ARIC Manuscript Proposal # 3306

PC Reviewed: 12/11/18          Status: _____          Priority: 2
SC Reviewed: _________        Status: _____        Priority: _____

1.a. Full Title: Adherence to commonly recommended heart healthy eating patterns and risk of diabetes in the Atherosclerosis Risk in Communities Study

b. Abbreviated Title (Length 26 characters): Heart healthy diets & diabetes

2. Writing Group:
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   Others welcome

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

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3. Timeline: Statistical analysis: Jan 2019-Feb 2019
   Manuscript preparation and revision: March 2019-May 2019
   Manuscript submission: June 2019
4. Rationale:

Adhering to a Mediterranean-style or a Dietary Approaches to Stop Hypertension-style (DASH Pattern) eating pattern is commonly recommended to reduce chronic disease risk in the U.S. Higher adherence to a Mediterranean Pattern is associated with reduced risk of cardiovascular events and higher adherence to a DASH Pattern can reduce blood pressure. Therefore, the American Diabetes Association recommends that individuals with diabetes should adhere to a Mediterranean or DASH Pattern to prevent cardiovascular complications. However, there is limited evidence and dietary guidance regarding whether these heart healthy eating patterns can prevent diabetes.

Moderate evidence indicates that adherence to heart healthy eating patterns, such as a Mediterranean or DASH Pattern, is associated with reduced diabetes risk, according to the 2015 Dietary Guidelines for Americans and supporting scientific report. The scientific report highlights that higher adherence to a Mediterranean Pattern was associated with up to a 35% reduced risk of developing diabetes in large Mediterranean cohorts (SUN in Spain, n=13,380 and EPIC in Greece, n=22,295) but showed no reduced risk in a smaller U.S. cohort (MESA, n=5,390). Further evidence supports this protective association in other European countries. However, it remains unclear if reductions in diabetes risk from adhering to a Mediterranean Pattern are translatable to U.S. populations that lack other aspects of a Mediterranean or European lifestyle. Further, the scientific report presents one relatively small (IRAS in U.S., n=820) cohort which reported that higher adherence to a DASH Pattern reduced the odds of developing diabetes in a Caucasian subgroup but not the total population or minority subgroups. Evidence from other U.S. cohorts (NHS, n=4,413 and HPFS, n=41,615) suggest up to a 40% reduction in diabetes incidence from higher adherence to a Mediterranean or DASH Pattern in predominantly higher socioeconomic Caucasian health professionals. Therefore, there is a paucity of evidence on associations between heart healthy eating patterns and diabetes in large, diverse, nationally representative U.S. populations.

The purpose of this proposal is to address current limitations in assessing associations between commonly recommended heart healthy eating patterns (Mediterranean and DASH Patterns) and incident diabetes for U.S. individuals. In addition to a lack of a representative U.S. cohort, most U.S. studies mentioned previously adjusting for BMI as a confounder, but European stratified analyses suggest an attenuated relationship in individuals who are obese. Further, none of these studies mentioned above consider carbohydrate intake type or amount as well as other diet-related diabetes risk factors that may contribute to inconsistent associations seen in the current literature. The ARIC cohort provides a large, community-based population of black and white adults with relevant lifestyle-related information to assess potential interactions between heart healthy eating patterns and lifestyle-related factors such as BMI and macronutrient intake. Therefore, this proposed manuscript will 1) assess appropriateness of Mediterranean and DASH Pattern scoring systems using ARIC data, 2) assess associations between Mediterranean and DASH Pattern adherence and incident diabetes, and 3) assess how certain diet-related factors may influence potential associations between Mediterranean and DASH Pattern adherence and incident diabetes. Results from this proposed manuscript may be helpful to inform future dietary guidance regarding type 2 diabetes prevention for U.S. populations.
5. **Main Hypothesis/Study Questions:**

Aim 1: To describe methodological differences between commonly used rank-based Mediterranean and DASH Pattern scoring systems and threshold-based scoring systems.

Hypothesis 1: The rank-based indices will differ from the threshold-based indices due to underestimation of absolute intake using the FFQ and incomplete collection of relevant dietary components.

Aim 2: To assess whether higher adherence to a Mediterranean or DASH Pattern is associated with lower risk of incident diabetes during follow-up compared to lower adherence to a Mediterranean or DASH Pattern.

Hypothesis 2: Higher adherence to Mediterranean or DASH Patterns will be modestly associated with a lower diabetes risk compared to lower adherence to a Mediterranean or DASH Pattern.

Aim 3: To assess potential effect modifiers of associations between Mediterranean or DASH Pattern adherence and incident diabetes risk including BMI/body weight and diet-related risk factors suspected to increase diabetes risk.

Hypothesis 3: Associations between Mediterranean or DASH Pattern adherence and incident diabetes will differ by BMI/body weight categories but will otherwise be unaffected by other diet-related factors.

