ARIC Manuscript Proposal # 1797

PC Reviewed: 5/10/11	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: The Association of AHA Ideal Cardiovascular Health with Cancer Incidence : The ARIC study

b. Abbreviated Title (Length 26 characters): Ideal CVD health and Cancer

2. Writing Group:

Writing group members: Laura Rasmussen-Torvik, Anna Prizment, Christina Shay, Judith Abramson, Aaron Folsom, Jennifer Nettleton, others welcome

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __LJRT___ **[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: AHA abstract submission by 6/1/11. Draft by 10/1/11

4. Rationale:

The AHA has recently set a 2020 goal that includes "improving CVD health of all Americans by 20%" (1). These recommendations include a suggested definition of ideal cardiovascular health which includes meeting all of the following criteria:
• Not smoking, quit >12 months prior
• BMI <25
• >=150 min/wk of moderate or >=75 min/wk vigorous exercise (or combination)
• Healthy diet score (4-5 components related to fruits/veggies, fish, whole grains, sodium and sugar-sweetened beverages)
• Untreated total cholesterol <200 mg/dl
• Untreated BP <120/<80
• Untreated Fasting glucose <100 mg/dl
Categories for "Intermediate" and "Poor" CV health" are also defined.

Previous analyses, including a recently published report from ARIC (2) \ have demonstrated that adults with optimal levels of readily-measured CVD risk factors at middle age rarely develop CVD (3; 4). However, the prevalence of ideal cardiovascular health (defined as having all 7 ideal health metrics) is very low (5; 6) ; in the recent ARIC analysis, only .1% of the cohort met the definition of ideal cardiovascular health. Major primordial prevention efforts are needed to increase the prevalence of ideal cardiovascular health.

Although the above construct has been labeled "Ideal *Cardiovascular* Health", many components of the metric are important risk factors for other chronic disease, notably cancer. Demonstrating that incidence of cancer is associated with number of ideal cardiovascular health metrics could set the stage for important cooperation between cardiovascular and cancer advocacy groups in promoting primordial prevention in the US and abroad. Such a paper written in the ARIC study would also highlight the unique combination of excellent CVD and cancer incidence information in a single prospective cohort study. Results of this paper can be compared to previous papers that have demonstrated a risk in cancer incidence among those adhering to prevention guidelines developed by cancer advocacy groups (7; 8).

The intent of this paper is to build on the results published in Dr. Folsom's recent paper (2) examining the prevalence of ideal cardiovascular health and the incidence of cancer in individuals with a given number of ideal health metrics. As, such, every attempt has been made to mirror the analysis techniques used in the Folsom paper.

5. Main Hypothesis/Study Questions:

What are the absolute incident rates of lung cancer, colon cancer, breast cancer, prostate cancer, individually and combined, among individuals with 0, 1, 2, 3, 4, 5, 6 or 7 ideal health metrics at baseline? What are the hazard ratios for different types of cancer by number of ideal health metrics (compared to a referent of 0 (or 0-1) ideal health metrics)?

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: prospective cohort
Exposure: Number of ideal health metrics present at baseline, by AHA definition (see above). These metrics have been previously defined for the ARIC cohort and were used in Dr. Folsom's paper.

A. Physical Activity (hours/week)
    a. $\geq$ 150 min/week moderate intensity or $\geq$ 75 min/week vigorous intensity or $\geq$ 150 min/week moderate + vigorous intensity (reference)
    b. 1-149 min/week moderate intensity or 1-74 min/week vigorous intensity or 1-149 min/week moderate + vigorous intensity
    c. 0 hours

