ARIC Manuscript Proposal # 890B

PC Reviewed: _6_/_5_/07   **Status:** __A__   **Priority:** _2__
SC Reviewed: _____   **Status:** _____   **Priority:** ____

1.a. Full Title:
Plasma Fatty Acid Composition and Incidence of Heart Failure in Middle Aged Adults: The Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters):
Plasma FA composition and HF

2. Writing Group:
Writing group members: Kazumasa Yamagishi, Jennifer A. Nettleton, Aaron R. Folsom

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

First author: Kazumasa Yamagishi
Address: Division of Epidemiology and Community Health,
School of Public Health, University of Minnesota
1300 South Second Street, Suite 300
Minneapolis, MN 55454
Phone: 612-626-1893   Fax: 612-624-0315
E-mail: k-yamagishi@umin.net
Dr. Yamagishi is a visiting scholar working with Dr. Folsom.

Corresponding/senior author (if different from first author correspondence will be sent to both the first author & the corresponding author): Aaron R. Folsom
Address: Division of Epidemiology and Community Health,
School of Public Health, University of Minnesota
1300 South Second Street, Suite 300
Minneapolis, MN 55454
Phone: 612-626-8862   Fax: 612-624-0315
E-mail: folsom@epi.umn.edu

3. Timeline: 6 months, but we do hope to submit an abstract for AHA (deadline: June 1st)

Approval of proposal
Literature review   - 2 weeks
Outline paper   - 1 week
Data analysis   - 6 weeks

Manuscript writing   - 8 weeks
    Review and edit   - 8 weeks

4. **Rationale**:
    Previous epidemiological studies have examined the association of several fatty
    acids with coronary heart disease, stroke, arrhythmia and risk factors (1-3), but
    evidence of an association between fatty acids composition and heart failure (HF) is
    limited. Mozaffarian et al. showed that fish and/or omega-3 polyunsaturated fatty
    acids (PUFA) intake measured by food frequency questionnaire was associated with
    reduced the risk of HF (4). However, to date, few studies have evaluated
    associations between fatty acids composition, including omega-3 PUFA, and HF.
    Furthermore, data on plasma fatty acids, common biomarkers of fatty acid intake,
    are quite limited.

    In the ARIC Minneapolis field center, fractions of cholesterol ester (CE) and
    phospholipids (PL) plasma fatty acids at baseline were measured by gas-liquid
    chromatography. The associations with carotid artery intima-media thickness (5),
    hypertension (6), diabetes (7), coronary heart disease (8) and cognitive decline (9)
    have been already examined. We propose to examine the association of CE and PL
    fractions of plasma fatty acids composition and HF in the ARIC Minneapolis cohort.

5. **Main Hypothesis/Study Questions**:
    (1) Plasma omega-3 PUFAs are associated inversely with HF. These associations
        persist for EPA, DPA, and DHA separately.
    (2) Plasma saturated fatty acids are associated positively with HF.
    (3) Plasma monounsaturated fatty acids, omega-6 and omega-9 PUFAs are
        associated inversely and modestly with HF.
    (4) We will further analyze association of HF with specific fatty acids, including
        linoleic acid, oleic acid etc.

**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).**

    Sample: Minnesota participants (n=4,009) with fatty acid data

    Exclusions: missing fatty acid compositions, prevalent HF, prevalent coronary heart
    disease, prevalent stroke, non-white

    Dependent variable: incident HF (n=245)

    Independent variable: PL and CE fatty acids

Covariates: age, smoking, alcohol intake, BMI, blood pressure, antihypertensive medication use, diabetes, plasma total cholesterol, total energy intake and other factors. Food frequency data will be used to help interpret our findings.

Analysis plan: Sex-specific hazard ratios and 95% confidence intervals of HF for quintiles of fatty acids composition will be calculated adjusted for age and other covariates using Cox proportional hazard model. Subgroup analysis will be conducted by stratification. Interactions will be tested using cross product terms.

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 ICTDER02 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 ICTDER02 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 ICTDER02 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
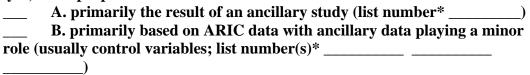
   ___X___ Yes   _____ No

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)?

#890 Plasma fatty acid composition and incidence of coronary heart disease in middle aged adults: The Atherosclerosis Risk in Communities (ARIC) Study
Lead author: Lu Wang

#1182 Diet and the risk of congestive heart failure in the Atherosclerosis Risk in Communities Study (ARIC)
Lead author: Jennifer A. Nettleton

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.

Reference
(1) Psota TL, Gebauer SK, Kris-Etherton P. Dietary omega-3 fatty acid intake and cardiovascular risk. *Am J Cardiol* 2006;98(suppl):3i-18i.
(2) Leaf A. Omega-3 fatty acids and prevention of arrythmias. *Curr Opin Lipidol* 2007;18:31-34.
(3) Balk EM, Lichtenstein AH, Chung M, Kupelnick B, Chew P, Lau J. Effects of omega-3 fatty acids on serum markers of cardiovascular disease risk: a systematic review. *Atherosclerosis* 2006;189:19-30.
(4) Mozaffarian D, Bryson CL, Lemaitre RN, Burke GL, Siscovick DS. Fish intake and risk of incident heart failure. *J Am Coll Cardiol* 2005;45:2015-2021.
(5) Ma J, Folsom AR, Lewis L, Eckfeldt JH. Relation of plasma phospholipid and cholesterol ester fatty acid composition to carotid artery intima-media thickness: the Athersoclerosis Risk In Communities (ARIC) Study. *Am J Clin Nutr* 1997;65:551-559.
(6) Zheng ZJ, Folsom AR, Ma J, Arnett DK, McGovern PG, Eckfeldt JH. Plasma fatty acid composition and 6-year incidence of hypertension in middle-aged adults: the Athersoclerosis Risk In Communities (ARIC) Study. *Am J Epidmiol* 1999;150:492-500.
(7) Wang L, Folsom AR, Zheng ZJ, Pankow JS, Eckfeldt JH; ARIC Study Investigators. Plasma fatty acid composition and incidence of diabetes in middle-aged adults: the Athersoclerosis Risk In Communities (ARIC) Study. *Am J Clin Nutr* 2003;78:91-98.
(8) Wang L, Folsom AR, Eckfeldt JH. Plasma fatty acid composition and incidence of coronary heart disease in middle-aged adults: the Athersoclerosis Risk In Communities (ARIC) Study. *Nutr Metab Cardiovasc Dis* 2003;13:256-266.
(9) Beydoun MA, Kaufman JS, Satia JA, Rosamond W, Folsom AR. Plasma n-3 fatty acids and the risk of cognitive decline in older adults: the Athersoclerosis Risk In Communities (ARIC) Study. *Am J Clin Nutr* 2007;85:1103-1111.