ARIC Manuscript Proposal Form

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Publication Committee Review Date: **09/17/24**
ARIC Manuscript Proposal Number: **# 4531**

1.a. Full Title: Planetary health diet index and incident cardiovascular disease, cardiovascular disease mortality, and all-cause mortality in the Atherosclerosis Risk in Communities Study

b. Abbreviated Title (Length 45 characters): Planetary health diet index, CVD, and death

2. Writing Group [please provide a middle initial if available; EX: Adam L Williams]:
Writing group members: Jiaqi Yang, Valerie K. Sullivan, Casey M. Rebholz, others welcome

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __JY___ **[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 (The ARIC author should be involved enough in ARIC to be able to point the lead author to appropriate ancillary study PIs and to be able to search ARIC manuscript proposals if the lead author doesn't have the access needed to do such a search).

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3. Timeline: After the manuscript proposal is approved, we will begin the data analysis. We anticipate that the first draft of the manuscript will be completed approximately within one year after proposal approval.

4. Rationale: Diet, climate change, and human health are deeply interconnected.[1] Diets higher in refined sugars, saturated fats, meats, and other processed foods are increasingly replacing traditional diets.[1] This global nutrition transition is contributing to rising obesity rates among both children and adults.[2,3] Moreover, this shift in dietary transitions is driving an increase in agricultural greenhouse gas emissions, as well as global land degradation and water pollution from intensive food production.[4] With the global population expected to reach nearly 10 billion by 2050, having sustainable access to a healthy diet is a major challenge.[5] In 2019, the EAT-*Lancet* Commission proposed an environmentally sustainable diet.[5] Along with reducing food waste and improving agricultural practices, adopting this diet could sustainably feed the growing population and reduce greenhouse gas emissions by 50% by 2050, potentially preventing 11 million premature deaths annually.[5,6]

In response to the EAT-*Lancet* Commission reports and growing global concerns about climate change, a novel dietary measure, the Planetary Health Diet Index (PHDI), was recently developed in three large, nationally representative U.S. cohorts.[5-7] Unlike other planetary health diet scores designed to quantify adherence to the EAT-*Lancet* reference diet, the PHDI captures a broad range of possible scores, having high discrimination in adherence levels and strong power to detect associations. Higher adherence to the PHDI has been associated with a lower risk of total and cause-specific mortality.[6] Yet, there is no evidence on the associations between the PHDI and cardiometabolic outcomes.

There are several key differences between the EAT-*Lancet* global reference diet and U.S. Dietary Guidelines for Americans (DGA). The EAT-*Lancet* diet emphasizes high-quality plant-based foods with low to moderate amounts of animal-sourced products like meat and dairy, and it restricts added sugar and saturated fat.[5] In contrast, the DGA recommends similar food groups but with less stringent limits on animal-sourced and refined products.[8] Given that the typical American diet is characterized by a high intake of animal-based foods and a low intake of plant-based foods, adapting the novel measure of PHDI, which assesses the health and sustainability of diets in the U.S., to the Atherosclerosis Risk in Communities (ARIC) study, a large U.S. community-based cohort, is necessary for understanding the potential health impact of the EAT-*Lancet* diet in the American context.

The present study aims to examine the associations between PHDI and incident cardiovascular disease (CVD), as well as the sub-components of this composite outcome [coronary heart disease (CHD), stroke, and heart failure], CVD mortality, and all-cause mortality in the ARIC study. We will adapt the novel PHDI to the food frequency questionnaire (FFQ) used in the ARIC study and provide key insights into whether an environmentally sustainable diet is associated with a lower risk of CVD outcomes and mortality.

5. Main Hypothesis/Study Aims:

Aim #1: We hypothesize that higher adherence to the PHDI will be associated with a lower risk of CVD (a composite outcome).

Aim #2: We hypothesize that higher adherence to the PHDI will be associated with a lower risk of CVD subtypes, including CHD, stroke, and heart failure.

