ARIC Manuscript Proposal #2431

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

1.a. Full Title: Ideal Cardiovascular Health during Adult Life and Cardiac Structure and Function among the Elderly

b. Abbreviated Title (Length 26 characters):
Ideal CV Health and Echocardiography in ARIC

2. Writing Group:
Writing group members: Amil M Shah, Brian Claggett, Aaron Folsom, Pamela Lutsey, Scott D. Solomon; Others welcome.

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

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3. Timeline:
Analysis will begin once this manuscript proposal is approved. Anticipate manuscript completion in October 2014.

4. Rationale:

Heart failure (HF) is a progressive disorder afflicting 5 million Americans, with 550,000 patients diagnosed annually, and is responsible for 53,000 deaths annually.[1] In

2010, the American Heart Association Strategic Planning Task Force and Statistics Committee identified seven metrics of ideal cardiovascular health, including three health behaviors (nonsmoking, body mass index <25 kg/m2, and ideal diet) and four health factors (untreated total cholesterol <200 mg/dL, untreated blood pressure <120/<80 mmHg, and fasting blood glucose <100 mg/dL).[2] The attainment of ideal CV health metrics is associated with a reduced subsequent incidence of cardiovascular disease,[3] including incident heart failure. Epidemiologic studies suggest that these risk factors account for over three-fourths of heart failure cases (population attributable fraction 77-89%).[4]

HF is predominantly a disease of the elderly, with over 80% of HF hospitalizations occurring in persons over 65 years of age.[5] Up to half of HF cases occur in the setting of preserved left ventricular ejection fraction (HFPEF), a syndrome for which there are currently no proven therapies. The aging U.S. population, along with increasing rates of hypertension,[6] diabetes,[7] and obesity,[8] create a growing pool of individuals at particularly high risk for HF development. HF risk factors are known to influence cardiac structure, systolic function, diastolic function, and arterial stiffness. However, little data exists regarding the impact of attaining ideal CV health metrics through mid-life and late-life on cardiovascular structure and function in the elderly. Furthermore, whether changes in the status of ideal CV health metrics between mid-life (<65 years old) and late-life (≥65 years old) impact cardiovascular structure and function in the elderly is not know but may have important implications of preventative care in the elderly.

5. Main Hypothesis/Study Questions:

We hypothesize that, among ARIC participants without prevalent CV disease at study initiation (Visit 1), a greater number of ideal cardiovascular health metrics consistently achieved over the following approximately 26 years (through Visit 5) will be associated with better measures of cardiac structure, LV systolic function, LV diastolic function, right ventricular function, and arterial stiffness at Visit 5.

Furthermore, we hypothesize that improvement in the number of ideal CV health metrics consistently achieved from (<65 years old) to late-life (≥65 years old) will be associated with better measures of cardiac structure and function at Visit 5.

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:
This will be a cross-sectional analysis of ARIC participants at Visit 5.

Inclusion/exclusion criteria:
Participants with prevalent cardiovascular disease (heart failure, prior myocardial infarction) at Visit 1 will be excluded from this analysis.

Key variables of interest:

1. Clinical covariates (visit 1 through visit 5): age, gender, race/ethnicity, height, weight, blood pressure, heart rate, history of hypertension, diabetes, dyslipidemia, current and former smoking status, coronary artery disease, prior MI or revascularization procedure, prior stroke or TIA, peripheral arterial disease, heart failure, prior hospitalization for heart failure, physical activity variables
2. Laboratory values (visits 1 through visit 5): glucose, hemoglobin A1C, total cholesterol, triglycerides, HDL, LDL; visit 5 only: high sensitivity troponin T, NT-proBNP, serum albumin and creatinine, urine albumin and creatinine, hemoglobin and hematocrit,
3. 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')
4. Pulse wave velocity values (visit 5): carotid-femoral pulse-wave velocity

Data analysis:

Six ideal CV health metrics will be assessed and classified at each study visit (1-5) according to the following criteria used in previous ARIC publications of ideal cardiovascular health:[3]

Metric	Status	Definition
Smoking	Ideal	Never or quit >12 months
	Intermediate	Former ≤12 months
	Poor	Current
Body mass index	Ideal	<25 kg/m2
	Intermediate	25-29.9 kg/m2
	Poor	≥30 kg/m2
Physical Activity	Ideal	≥150 min/week moderate, or ≥75 min/week vigorous, or ≥150 min/week moderate+vigorous
	Intermediate	1-149 min/week moderate, or 1-74 min/week vigorous, or 1-149 min/week moderate+vigorous
	Poor	None
Total Cholesterol	Ideal	<200 mg/dl without medications
	Intermediate	200-239 or treated to <200 mg/dl
	Poor	≥240 mg/dl
Blood pressure	Ideal	<120/<80 mmHg without medications
	Intermediate	SBP 120-139 or DBP 80-89 or treated to <120/<80 mmHg
	Poor	SBP ≥140 or DBP ≥90 mmHg
Fasting serum glucose	Ideal	<100 mg/dl without medication
	Intermediate	100-125 mg/dl or treated to <100 mg/dl
	Poor	≥126 mg/dl

Physical activity was only assessed at Visits 1, 3, and 5. Status of physical activity metric at Visits 2 and 4 will be assigned the lowest value from the two shouldering measurements. Healthy diet will not be assessed due to lack of adequate serial data on diet.