B. Body Mass Index
    a. BMI <24.9 kg/m^2
    b. BMI 25.0-29.0 kg/m^2
    c. BMI $\geq$ 30.0 kg/m^2

C. Smoking
    a. Never a smoker or Former > 12 mo.
    b. Former smoker ($\leq$ 12 mo)
    c. Current smoker

D. Diet (AHA Definition):
    a. Adherence to 4-5 (a), 2-3 (b), or 0-1 (c) of the following dietary intake guidelines:
        i. Fruits and Vegetables $\geq$ 4.5 cups/day
        ii. Fish $\geq$ 2 servings/week
        iii. Whole Grain (1 oz serving or 1.1 g/10 g carbohydrates) $\geq$ 3 servings/day
        iv. Sodium $\leq$ 1500 mg/day
        v. Sugar Sweetened Beverages (< 450 kcal or 36 oz/week)
    b. Modified to fit ARIC
        i. Fruits and vegetables: ≥4.5 servings per day (as estimated from FFQ—includes fruits in Q9-Q14 & vegetables in Q15-Q25 + Q56-*excluding Q21 and Q24 (peas/lima beans and lentils/beans, respectively*)
        ii. Fish: ≥two servings per week (preferably oily fish) (as estimated from FFQ—includes Q34, Q35, Q36)

iii. Fiber-rich whole grains: > three servings per day (as estimated from FFQ—includes Q48 (if whole grain), Q49 and Q51)
iv. Sodium: <1500 mg per day
v. Sugar-sweetened beverages: ≤ 4 glasses (assuming ~10-oz glass) per week. (as estimated from FFQ—includes Q64 & Q65)

E. Fasting Plasma Glucose
   a. <100 mg/dL, untreated
   b. 100-126 mg/dL or treated to goal
   c. > 126 mg/dL

F. Total Cholesterol
   a. < 200 mg/dL, untreated
   b. 200-239 mg/dL or treated to goal
   c. ≥ 240 md/dL

G. Blood Pressure
   a. SBP/DBP <120/80 mm/Hg, untreated
   b. SBP/DBP 120-139/80-89 mm/Hg or treated to goal
   c. SBP/DBP >140/90 mm/Hg

Outcome: Incidence rates of colorectal cancer, breast cancer, prostate cancer, and lung cancer, as well as a composite of any of the four cancer outcomes. Recently, Dr. Prizment updated cancer cases in the ARIC cohort through 2006, and there are now 344 colorectal cases, 567 breast cases, 679 prostate cases, and 471 lung cases in the cohort. Sensitivity analyses may be undertaken excluding lung cancer cases from the composite (given the presumed very strong association between lung cancer and smoking). We may also separate pre- and post- menopausal breast cancers for analysis, if the numbers allow.

Covariates for adjustment or stratification: age, race, center, sex (where appropriate--breast cancer analyses will occur only in women, prostate cancer analyses only in men, and we will conduct race-specific analyses).

We will also consider analyses additionally adjusting for additional cancer risk factors (e. g. breast cancerage at first birth, age at menarche, HRT etc.) and compare these analyses to minimally adjusted models.

Analysis:
1. Exclude non-fasters, those with missing data, individuals with cancer at baseline, those not agreeing to participate in non-CVD analyses
2. Compute absolute rates of cancers by number of ideal health factors. Use

Poisson regression models for covariate adjustment. Compute both race-specific and race-combined rates. Assemble figures comparing incidence rates using a life-table approach.

3. Use Cox regression to compute HR for cancer incidence, by number of ideal health factors, using 0 ideal health factors as the referent (or 0-1, 0-2 if the 0 group is too small).

7.a. Will the data be used for non-CVD analysis in this manuscript? _X___ 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 __x__ 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"?
_x___ 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)?

#1631 CVD Health: Prevalence and Outcomes. Now Published in JACC—Community Prevalence of Ideal Cardiovascular Health, by the American Heart Association Definition, and Relationship with Cardiovascular Disease Incidence. AR Folsom et al. PMID: 21492767
We have spoken to Dr. Folsom and there is no anticipated overlap as his paper focused on CVD incidence, not cancer.

#1683 Ideal Cardiovascular Health Behaviors and Progression of Intima Media Thickness. First Author –Shay. Dr. Shay is a co-author on this project and no overlap is anticipated as this paper focuses on IMT progression.

This proposal was discussed briefly at the last ARIC Cancer working group meeting and will be discussed more at the upcoming May meeting. Although several previous papers have examined the association of *individual* elements of ideal health with cancer incidence, no paper has examined the combination of factors as assembled in the AHA 2020 guidelines with cancer incidence.

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

_X__ A. primarily the result of an ancillary study (list number* _1995.04—ARIC cancer study)

___ 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/

11. 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

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