Aim #3: We hypothesize that higher adherence to the PHDI will be associated with a lower risk of CVD mortality and all-cause mortality.

6. Design and analysis - please address the following aspects:

a) **inclusion/exclusion**
b) **study design**
c) **outcome and other variables of interest with specific reference to the time of their collection**
d) **summary of data analysis**
e) **Any anticipated methodologic limitations or challenges if present**

Study Design: For all aims, this study will use a prospective design. The baseline will be visit 1 (1987-1989), and the prospective analyses will conducted through the most recent follow-up data that are available. Dietary data from visit 1 and visit 3 (1993-1995) will be averaged for dietary exposure assessment. Longitudinal analyses using the latest follow-up data that are available will be conducted to estimate risk of CVD (a composite outcome), CVD subtypes (CHD, stroke, and heart failure), CVD mortality, and all-cause mortality.

Eligibility Criteria: Participants must have completed FFQ at visit 1 and been followed up for CVD outcomes and all-cause mortality. Participants with unrealistic total caloric intake (>4200 or <600 kcal/day for male; >3600 or <500 kcal/day for female), missing 10+ items on FFQ at visit 1, missing covariates, prevalent coronary heart disease, stroke, or heart failure at visit 1, missing follow-up data, and missing food components of PHDI will be excluded.

Exposure: The exposure will be modified PHDI.

Modified PHDI: Dietary data were assessed by trained interviewers using a semi-quantitative 66-item FFQ at visits 1 and 3. The FFQ, adapted from the Willett questionnaire, has been validated within the ARIC study.[9] Participants self-reported the frequency of consumption for each food item over the previous year, using a scale ranging from "almost never" to "more than 6 times per day." We will modify an existing scoring system, the PHDI, recently developed in a large U.S. population in response to the EAT-*Lancet* Commission's report, i.e., soy foods will not be included as a component since it was not assessed in the ARIC study. To better reflect usual intake and reduce within-individual variation, we will calculate the average PHDI using dietary data from visits 1 and 3.[10,11] We will average the score only for individuals who did not experience an event, were not censored between visits 1 and 3, and had complete food component data at visit 3. This average PHDI will then be used to assess associations with CVD events and mortality, with participants divided into quintiles based on their adherence to the PHDI, as well as analyzed continuously.

- Ranges from 0 (the lowest) to 140 (the highest)
- 7 emphasized components: whole grain, vegetable, whole fruit, fish and shellfish, nuts, non-soy legumes, added fat-unsaturated
- 7 limited components: chicken and other poultry, eggs, tubers, dairy foods, red/processed meats, added fat-saturated, added sugar and sugar from fruit juice
- Each of the components will be scored from 0 to 10, according to Table 1.