Key exposure variables will be:
(1) Degree of ideal CV health consistently attained in adulthood, defined as the minimum number of ideal CV health metrics attained at Visits 1-5;
(2) Average CV health in adulthood, defined as the mean number of ideal CV health metrics attained at Visits 1-5;
(3) Change in CV health from mid- to late-life, defined as the difference between the minimum number of ideal CV health indicators attained when <65 years old and when ≥65 years old.

Primary outcome variables will be:
(1) Echocardiographic measures of cardiac structure and function at Visit 5;
(2) Arterial stiffness at Visit 5;
(3) Serum biomarkers of myocardial stress (NT-proBNP) and injury (high-sensitivity troponin) at Visit 5

The primary analysis will include all ARIC participants free of prevalent HF or MI at Visit 1. Sensitivity analysis will be performed further excluding participants with interval HF or MI between Visit 1 and Visit 5.

To address our first hypothesis, the distribution of number of ideal CV health indicators consistently attained from Visits 1-5 will be described. Clinical, echocardiographic, arterial stiffness, and biomarker data will be described based on the number of ideal CV health indicators consistently attained (0, 1, 2, 3, ≥4). For echocardiographic, arterial stiffness, and biomarker data, trend test will be performed using multivariable modeling (linear or logistic regress as appropriate) to test for trend across categories after adjusting for age, gender, race, and study field center. Analysis will be performed in the study population overall and stratified by gender and race. An additional sensitivity analysis will be performed using the average number of ideal CV health metrics obtained from Visits 1-5.

To address our second hypothesis, the distribution in the change in consistently attained CV health indicators from prior to age 65 to age 65 or older will be described. Clinical, echocardiographic, arterial stiffness, and biomarker data will be described based on the change in the number of indicators (≤-2, -1, no change, +1, ≥+2). Given the likelihood that the number of consistently ideal health indicators prior to age 65 will differ between change groups, multivariable adjusted mean values for echocardiographic, arterial stiffness, and biomarker will be displayed, adjusting for number of consistent ideal indicators achieved prior to age 65, age, gender, race, and field center. Adjusted trend test will similarly be performed using linear or logistic regression as appropriate.

Anticipated methodologic limitations:

A limitation of this analysis is missing exposure assessment at serial visits. As noted above, physical activity was only assessed at Visits 1, 3, and 5. Status of physical activity metric at Visits 2 and 4 will be assigned the lowest value from the two shouldering measurements. Healthy diet will not be assessed due to lack of adequate serial data on diet. In addition, the appreciable rate of non-attendance at Visit 5 may limit the generalizability of our findings to the community more generally and bias our findings.

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 ____ 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)?

MS#1797- (Rasmussen-Torvik et al) The Association of AHA Ideal Cardiovascular Health with Cancer incidence: The ARIC Study (MS1797)

MS#1683- (Shay et al) Ideal Cardiovascular Health Behaviors and Progression of Intima Media Thickness

MS#1993 (Allen et al) Genome-wide Association of Ideal Cardiovascular Health

MS#2093 (Cheng et al) Characterizing Healthy Cardiac Aging and Its Correlates in the Community

MS#2383 (Windham et al) Relationship of Life's Simple 7 Score in Midlife to Late Life Physical Function

MS#1905 (Bower et al) The Association of Lifestyle Factors with circulating levels of the Soluble Receptor for Advanced Glycation End Products (sRAGE)

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? ____ Yes __x__ 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.cscc.unc.edu/aric/forms/

12. 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.

References

[1] American Heart Association. Heart disease and stroke statistics – 2009 update. Dallas, Texas:American Heart Association;2009.

[2] Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, Greenlund K, Daniels S, Nichol G, Tomaselli GF, Arnett DK, Fonarow GC, Ho PM, Lauer MS, Masoudi FA, Robertson RM, Roger V, Schwamm LH, Sorlie P, Yancy CW, Rosamond WD. 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.

[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. *J Am Coll Cardiol* 2011;57:1690-6.

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[6] Herz RP, Unger AN, Cornell JA, Saunders E. Racial disparities in hypertension prevalence, awareness, and management. *Arch Intern Med* 2005;165:2098-2104.

[7] Geiss LS, Pan L, Cadwell B, Gregg EW, Benjamin SM, Engelgau MM. Changes in incidence of diabetes in U.S. adults, 1997-2003. *Am J Prev Med* 2006;30:371-7.

[8] Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA* 2006;295:1549-55.