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 proposal is a prospective analysis of the ARIC cohort using dietary intake data averaged from visit 1 (1987-1989) and visit 3 (1993-1995) to assess how adherence to a Mediterranean or DASH Pattern relate to incident diabetes during the available follow-up period.

**Inclusion/exclusion criteria:** Baseline prevalent cases of diabetes, cardiovascular disease, and cancer will be excluded from all analyses. Participants with implausible energy intakes (<600 or >4200 kcal for men and <500 or >3600 for women), have ≥10 missing food frequency questionnaire items, or missing covariates will be also excluded from all analyses.

**Exposures:** Dietary intake data was ascertained at visit 1 (1987-1989) and visit 3 (1993-1995) using an interview-administered 66-item semi-quantitative food frequency questionnaire to ascertain more details pertaining to fish intake and cooking fat. Participants reported average intake frequency and portion size of various food items during the previous year. In this proposal, we will calculate various eating pattern scores to the extent possible using self-reported dietary intake data. Table 1 describes the Mediterranean eating pattern indices and Table 2 describes the DASH eating pattern indices. Aim/hypothesis #1 will assess the appropriateness of these indices for the ARIC study population considering the food frequency questionnaires items assessed at visits 1 and 3.
**Covariates:** We will adjust analyses for age, sex, race, testing center, family history of diabetes, and level of education as well as total energy intake. The following lifestyle-related factors that are recognized or suspected to influence diabetes risk will be assessed as possible effect modifiers of the association of dietary patterns and diabetes risk: dietary risk factors recognized by the American Diabetes Association\(^3\) including refined carbohydrate intake,\(^3,21\) sugar sweetened beverage intake,\(^3,21\) red and processed meat intake,\(^3,21\) and macronutrient (carbohydrate) distribution,\(^3,21\) as well as BMI and reported body mass changes.\(^19,20\)

**Outcome:** Incident diabetes cases will be ascertained from visit 1 (1987-1989) to visit 6 (2015-2018) as defined by the following criteria: 1) self-reported physician diagnosis, 2) self-reported use of diabetes-related medication during previous 2 weeks, 3) fasting blood glucose concentration ≥126 mg/dL, or 4) non-fasting blood glucose concentration ≥200 mg/dL. These criteria were validated previously in the ARIC cohort and this definition is highly specific for the classification of newly diagnosed diabetes cases.\(^22\)

**Table 1: Mediterranean Pattern scoring systems**

<table>
<thead>
<tr>
<th>Category</th>
<th>Alternate Mediterranean Diet Score(^{23})</th>
<th>Mediterranean Diet Assessment (MEDAS)(^{24})</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Description</strong></td>
<td><strong>Description</strong></td>
</tr>
<tr>
<td></td>
<td>1 point if…</td>
<td>1 point if…</td>
</tr>
<tr>
<td>Vegetables</td>
<td>Total vegetables above median</td>
<td>Total vegetables ≥3 cups/d</td>
</tr>
<tr>
<td>Fruits</td>
<td>Total fruit above median</td>
<td>Total fruit ≥3 servs/d</td>
</tr>
<tr>
<td>Grains</td>
<td>Whole grain above median</td>
<td>Commercial sweets/pastries ≤3 /wk</td>
</tr>
<tr>
<td>Nuts</td>
<td>Nuts above median</td>
<td>Nuts, not including nut butters ≥3/4 cup or more/wk</td>
</tr>
<tr>
<td>Legumes</td>
<td>Legumes above median</td>
<td>Cooked legumes ≥3 or more cups/wk</td>
</tr>
<tr>
<td>Meats</td>
<td>Red and processed meat below median</td>
<td>Red meat and meat products ≤150g per/d preference for white</td>
</tr>
<tr>
<td>Fish</td>
<td>Fish above median</td>
<td>Fish/shellfish ≥3 servs/wk</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Alcohol, general above median</td>
<td>Wine ≥7 glasses/wk</td>
</tr>
<tr>
<td>Fat</td>
<td>MUFA:SFA above median</td>
<td>Olive oil* main fat used ≥1/4 cup/d</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Olive oil* White meat: red meat ≤1 tbsp/d</td>
</tr>
<tr>
<td>Other</td>
<td>n/a</td>
<td>Sofrito* Carbonated/sweetened beverages ≥2/wk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>9 points</td>
<td>14 points</td>
</tr>
</tbody>
</table>

*indicates items that are not assessed in the ARIC food frequency questionnaire.

