

ARIC Manuscript Proposal # 1180

PC Reviewed: 08 / 15 /06

Status: A

Priority: 2

SC Reviewed: 08 / 17 /06

Status: A

Priority: 2

1.a. Full Title: Dietary influence on pulmonary function, respiratory symptoms and retinal abnormalities in the Atherosclerosis Risk in Communities (ARIC) study

b. Abbreviated Title (Length 26 characters):

2. Writing Group:

Writing group members: **Haidong Kan, June Stevens, Gerardo Heiss, Ronald Klein, Kathryn M. Rose, Stephanie J. London**

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

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3. Timeline: A first manuscript should be available for circulation to the ARIC investigators before Feb. 1, 2007.

4. Rationale:

There is increasing evidence that dietary nutrients modulate oxidative stress-induced lung damage and influence pulmonary function and respiratory symptoms. For example, individuals with a higher intake of fruit have a higher FEV₁ and fewer respiratory symptoms than those who eat fruit infrequently^{1, 2, 3}. Also, both the serum concentrations and the dietary intake of antioxidant nutrients such as omega-3 polyunsaturated fatty acids, Vitamin C, E and beta-carotene have been positively associated with lung function^{4, 5}. Dietary fiber, especially from fruits, was found to reduce the incidence of chronic respiratory symptoms⁶. However, the relationship between dietary components and respiratory health is still not clear and needs to be validated in large studies with detailed phenotypes⁷.

Diet has been associated with cardiovascular disorders such as coronary heart disease^{8,9} and stroke¹⁰. In recent studies, retinal abnormalities have been shown to be structural markers of microvascular damage. Retinal abnormalities predict incident congestive heart failure and coronary heart disease^{11,12}. Moreover, retinal abnormalities might be useful tools to investigate the contribution of environmental exposures such as smoking, environmental tobacco smoke and air pollution to cardiovascular disorders. Among different dietary nutrients, omega-3 polyunsaturated fatty acids has been related with subclinical pathology such as retinal microvascular disorders¹³. To our knowledge, there have been few studies investigating other nutrients in relation to retinal microvascular caliber and other manifestations of microvascular disease.

Dietary assessment at the 1st and 3rd visit of the ARIC study provides us an opportunity to examine the relation between dietary nutrients and respiratory health/retinal abnormalities.

5. Main Hypothesis/Study Questions:

Intake of nutrients that influence antioxidant pathways and other mechanisms implicated in the pathophysiology of lung and cardiovascular abnormalities impact lung function and retinal abnormalities. Nutrients of interest are limited to those which can be reasonably well assessed by the ARIC dietary questionnaire and include omega-3 fatty acids, Vitamin C, beta-carotene, dietary fiber, fruit and vegetable intake and Vitamin D. On the other hand, dietary intake of saturated fatty acids and cholesterol may have adverse effect on lung function and retinal abnormalities. We will examine the effect of nutrients on retinal abnormalities in subjects with diabetes and without diabetes separately. We will also consider effect modification by smoking and environmental tobacco smoke exposure.

6. Data (variables, time window, source, inclusions/exclusions):

Dietary data were collected at visits 1 and 3.

Visits 1: dietary assessment including both dietary questionnaires and supplement data, pulmonary function measures (FEV₁ and FVC), respiratory symptoms (cough, phlegm, wheeze, breathlessness), cardiovascular outcomes (heart rate variability, plaque, carotid thickness, blood pressure, fibrinogen, lipids etc), research center, race group, age, smoking (status including never, former and current smokers, and pack years), exposure to environmental tobacco smoke, BMI, occupation, educational level and height.

Visit 3: dietary assessment including both dietary questionnaires and supplement data, retinal abnormalities (arteriovenous nicking, generalized arteriolar narrowing, venular dilation, and retinopathy), cardiovascular outcomes (heart rate variability, plaque, carotid thickness, blood pressure, fibrinogen, lipids etc), diabetes status, anthropometric measures, blood pressure at the time of the retinal exam, demographic characteristic, smoking, exposure to environmental tobacco smoke, diabetes, and other cardiovascular risk factors at visit 3.

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 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 ☒ 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.cscce.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)?

450, 760, 782, 860, 861, 907

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*AS#2003.03)

☐ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____)

Note – original ancillary study proposal expansion to include cardiovascular endpoints was approved by the Steering Committee at the meeting on April 14, 2004.

*ancillary studies are listed by number at <http://www.cscce.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 Strachan DP, Cox BD, Erzincinoglu SW, Walters DE, Whichelow MJ. Ventilatory function and winter fresh fruit consumption in a random sample of British adults. Thorax. 1991; 46(9):624-9.
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- 4 Shahar E, Folsom AR, Melnick SL, Tockman MS, Comstock GW, Gennaro V, Higgins MW, Sorlie PD, Ko WJ, Szklo M. Dietary n-3 polyunsaturated fatty acids and smoking-related chronic obstructive pulmonary disease. Atherosclerosis Risk in Communities Study Investigators. N Engl J Med. 1994; 331(4):228-33.

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 - 6 Butler LM, Koh WP, Lee HP, Yu MC, London SJ. Dietary fiber and reduced cough with phlegm: a cohort study in Singapore. *Am J Respir Crit Care Med.* 2004; 170(3):279-87.
 - 7 Smit HA, Grievink L, Tabak C. Dietary influences on chronic obstructive lung disease and asthma: a review of the epidemiological evidence. *Proc Nutr Soc.* 1999; 58(2):309-19.
 - 8 Hu FB, Willett WC. Optimal diets for prevention of coronary heart disease. *JAMA.* 2002 Nov 27;288(20):2569-78.
 - 9 Hu FB, Bronner L, Willett WC, Stampfer MJ, Rexrode KM, Albert CM, Hunter D, Manson JE. Fish and omega-3 fatty acid intake and risk of coronary heart disease in women. *JAMA.* 2002;287(14):1815-21.
 - 10 Fung TT, Stampfer MJ, Manson JE, Rexrode KM, Willett WC, Hu FB. Prospective study of major dietary patterns and stroke risk in women. *Stroke.* 2004; 35(9):2014-9.
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 - 12 Wong TY, Klein R, Sharrett AR, Duncan BB, Couper DJ, Tielsch JM, Klein BE, Hubbard LD. Retinal arteriolar narrowing and risk of coronary heart disease in men and women. The Atherosclerosis Risk in Communities Study. *JAMA.* 2002; 287(9): 1153-9.
 - 13 SanGiovanni JP, Chew EY. The role of omega-3 long-chain polyunsaturated fatty acids in health and disease of the retina. *Prog Retin Eye Res.* 2005, 24(1):87-138.