Table 1. PHDI scoring system in the ARIC study

Components		Food items and nutrients	Criteria for scoring	
			Min score (0) in g/d	Max score (10) in g/d
Emphasized components	Whole grain	Whole grain cold breakfast cereal; cooked cereals such as oatmeal, grits, cream of wheat; dark or whole grain bread	0	≥75 g/d for females ≥90 g/d for males
	Vegetable	Carrots; corn; spinach, collards or other green; broccoli; string beans; cabbage; cauliflower; brussels sprouts; peas or lima beans; dark yellow, winter, squash such as acorn, butternut; sweet potatoes; tomatoes	0	≥300
	Whole fruit	Apples or pears; oranges; peaches, apricots or plums, canned or dried; bananas, other fruits, canned, including fruit cocktail	0	≥200
	Fish and shellfish	Canned tuna fish; dark meat fish, such as salmon, mackerel, swordfish, sardines, bluefish; other fish, such as cod, perch, catfish; shrimp, lobster, scallops as main dish	0	≥28
	Nuts	Peanut butter, nuts	0	≥50
	Non-soy legume	Beans or lentils, dried cooked, or canned, such as pinto, blackeye, baked beans	0	100
	Added fat - unsaturated	Monounsaturated and polyunsaturated fat	≤3.5% of TEI	≥21% of TEI
Limited components	Dairy food	Skim milk or low-fat milk; whole milk; yogurt; cottage or ricotta cheese; other cheeses, plain or as part of a dish	≥1000	≤250
	Red/processed meat	Hamburgers; hot dogs; processed meats: sausage, salami, bologna, etc.; bacon; beef, pork or lamb as a sandwich or mixed dish, stew, casserole, lasagna, or in spaghetti; liver	≥100	≤14
	Tuber	Potato chips or corn chips, French fried potatoes, potatoes, mashed or baked	≥200	≤50
	Chicken and other poultry	Chicken or turkey without skin, chicken or turkey, with skin	≥100	≤29
	Egg	Eggs	≥120	≤13
	Added fat - saturated	Saturated fat	≥10% of TEI	0%
	Added sugar and sugar from fruit juice	Ice cream; orange or grapefruit juice; chocolate bars or pieces, such as Hershey's plain M & M's, snickers, reeses; candy without chocolate; pie, homemade from scratch; pie, ready-made or from a mix; donut; Danish pastry, sweet roll, coffee cake, croissant; cake or brownie;	≥25% of TEI	≤5% of TEI

		cookies; low calorie soft drinks, such as any diet Coke, diet Pepsi, diet 7-Up; fruit-flavored punch or non-carbonated beverages, such as lemonade, Kool-Aid or Hawaiian punch; not diet; teaspoons of sugar, including coffee, tea, cereal, etc.		

Abbreviations: TEI, total energy intake; g, grams; d, day

Incident cardiovascular disease: Incident CVD will be defined as a combination of fatal or nonfatal CHD (hospitalized myocardial infarction or fatal CHD), adjudicated definite or probable stroke, and heart failure (hospitalization or death, identified using International Classification of Diseases (ICD)-9 code 428 or ICD-10 code I50).[12] Incident CVD was assessed through annual telephone interviews, active surveillance of local hospital discharge records, death certificates, and linkage to the National Death Index. A physician review panel used this information to adjudicate CVD outcomes.

Cardiovascular disease mortality and all-cause mortality: Cardiovascular disease mortality was defined as deaths with ICD-9 codes 390 to 459 or ICD-10 codes I00 to I99, and all-cause mortality was defined as deaths from any cause.[13]

Other Variables of Interest: Covariates we would like to consider include age, sex, race, study center, area deprivation index, body mass index, total energy intake, smoking status, physical activity, alcohol consumption, lipid-lowering medication use, estimated glomerular filtration rate (eGFR), hypertension status, and diabetes status.

Statistical Analysis: Baseline and nutritional characteristics of the analytic sample will be analyzed across quintiles of the PHDI. Cox proportional hazard models will be used to estimate hazard ratios and 95% confident intervals for incident CVD, CVD subtypes, CVD mortality, and all-cause mortality in relation to adherence to the PHDI, while adjusting for key covariates.

- **Model 1** will adjust for demographics, including age, sex, race, study center, area deprivation index, and total energy intake.
- **Model 2** will further adjust for health behaviors, including smoking status, physical activity, and alcohol consumption.
- **Model 3** will further adjust for potential mediators, including body mass index, lipid-lowering medication use, eGFR, hypertension, and diabetes status.

For the primary analysis, we will model the exposure as a categorical variable and use the lowest quintile of PHDI as the reference group.

As secondary analyses, the PHDI will be modeled as a continuous variable (per 10-point higher). We also plan to examine whether any of the 14 components of the PHDI (food intake or score) are independently associated with CVD outcomes and all-cause mortality.

As subgroup analyses, we will identify potential effect modifiers, such as race (white or non-white), sex (female or male), and area deprivation index (below or above median), and test for interaction terms using likelihood ratio tests. If effect modification is present, stratified results will be presented.

