch.html

___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)?

#2966: LS7 & AF in ARIC (Garg)
#2280: Zio arrhythmia burden (Rooney)

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* 2013.14_____)
___ 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 https://www2.cscc.unc.edu/aric/approved-ancillary-studies

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.

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