

ARIC Manuscript Proposal # 1173r

PC Reviewed: 08 / 15 /06

Status: A

Priority: 2

SC Reviewed: 08 / 17 /06

Status: A

Priority: 2

1.a. Full Title: Dietary intake and the development of the metabolic syndrome: The ARIC study.

b. Abbreviated Title (Length 26 characters): Diet and the metabolic syndrome

2. Writing Group:

Writing group members: Pamela L. Lutsey, Lyn M. Steffen, June Stevens, and other interested investigators

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. PLL

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3. Timeline: Literature review – completed

Data analysis – 3 months

Writing the manuscript – 6 months

Coauthor review and revisions – 4 months

4. Rationale:

The aim of this paper is to evaluate the relationship between dietary intake and the development of the metabolic syndrome. Metabolic syndrome is characterized by the presence of any 3 of the following risk factors, according to NHLBI/NCEP/ATP3 guidelines: waist circumference > 102 cm in men and > 88 cm in women; triglycerides \geq 150 mg/dL; HDL-C < 40 mg/dL in men and < 50 mg/dL in women; blood pressure \geq 130/ \geq 85 mmHg; and fasting glucose \geq 110 mg/dL. Individuals with the metabolic syndrome are at increased risk for developing diabetes mellitus (Haffner, 1992) and cardiovascular diseases (Isomaa, 2001), and have increased mortality from cardiovascular disease and all causes (Trevisan, 1998). According to NHANES III data, approximately 24% of Americans, or nearly 47 million U.S. residents, have the metabolic syndrome (Ford, 2002). Given the present obesity epidemic in the U.S. (Mokdad, 2000), the current prevalence of metabolic syndrome is likely higher than that estimated from the 1988-1994 NHANES III data (Ford, 2002).

Whereas aspects of diet have been linked to individual metabolic features of the syndrome, the role of diet in the etiology of the metabolic syndrome is not well understood. Cross-sectionally, dietary intakes rich in whole-grain foods have been linked to a lower prevalence of metabolic syndrome (McKeown, 2004; Esmailzadeh, 2005; Sahyoun, 2006). The evidence is less consistent for refined-grain intake, with some cross-sectional studies reporting a positive association (Esmailzadeh, 2005; Sahyoun, 2006), and others finding no relation (McKeown, 2004). Dairy has been inversely associated with metabolic syndrome both cross-sectionally (Azadbakht, 2005; Mennen, 2000) and prospectively (Pereira, 2002). No association has been found between the metabolic syndrome and intakes of meat and fish (Mennen, 2000). To our knowledge, relationships between the metabolic syndrome and intakes of fruits, vegetables, meat subtypes (i.e. poultry vs. red meat), a Mediterranean diet score, and dietary patterns (i.e. “Western vs. Prudent” using principal components analysis) have not been assessed. The Bogalusa Heart Study did, however, find that young adults who had no components of the metabolic syndrome consumed more fruits, fruit juice, vegetables, alcohol, low fat dairy products, and diet beverages and fewer sweetened beverages than those who had \geq 1 metabolic syndrome component (Yoo, 2004). The number of metabolic syndrome components among these young adults did not vary according to consumption of refined grains, whole grains, meat, and seafood.

Most previous studies relating the metabolic syndrome to diet have focused on a single food group, and all but one (Pereira, 2002) were cross-sectional. The proposed study expands upon previous research in that it will explore prospective relationships between metabolic syndrome and major food groups and dietary patterns.

5. Main Hypothesis/Study Questions:

We hypothesize that dietary intake, as measured through both food groups and dietary patterns, will be associated with development of the metabolic syndrome within the ARIC cohort. Specifically, we expect that consumption of whole grains, low fat dairy, fruits, and vegetables will be inversely associated with the development of metabolic syndrome, while consumption of refined grains and red/processed meats will

be positively related. Additionally, we hypothesize that the prudent dietary pattern, which includes a diet rich in whole grains, fruit and vegetables, fish and some dairy products, will be inversely associated with metabolic syndrome, while the western dietary pattern, which is rich in red and processed meat, will be positively associated with incident metabolic syndrome. We expect the Mediterranean diet score to follow a pattern similar to that observed with the prudent diet pattern. Additionally, we intend to test for sex, race, and BMI interactions in the diet/metabolic syndrome relationship.

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

The analysis will be prospective. ARIC baseline and all follow-up datasets will be used.

Inclusions/Exclusion

Excluded from this analysis will be participants with CVD, diabetes, cancer, and metabolic syndrome at baseline, and those with missing or implausible energy intakes.

Variables

Outcome variable: Incident metabolic syndrome. Metabolic syndrome will be defined according to the NHLBI/NCEP/ATP3 guidelines. Participants identified as having 3 or more of the following risk factors will be identified as having incident metabolic syndrome: waist circumference > 102 cm in men and > 88 cm in women; triglycerides \geq 150 mg/dL; HDL-C < 40 mg/dL in men and < 50 mg/dL in women; blood pressure \geq 130/ \geq 85 mmHg; and fasting glucose \geq 110 mg/dL.

Exposure variables: Food groups as previously defined within the ARIC dataset. Dietary patterns will also be derived via principal components analysis (we anticipate that “Western” and “Prudent” dietary patterns will emerge from this analysis). All of the individual foods, including the associated frequency and portion size information, will be used to develop the dietary patterns. We will also use the food frequency questionnaire to create a Mediterranean diet score, similar to that used by Trichopoulou (2003).

Additional notes:

- To increase the reliability of dietary measures, exposures will be based on cumulative average diet. Specifically, between baseline and exam 3 dietary exposures will be based on diet as measured at the baseline exam. After exam 3, dietary exposures will be based on the mean of baseline diet and exam 3 diet.
- Energy intake will be controlled for using nutrient-residual method (Willett, 1986).

Potential confounding factors: Age, sex, race, center, education, income, energy intake (kcal/day), smoking status (former, current, never), pack-years (continuous), vitamin supplements (yes/no), physical activity (Baecke score).

Data Analysis Summary

1. Distributions of dietary variables and potential confounding factors will be reported. Characteristics of participants will also be stratified by quintile of food group and dietary pattern intake, after adjustment for sex, race, center, and baseline energy intake.
2. In describing metabolic syndrome, we intend to determine the prevalence of components that contribute to metabolic syndrome incidence. Mean levels of individual metabolic syndrome components and percent of participants meeting metabolic syndrome definitions will also be reported.
3. The primary analysis will use Cox regression to evaluate the relationship between incident metabolic syndrome and diet. Model 1 will adjust for age, sex, race, center, education, income, and energy intake. Model 2 will adjust for Model 1 covariates and non-dietary lifestyle factors, such as smoking and physical activity. Model 3 will further adjust for other food groups or food patterns, as appropriate. We will also explore interactions of the diet/metabolic syndrome relationship by sex, race, and BMI.
4. To assess whether the relations between diet and incident metabolic syndrome are driven by only a few of the metabolic syndrome components, we will explore the relations between dietary intake and incidence of individual components of the metabolic syndrome. To maintain consistency, we will use the same statistical models as in the primary analysis.

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.csc.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)?

1006 Full Title: Associations of dairy products, dietary calcium and calcium supplementation with the incidence of metabolic syndrome and its components. 05/07/04

June Stevens is also an author on manuscript #1006; she does not feel the present proposal would overlap with #1006.

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* _____)**

☐ **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.csc.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.