Anticipated Methodologic Limitations or Challenges: One of the anticipated limitations is that self-reported dietary intake is subject to measurement error. Yet, we plan to incorporate dietary data from visits 1 and 3 FFQs to improve the estimation of typical consumption patterns and adjust for total energy intake to reduce bias.[11] In addition, the nutrient characteristics of the PHDI and its associations with cardiovascular events may differ from current consumption patterns, as the dietary data were collected three decades ago. Moreover, while we will adjust for sociodemographic factors and health behaviors, we cannot entirely rule out the possibility of residual confounding due to unmeasured variables. Lastly, the observational design of the current study limits our ability to establish causality between the PHDI and CVD outcomes as well as mortality.

f) Will the author need Limited data to complete the proposed manuscript? ☐ Yes, Limited data is needed (Provide a brief (2-3 sentences) justification for requesting PHI data) . ☒ No, De-identified data will be sufficient.

*Please note, Limited dataset access is strict and rarely provided. Limited data includes identifiable information such as dates (birthdays, visit dates, etc.). CMS, Genomic, Geocoded, Proteomics/Somalogic, and other -omic data all fall under the limited data category. De-identified data does not include dates. All dates are date adjusted to "Days since Visit 1".

7.a. Will the data be used for non-ARIC analysis or by a for-profit organization in this manuscript? (Non-ARIC analysis means that the authors are not regarded as ARIC investigators and the "ARIC author" is essentially just a facilitator rather than an integral part of the writing group.) ☐ Yes ☒ No

b. If Yes, is the author aware that the current derived consent file ICTDER05 must be used to exclude persons with a value RES_OTH and/or RES_DNA = "ARIC only" and/or "Not for Profit" ? ☐ Yes ☐ No
(The file ICTDER is distributed to ARIC PIs annually, 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 current derived consent file ICTDER05 must be used to exclude those with value RES_DNA = "No use/storage DNA"? ☐ Yes ☐ No

9. The lead author or the "sponsoring" ARIC 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 website at: https://aric.cscc.unc.edu/aric9/proposalsearch [ARIC Website□Publications□Proposal Search]

☒ 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)?

MS#4481 Association Between the EAT-Lancet Planetary Health Diet and Incidence of Chronic Kidney Disease in the Atherosclerosis Risk in Communities (ARIC) Study (lead author: Dawit Girma)

The manuscript based on this proposal is currently in progress. This prior proposal focused on chronic kidney disease, whereas our study will focus on CVD outcomes and all-cause mortality.

MS#3098A Plant-Based Diets Are Associated With a Lower Risk of Incident Cardiovascular Disease, Cardiovascular Disease Mortality, and All-Cause Mortality in a General Population of Middle-Aged Adults (lead author: Hyunju Kim)

The manuscript based on this proposal has been published [Kim H, Caulfield LE, Garcia-Larsen V, Steffen LM, Coresh J, Rebholz CM. Plant-Based Diets Are Associated With a Lower Risk of Incident Cardiovascular Disease, Cardiovascular Disease Mortality, and All-Cause Mortality in a General Population of Middle-Aged Adults. *J Am Heart Assoc*. 2019;8(16):e012865.] This prior manuscript focused on plant-based diets, whereas our study will focus on PHDI, an environmentally sustainable diet.

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or does it use current [or ongoing] ancillary study data (this includes ACHIEVE)? ☐ **Yes** ☒ **No → Skip to question 12**

11.b. If yes to 11.a., is the proposal

☐ **A. primarily the result of an ancillary study**

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

11.c. If yes to 11.a., list number_

*ancillary studies are listed by number
https://aric.cscc.unc.edu/aric9/researchers/ancillary_studies/approved_ancillary_studies [ARIC Website□Ancillary Studies□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 https://aric.cscc.unc.edu/aric9/publications/policies_forms_and_guidelines [ARIC Website□Publications□Publication Policies, Forms, and Guidelines].

http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

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