1.a. **Full Title:** Six-Year Change in Diet Quality and Risk of Incident Diabetes: The Atherosclerosis Risk in Communities (ARIC) Study

b. **Abbreviated Title (Length 26 characters):** Diet Quality Change and Diabetes

2. **Writing Group:**
   Writing group members: Zhe Xu, BM, ScM
   Menglu Liang, ScM, MPH
   Lyn M. Steffen PhD, MPH, RD
   Elizabeth Selvin, PhD, MPH
   Casey M. Rebholz, PhD, MS, MPH

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

**First author:** Zhe Xu  
Address: Johns Hopkins Bloomberg School of Public Health  
2024 E. Monument Street  
Baltimore, MD 21287

Phone: 443-850-6808  
Fax: N/A  
E-mail: xuzhe922@gmail.com

**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).  
Name: Casey M. Rebholz  
Address: 2024 E. Monument Street, Suite 2-600  
Baltimore, MD 21287

Phone: 410-502-2049  
Fax: N/A  
E-mail: crebholl@jhu.edu

3. **Timeline:**

Statistical Analysis: May 2017 – August 2017  
Manuscript Preparation and Revision: September 2017 – December 2017  
Manuscript Submission: January 2018
4. Rationale:

Trends of prevalence and incidence of diabetes

Type 2 diabetes mellitus is one of the fastest growing diseases. Over the past 2 decades, the prevalence of diabetes has increased substantially and 21 million adults are affected in the United States. The prevalence of total diabetes (defined as diagnosed diabetes or calibrated HbA1c levels $\geq 6.5\%$) increased over the 20-year period from 6.2\% in 1988 – 1994, 8.8\% in 1999 – 2004, and 9.9\% in 2005 – 2010. The most recent Centers for Disease Control and Prevention report shows that from 1980 to 2014, the age-adjusted incidence of diagnosed diabetes mellitus nearly doubled from 3.5 to 6.6 per 1,000 persons.

Dietary risks for type 2 diabetes

Dietary risks account for 26\% of deaths and 14\% of disability-adjusted life years in the United States. Unhealthful diet is also an important modifiable risk factor for many major chronic diseases, including type 2 diabetes mellitus. Previous studies have demonstrated that a healthful diet pattern is associated with type 2 diabetes prevention. Improvement in diet represents a potential intervention for disease reduction either directly or indirectly through reducing intermediate risk factors, such as blood pressure, fasting glucose, and body weight.

Change in diet quality

Despite the well-established association between diet and chronic disease risk, it is inherently difficult to change health behaviors including dietary intake at the individual level and the population level. An evaluation of trends in U.S. diet revealed that diet quality has improved modestly and steadily from 1999 to 2010; however, the overall dietary quality remains far from optimal. In particular, the consumption fruits, vegetables, whole grains, nuts and legumes, and long-chain omega-3 fatty acids remains low.

There is limited evidence on the association between diet change and risk of diabetes with long-term follow-up in large prospective cohorts of the general population in the U.S. The majority of previous studies focused only one assessment of dietary intake. Repeated assessments of dietary intake could be useful to describe change in diet quality in the U.S. and its relation to diabetes risk. This information could be used to inform intervention strategies for diabetes prevention.

The Healthy Eating Index (HEI)-2015

As a measure of diet quality, the Healthy Eating Index (HEI)-2015 is the latest iteration of the index and was designed to assess adherence with the 2015-2020 Dietary Guidelines for Americans (DGAs). Compared to HEI-2010, the HEI-2015 retained most of the previous existing components; however, the “empty calories” component has been replaced by two separate components, “added sugars” and “saturated fats”, to better align with the newly quantified added sugars recommendation. Previous prospective studies had shown significant association between HEI-2010 and all-cause and cardiovascular disease, but not significant relation between adherence to HEI-2010 and risk of type 2 diabetes. The association between HEI-2015 and the risk of diabetes has not been previously studied.

The Alternative Healthy Eating Index (AHEI)-2010
The Alternative Healthy Eating Index (AHEI) was created in 2002 as an alternative to the Health Eating Index (HEI) and was based on foods and nutrients predictive of chronic disease risk.\(^7\) Updated from the original AHEI, the AHEI-2010 was then created based on a comprehensive review of the relevant literature to identify foods and nutrients that have been consistently associated with a lower risk of chronic disease in clinical and epidemiologic studies.\(^7\) AHEI-2010 is mainly used to represent adherence to healthy eating for chronic disease prevention.\(^7\) Previous studies have shown that the AHEI-2010 was inversely associated with risk of major chronic diseases, and was more strongly associated with risk of diabetes in both women and men.\(^7\) Therefore, using both the HEI-2015 and AHEI-2010 can provide information on change of diet quality and the association between diet quality changes and the risk of diabetes. These study findings may inform the implementation of public health policies on healthful diets for diabetes prevention.

5. **Main Hypothesis/Study Questions:**


Aim 2: To assess the association between six-year change in diet quality and subsequent risk for the development of type 2 diabetes.

Hypothesis: Decrease in dietary quality score is associated with an increased risk for incidence of diabetes.

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**

Prospective analysis of the ARIC study, using study visit 1 (1987-1989) to study visit 3 (1993-1995) to assess change in diet quality, and using data collected during subsequent follow-up to assess the incidence of diabetes.

**Inclusion/Exclusion**

Participants with prevalent diabetes, cardiovascular disease, or cancer at baseline will be excluded. Further, participants who had 10 or more missing food items on the food frequency questionnaire at either time point will be excluded. Low caloric intake (<600 kcal for men and <500 kcal for women) and implausible high caloric intake (>4200 kcal for men and >3600 kcal for women). Participants with missing data on covariates will be excluded.

**Exposure**

Dietary intake was assessed at ARIC study visit 1 and study visit 3. Usual dietary intake was assessed with a semi-quantitative 66-item food frequency questionnaire (FFQ), modified from the Willett questionnaire.\(^11-13\) Participants reported the average frequency of each food item they consumed of a particular portion size in the preceding year. Nutrient intake was calculated by multiplying self-reported frequency of consumption and portion size by the nutritional content of
each food item from US Department of Agriculture data sources. The HEI-2015 and AHEI-2010 will both be used to represent dietary quality and adherence to healthy eating for chronic disease prevention. After revisions, the HEI-2015 contains 13 components that sum to a total maximum score of 100 points. The 13 components are: total fruits, whole fruits, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, fatty acids, refined grains, sodium, added sugars, and saturated fats. Each of the components is scored on a density basis out of 1,000 calories, with the exception of fatty acids, which is the ratio of unsaturated to saturated fatty acids. In the AHEI-2010, there are 11 food components, including higher intake of vegetables, fruits, whole grains, nuts and legumes, long-chain n-3 fatty acids, and polyunsaturated fatty acids (excluding long-chain n-3 fatty acids); lower intake of red/processed meat, sugar-sweetened beverages and fruit juice, trans fat, and sodium; and moderate alcohol consumption. Each component is scored from 0 (worst) to 10 (best), and the total AHEI-2010 score ranges from 0 (nonadherence) to 110 (perfect adherence).

We will assess change in diet quality using HEI-2015 and AHEI-2010 scores from study visit 1 to visit 3. Change in scores will be classified into quintiles (moderate to large decrease, small to moderate decrease, stable, small to moderate increase, moderate to large increase).

Outcome

Incident cases of diabetes will be ascertained from visit 3 (1993-1995) to visit 5 (2011-2013). Diabetes will be defined as any of the following: self-reported physician’s diagnosis of diabetes; reported the use of diabetes medication in the past 2 weeks; fasting (≥8 hours) glucose measurement of ≥126 mg/dL; or nonfasting glucose measurement of ≥200 mg/dL. This definition of incident diabetes in the ARIC Study has been shown to be valid and highly specific for the classification of newly diagnosed cases.

Covariates

The main covariates include: demographic characteristics (age, sex, and race-center), socioeconomic status (education level), body mass index (BMI), health behaviors (physical activity and smoking), total energy intake (the standard method for energy adjustment), health status (hypertension), kidney function [estimated glomerular filtration rate (eGFR)], and family history of diabetes.

Statistical Analysis

Study participant characteristics at baseline will be compared across the quintiles of change in diet quality (HEI-2015 and AHEI-2010 scores). To better describe dietary intake in the ARIC study population, we will use descriptive statistics to report the baseline level of the overall HEI-2015 dietary quality score, AHEI-2010 diet quality score, and individual food and nutrient components of these two scores at the two time points (visit 1 and visit 3).

Cox proportional hazard regression will be used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for the association between HEI-2015/AHEI-2010 scores and diabetes, incorporating time to event. Different regression models will be developed to account for adjusting potential confounders. The basic model (model 1) will adjust for demographic characteristics (age, sex, and race-center), socioeconomic status (education level), health behaviors (physical activity and smoking), total energy intake, and diet quality score at the first time point (HEI-2015 or AHEI-2010). In model 2, body mass index (BMI), health status (hypertension status, systolic blood pressure, medication use), kidney function, and family
history of diabetes will be added to model 1 for adjustment. Statistical tests will be based on a 2-sided probability of alpha = 0.05.

To assess the robustness of our findings, we will perform sensitivity analyses. In addition to the quintiles, we will use classify change in diet quality as decrease, stable, or increase. We will perform analyses using different definitions for diabetes (doctor diagnosis only; medication use only; doctor diagnosis or medication use).

**Limitations**

Self-reported dietary intake is subject to recall bias and measurement error. We will mention this limitation in the discussion section. Dietary intake may change after the development of the disease. To address this issue, we will exclude participants with the prevalent disease at baseline and will adjust for intermediate risk factors.

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.escc.unc.edu/ARIC/search.php](http://www.escc.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)?

MP989: “Associations of plant- and animal-based food consumption with risk of developing type 2 diabetes: the Atherosclerosis Risk in Communities (ARIC) Study”; Lead author: Lyn M. Steffen

Dietary intake as a predictor of incidence of type 2 diabetes in African Americans (AAs) and Whites; Lead author: June Stevens

These prior manuscript proposals did not evaluate changes in diet quality and ascertained incident diabetes over a shorter follow-up time period. We have invited Lyn Steffen, an author on both of these previous proposals, to be a co-author on the present manuscript proposal.

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 http://www.cscu.unc.edu/aric/forms/

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.cscu.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.

13. Per Data Use Agreement Addendum, approved manuscripts using CMS data shall be submitted by the Coordinating Center to CMS for informational purposes prior to publication. Approved manuscripts should be sent to Pingping Wu at CC, at pingping_wu@unc.edu. I will be using CMS data in my manuscript ____ Yes  ____ X ____ No.

References


