RESEARCH
Commentary

From Neighborhood to Genome: Three Decades of Nutrition-Related Research from the Atherosclerosis Risk in Communities Study

Margaret R. Savoca, PhD; Lyn M. Steffen, PhD, MPH, RD; Alain G. Bertoni, MD, MPH; Lynne E. Wagenknecht, DrPH

ARTICLE INFORMATION

Article history:
Submitted 10 February 2017
Accepted 7 August 2017

Keywords:
Cohort studies
Dietary quality indices
Epigenetics
Geographical information systems
Nutrigenomics

Supplementary materials:
The Table is available at www.jandonline.org

http://dx.doi.org/10.1016/j.jand.2017.08.008

FOR 30 YEARS, THE ATHEROSCLEROSIS RISK IN COMmunities (ARIC) cohort study has examined the etiology and progression of atherosclerosis and atherosclerotic diseases.[1] This research has evaluated variations in cardiovascular disease (CVD) risk in relation to age, race, sex, location, and lifestyle factors, including diet. In this commentary, we describe ARIC research that illustrates an expanded view of the relationship between diet and health and suggest ways that future cohort studies can influence the direction of nutrition and dietetics practice.

ARIC BACKGROUND

In the early 20th century, food policy and dietary guidance focused on prevention of foodborne illnesses and nutritional deficiencies. Later in the century, the prevention and control of chronic disease became priorities.[2,3] The nutrition and dietetics professions have evolved in response to increasing knowledge of chronic disease risk factors; new treatments and lifestyle strategies for prevention[4]; rising rates of obesity and obesity-related chronic diseases; and persisting racial and ethnic health disparities in heart disease, hypertension, and diabetes.[5-7] Beginning with the Framingham Heart Study in 1949, multicenter cohort prospective observational studies have examined the relationships between chronic disease and diet.[8] Starting in 1987 and sponsored by the National Institute of Health's Heart, Lung and Blood Institute, ARIC has been studying a cohort of individuals born before or during World War II through four field centers (Wake Forest Baptist Medical Center [Forsyth County, NC], University of Mississippi [Jackson, MS], University of Minnesota [Minneapolis suburbs], and John Hopkins University [Washington County, MD]), a coordinating center (the University of North Carolina), and numerous collaborating centers.[1] From 1987 through 1989, a sample of 15,792 white and African-American participants aged 45 to 64 years were recruited. Using probability sampling, each ARIC field center recruited approximately 4,000 individuals aged 45 to 64 years from a defined population in their community.[9] Only African Americans were recruited in Jackson, MS; the remaining sites reflected local populations, mostly white in Minneapolis and Washington County and both races in Forsyth County. The Institutional Review Boards from all centers approved ARIC protocols, including compliance with National Institutes of Health protocols for the protection of genetic information. Participants provided written consent for their study participation and for use of their genetic data. To date, there have been six examinations, baseline/visit 1 (1987 to 1989), visit 2 (1990 to 1992), visit 3 (1993 to 1995), visit 4 (1996 to 1998), visit 5 (2011 to 2013), and visit 6 (2016 to 2017), with telephone follow-up conducted annually between visits. Examinations occurred at a local research clinic; if necessary, a shorter examination at the clinic or at the participant's home or care facility was substituted. Participants were compensated for their time and travel. As of 2016, the cohort was composed of approximately 9,000 participants. ARIC funding continues through 2021 and new investigators are invited to become involved in the study.[10]

Assessments include, but are not limited to, medical history, anthropometrics, blood pressure, glucose, biochemical measures, pulmonary function, carotid artery ultrasound measures, genotyping, and behaviors (smoking, diet, and physical activity). Investigators have received additional funding for ancillary studies that have supported magnetic resonance imaging of the brain, cognitive and physical function, and other topics.

Dietary data were obtained with the interviewer-administered ARIC 66-item modified Harvard food frequency questionnaire (FFQ) at visits 1 and 3.[11] From the FFQ, dietary intake was calculated using the Harvard Nutrient Database.[12] The original validated 61-item Harvard FFQ, developed primarily among white women, was modified by ARIC to include four fish categories, pasta, cake and bread items, and a single sugar-sweetened soft drink category; alcohol items were removed and queried separately. The reliability of the ARIC FFQ was assessed using dietary data from the baseline/visit 1 (1987 to 1989) obtained from all

participants and from an additional dietary assessment obtained in visit 2 (1990 to 1992) from a subset of 443 subjects randomly selected from all sites.[13] Mean time elapsed between these exams was 3 years. Reliability coefficients were higher among men, whites, individuals with >12 years of education, and those between 45 and 49 years old.

ARIC published 117 nutrition-related articles from 1992 through August 2016. For this commentary, the first author constructed a database documenting each report's aims, dietary or nutrition-related measures, participant characterization, biochemical and metabolic assessments, health outcomes, statistical analysis, and key findings (Microsoft Access[14]). A review by all authors of the methods in the database found that most articles evaluated single foods or nutrients in relation to advanced biochemical and metabolic assessments, chronic disease and mortality outcomes, and demographic characteristics (age, sex, race, and education). Studies investigated micronutrients (phosphorus, magnesium, iron, potassium, zinc, choline and betaine, vitamins A, C, D, E, and B vitamins), macronutrients with an emphasis on dietary fats (cholesterol, saturated and monounsaturated fats, and types of polyunsaturated fats), and individual foods (fruits, vegetables, dairy, fish, eggs, red and processed meats, poultry, whole and refined grains, salty snacks, nuts, sweets, soft drinks, alcohol, and coffee).[15-24] Details of these reports are found in the Table (available online at www.jandonline.org). However, there were three investigative approaches that expanded ARIC's nutrition-related methods; these were dietary pattern analysis, neighborhood effects on diet and health, and nutritional genomics techniques. This commentary provides an overview of these three methodological approaches using 27 ARIC reports to illustrate the methodologies. Details of these 27 reports are also found in the Table (available online at www.jandonline.org).

DIETARY PATTERN ANALYSIS

Beginning with 19th century research about vitamin structure and function, investigations of individual nutrients became critical to understanding metabolic pathways and biomarkers of disease.[2,25] However, many nutrients and foods influence similar pathways, making it difficult to separate the multiple small health effects of a single nutrient or food from the rest of the diet.[25-27] As early as 1950, researchers identified the effects of food patterns on health, such as the diets of Mediterranean countries on CVD risk.[28] Today, supported by evidence from nutrition epidemiology and lifestyle and clinical interventions, research on the cumulative and synergistic effects of dietary patterns has expanded using both *a posteriori* and *a priori* methods.[29-31]

A posteriori or "data-driven" methods use existing datasets and multivariate analysis to identify dietary patterns within a sample and relate these patterns to characteristics of that same sample.[32] With 10,000 participants from all sites, Lutsey and colleagues[33] examined the relationship between dietary patterns and onset of metabolic syndrome up to 9 years after baseline. Dietary patterns as measured by ARIC's 66-item FFQ were based on the average of dietary intakes from visit 1 (1987 to 1989) and visit 3 (1993 to 1995). Similarly, Steffen and colleagues[22] related dietary patterns of 15,000 ARIC participants to the development of venous thromboembolism over a 12-year period. In a third study, diet was assessed in 2005 to 2006 among 1,000 white participants using the Willett 131-item FFQ and dietary patterns were related to cell activation and inflammation markers.[34] The principal components analyses from these three studies identified similar dietary patterns.[22,33,34] "Western" patterns were characterized by high intakes of refined grains, processed meat, fried foods, red meat, refined grain desserts, sweetened beverages, and cheese and whole milk. "Prudent" or "healthier" patterns reflected higher consumption of vegetables, fruit, fish, poultry, and whole grains. Metabolic syndrome and venous thromboembolism were positively associated with Western pattern and five cell activation and inflammation markers were positively associated with Western pattern and inversely with the healthier pattern. Although studies differed in sample size, racial composition, and participants' age at the time when diets were assessed, these results demonstrate generalizability of "healthy" and "unhealthy" dietary patterns and suggest stability of these patterns over time.

A priori composite measures utilize results from prior epidemiologic or clinical research to create standardized tools for dietary assessment, such as dietary quality indices.[31] These indices provide component scores representing food categories relevant to health and a total score representing overall dietary quality.[35] Indices, such as Healthy Eating Indices,[36,37] Dietary Approaches to Stop Hypertension Index,[38] and Mediterranean Diet Index,[39,40] share food groups including fruits and vegetables, whole grains, nuts, legumes, unsaturated fats, red meat, processed foods, sodium and sugar-sweetened beverages. ARIC's Healthy Food Score identified similar dietary components based on evidence from prior research about the relationship between diet and blood pressure.[41] Hypertension was inversely associated with Healthy Food total score and its dairy and nut components, and positively associated with the meat component.[41] In 2010, the American Heart Association defined the concept of cardiovascular health using ideal health behaviors (nonsmoking, body mass index <25, and adherence to current dietary and physical activity guidelines) and ideal health factors (untreated total cholesterol <200 mg/dL [<5.17 mmol/L], untreated blood pressure <120/<80 mm Hg, and fasting blood glucose <100 mg/dL [<5.51 mmol/L]).[42] To monitor these factors over time, the organization developed metrics known as Life's Simple 7. Metrics included three health behaviors (diet, exercise, and smoking) and four health factors (cholesterol, body mass index, blood pressure, and fasting blood glucose). Diet is assessed with the Healthy Diet Score, which contains recommended intakes of fruit and vegetables, fish, fiber-rich foods, sweetened beverages, and sodium. ARIC has shown that African Americans have the lowest rate of compliance for Healthy Diet Score and other Simple 7 measures.[43] However, African Americans with high rates of Simple 7 compliance have comparable CVD risk as whites with similar compliance rates.[43]

Future Applications

In future cohort studies, both dietary pattern analysis and quality indices should be assessed at each time point. Dietary pattern analysis provides a way to identify subgroups with common food habits and to monitor changes in their dietary patterns and biomarkers over time. Standardized dietary