**Table 2: DASH Pattern scoring systems**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th><strong>Fung et al.(^{25})</strong></th>
<th><strong>Dixon et al.(^{26})</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Description</strong></td>
<td>5 points if…</td>
<td>Description</td>
</tr>
<tr>
<td>Vegetables</td>
<td>Vegetables</td>
<td>highest quintile</td>
<td>Vegetables</td>
</tr>
<tr>
<td>Fruits</td>
<td>Fruits</td>
<td>highest quintile</td>
<td>Fruits</td>
</tr>
<tr>
<td>Grains</td>
<td>Whole grains</td>
<td>highest quintile</td>
<td>Whole grains</td>
</tr>
</tbody>
</table>
Data analysis:

Aim 1:
Mediterranean Pattern: Dietary data obtained from the ARIC food frequency questionnaire will be scored using the aMed scoring system. The aMed assigns 1 adherence point for reported consumption above or below the cohort’s calculated median intake of desirable or undesirable food groups, respectively, as listed in Table 1. The calculated median intake cut-offs derived from our ARIC cohort sample will then be qualitatively compared to cut-offs for the MEDAS scoring system. This will allow us to compare a Mediterranean Pattern identified in the ARIC cohort to a “true” Mediterranean Pattern as characterized in a trial of the Mediterranean diet, i.e. the PREDIMED trial.

DASH Pattern: Similar to above, dietary data obtained from the ARIC food frequency questionnaire will be used to characterize DASH Pattern adherence using the Fung et al. DASH Pattern scoring system. Fung et al. assign points for reported consumption based on quintiles of intake for desirable or undesirable food groups, as listed in Table 2. The calculated quintile intakes derived from our ARIC cohort sample will then be qualitatively compared to cutoffs of Dixon et al. The Dixon et al. scoring system is based on the 2010 Dietary Guidelines for Americans summary of the DASH Pattern which were derived from the original DASH Pattern trials. This will allow us to compare a DASH Pattern identified in the ARIC cohort to how the DASH Pattern was originally described.

Aim 2:
We will examine differences in demographic and behavioral risk factors across quintiles of eating pattern scores to assess possible confounders. Hazard ratios and 95% confidence intervals for incident diabetes, using Cox regression models, will estimate associations with one point increases in eating pattern scores, as well as according to quintiles. Model 1 will be adjusted for energy intake and Model 2 will be adjusted additionally for age, sex, race, testing center, family history of diabetes, and level of education. We will use restricted cubic splines to model dietary pattern scores to more flexibly illustrate the association of eating pattern scores with incident diabetes. If relationships appear non-linear, we will report the findings by quintiles and splines. Calendar time will be the time metric and will start from visit 1.
Aim 3:

If hypothesized associations between higher vs lower Mediterranean or DASH Pattern adherence and diabetes risk are supported by the data, we will explore potential effect modifiers to test the robustness of observed associations. The following diet-related factors that are recognized or suspected to influence diabetes risk will be assessed as possible effect modifiers via stratified comparisons and tests for interaction: dietary risk factors recognized by the American Diabetes Association including refined carbohydrate intake, sugar sweetened beverage intake, red and processed meat intake, and macronutrient distributions (carbohydrate), as well as BMI and reported body mass changes.

Methodological limitations: Use of self-reported food frequency questionnaires and diabetes diagnoses for the majority of follow-up are two limitations of this proposed manuscript. Self-reported dietary data is often underestimated by up to 38% in food frequency questionnaires and limits the granularity that is desired to assess diet and disease associations. While inferences about absolute intake quantities are limited, it is still feasible to make inferences about overall food intake patterns by ranking participants within the study population according to intake. Clinical diabetes-related outcomes were not measured at each visit, such as HbA1c, which limits inferences to mainly self-reported diagnoses. Low power and possible residual confounding from categorizing continuous variables are also potential limitations for proposed stratified analyses.

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 ICTDER 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/mantrack/maintain/search/dtSearch.html

____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)?
Five related manuscript proposals are presented below as proposal #: title; first author, ARIC investigator. These previous proposals did not assess associations between adherence to a Mediterranean-style or DASH eating pattern at baseline and incident type 2 diabetes cases during follow-up.

a. 2990: Six-Year Change in Diet Quality and Risk of Incident Diabetes: The Atherosclerosis Risk in Communities (ARIC) Study; Zhe Xu, Casey Rebholz
b. 3155: Diet quality scores and incident kidney disease in the ARIC study; Emily Hu, Casey Rebholz
c. 3239: Dietary patterns and risk of incident dementia and cognitive decline: Results from the ARIC study; Emily Hu, Casey Rebholz
d. 2474: Associations between diet patterns and diabetic retinopathy in a biracial cohort; Michelle Sahli, Ronald Klein
e. 1173r: Dietary intake and the development of the metabolic syndrome: The ARIC study; Pamela Lutsey, Lyn Steffen

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 https://www2.cscc.unc.edu/aric/approved-ancillary-studies

12a. 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.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is your responsibility to upload manuscripts to PubMed Central whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.
References:


