



Published in final edited form as:

Eur J Clin Nutr. 2020 July ; 74(7): 1084–1090. doi:10.1038/s41430-019-0539-1.

Associations of Diet Quality and Blood Serum Lipoprotein Levels in a Population at High Risk for Diabetes: The Strong Heart Family Study

Sophie A.E. Kauffman¹, Michelle M. Averill², Joseph A C Delaney^{3,4}, Rozenn N. Lemaitre^{4,5}, Barbara V. Howard^{6,7}, Amanda M. Fretts^{3,4}

¹Nutritional Sciences Program, University of Washington, Seattle WA

²Department of Environmental and Occupational Health Sciences, University of Washington, Seattle WA

³Department of Epidemiology, University of Washington, Seattle, WA

⁴Cardiovascular Health Research Unit, University of Washington, Seattle, WA

⁵Department of Medicine, University of Washington, Seattle WA

⁶MedStar Health Research Institute, Washington, DC

⁷Georgetown and Howard Universities Center for Translational Science, Washington DC

Abstract

Background/Objectives—Previous studies consistently report that diet quality is inversely associated with risk of cardiovascular disease (CVD) and type 2 diabetes. However, few studies have assessed the association of diet quality with serum lipoproteins, an intermediate-marker of cardio-metabolic health, or assessed whether type 2 diabetes modifies these associations. This study assessed associations of diet quality (evaluated using the Alternative Healthy Eating Index (AHEI)), and the interaction of diet quality with diabetes, on total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL-C), high density lipoprotein (HDL-C), apolipoprotein A (apoA1) and apolipoprotein B (apoB) among American Indians (AIs).

Subjects/Methods—Participants comprised AIs who participated in the Strong Heart Family Study (SHFS)—a study of CVD and its risk factors in 12 AI communities. Generalized estimated equations (GEE) were used to examine the: (1) cross-sectional associations of diet quality (as determined by AHEI) with serum lipoproteins (n=2 200); and (2) the prospective associations of the AHEI measured at baseline with serum lipoproteins (n=1 899).

Users may view, print, copy, and download text and data-mine the content in such documents, for the purposes of academic research, subject always to the full Conditions of use:http://www.nature.com/authors/editorial_policies/license.html#terms

Corresponding Author: Amanda M Fretts, PhD, amfretts@u.washington.edu.

Author Contributions

SAEK, MMA, JACD, and AMF designed the research question. SAEK and AMF analyzed the data. BVH provided essential material. SAEK and AMF wrote the paper. MMF, JACD, RNL, and BVH provided content expertise, and edited and revised drafts of the manuscript. AMF had primary responsibility for the final content.

Conflicts of Interest

There are no conflicts of interest for any authors.

Results—The association of AHEI with TC, LDL-C, and ApoB differed according to diabetes status. In prospective analysis, AHEI was associated with more favorable levels of TC ($p=0.029$) and LDL-C ($p=0.008$) among participants with diabetes independent of other demographic, behavioral, and health factors. The association of diet quality with TC, LDL-C, and ApoB were much weaker among participants without diabetes. There was no association of diet quality with TG, HDL-C, or ApoA.

Conclusions—The associations of diet quality with TC, LDL-C, and ApoB differ according to diabetes status.

Introduction

Previous studies have demonstrated the importance of diet quality with health outcomes, and a healthy diet has consistently been shown to be associated with a lower risk of obesity, type 2 diabetes, and cardiovascular disease (CVD) (1–3). One of the mechanisms by which diet may impact cardio-metabolic diseases is by influencing lipoprotein levels. Although few studies have assessed the prospective associations of dietary patterns with lipoprotein levels, studies in American Indian populations show diets low in saturated fat have been shown to have a beneficial effect on high density lipoprotein (HDL-C) and triglycerides (TG) (4–7), while diets high in saturated fat have been shown to increase low-density lipoprotein (LDL-C), TG, and apolipoprotein B (ApoB)—major contributors to atherosclerosis (4–7). Further, both dietary patterns and dyslipidemia have been shown to influence insulin-mediated glucose management and disposal—implicating the importance of considering diabetes in an evaluation of diet quality and lipoproteins (8).

Using data available from the Strong Heart Family Study (SHFS), a cohort study of cardio-metabolic diseases and their risk factors among American Indians (AIs), we investigated the interplay of diet quality (using the Alternative Healthy Eating Index (AHEI)) and diabetes with total cholesterol (TC), TG, LDL-C, HDL-C, and apolipoprotein A (apoA1) and ApoB among 2200 AIs 14 years of age or older. Though diabetes and CVD are major health concerns that influence all Americans, the burden of these diseases among AIs is particularly high. AIs are 2.3 times more likely to have diagnosed diabetes than non-Hispanic whites of the same age (9–11), and are 20% more likely to die of CVD (12). As such, a better understanding of the relationship between diet quality, diabetes, and lipoproteins is warranted.

Materials/Subjects & Methods

Setting & Study Population

The SHFS is a family-based cohort study of risk factors for CVD among AIs from 12 communities in Arizona, North Dakota, South Dakota, and Oklahoma. The study comprised two examinations—a baseline examination in 2001–2003 and a follow-up examination in 2007–2009. Specifics of study design have been previously described (13, 14). In total, 2 780 participants from 91 large families participated in the baseline examination and 91% of participants then went on to participate in the follow-up examination. Both examinations included a personal interview, laboratory work-up, physical assessment, and medication

review. Written informed consent was obtained from all participants at each examination. The institutional review boards from each Indian Health Service region for the 12 participating communities approved the study.

This investigation included all SHFS participants with available measures related to diet, lipoproteins, and diabetes. Participants with missing diet (n=194), lipoproteins (n=41), or diabetes (n=1) data were excluded. Additionally, participants who skipped more than 10% of questions on the food frequency questionnaire (FFQ) (n=39) or with caloric intakes less than 600 kilocalories for women and men (n=49), or greater than 6,000 kilocalories for women (n=56) or 8,000 kilocalories for men (n=34) were excluded. The exclusion cut-points for low or high estimated daily caloric intake were determined by nutritionists who work in American Indian communities, and these criteria have been used consistently across all SHFS publications that involve diet measures (15–18). Finally, participants missing key covariates of interest (<1% of study participants for most covariates) were excluded. The final sample size included 2 200 participants for the cross-sectional analyses (i.e., 411 participants with prevalent diabetes; 1789 participants without prevalent diabetes) and 1 899 participants for the prospective analyses (i.e., 344 participants with prevalent diabetes; 1555 participants without prevalent diabetes).

Data Collection

Information on participants' demographics and medical history were collected at the personal interview at baseline. Anthropometric measures were obtained with the participant wearing lightweight clothing and no shoes. Body weight was measured using a Tanita BWB-800 5 Adult Digital Scale, and height was measured using a vertical mounted ruler. Body mass index (BMI) was calculated as body weight divided by height-squared (kg/m^2). Prevalent CVD was defined as self-reported history of myocardial infarction, stroke, heart failure, or angioplasty (13, 14).

Blood samples were collected after a 12-hour overnight fast and were stored at -70 degrees Celsius. Plasma glucose were measured using enzymatic methods (19), and prevalent diabetes was assessed using the American Diabetes Association criteria, including use of insulin or oral anti-diabetes medication or fasting plasma glucose level greater than or equal to 126 mg/dL (20).

Assessment of Dietary Quality

A Block 119-item FFQ was administered at the baseline examination to estimate usual dietary intake during the previous year. The Block FFQ is a well-established and widely used FFQ, demonstrating both reliability and validity in previous studies (21, 22). In addition to food items on the standard Block FFQ, participants were asked additional supplemental questions about intake of common AI foods, such as menudo, pozole, guysava, red or green chili, Indian taco, fry bread, corn tortilla, flour tortilla, and spam. For certain ethnic groups, the inclusion of an ethnic foods section on the FFQ contributes considerably to group mean nutrient estimates (23). In the SHFS, it was hypothesized that these foods may represent commonly consumed foods in these AI communities, and including them in the dietary assessment may have produced more accurate nutrient estimates. For each food

item listed on the FFQ or supplement, participants were asked on average how often a specific food item was consumed during the year prior. Frequency was assessed using measures of regularity—i.e. seasonally, never, a few times per year, once per month, 2–3 times per month, once per week, twice per week, 2–3 times per week, 5–6 times per week, or daily—and quantity was measured via portion size as small, medium, or large. Average daily energy and macronutrient intakes were calculated for each study participant using the Block database (Block Dietary Systems, Berkeley, CA) by multiplying the frequency response for each food on the FFQ and AI supplemental foods questionnaire by the nutrient content of the documented portion size of the food, then summed for all foods (24).

For the present analysis, the primary exposure of interest was diet quality. This was assessed using the AHEI. Details of the AHEI have been described previously (3). In brief, the AHEI is an eating index designed to estimate dietary patterns associated with risk of chronic diseases, including diabetes, cardiovascular disease, and cancer (25–33). It is based on 11 foods and nutrients: vegetables, fruit, whole grains, nuts and legumes, long chain omega-3 fatty acids, polyunsaturated fatty acids, alcohol, sugar sweetened beverages (SSBs) and fruit juice, red and processed meat, trans fat, and sodium. Each of these dietary factors has the potential to contribute zero (least healthy) to 10 (most healthy) points to the AHEI, with total score ranging from zero (unhealthiest diet) to 110 (healthiest diet) (34, 35) (Supplementary Table 1).

Measurement of lipoproteins

The procedures and assays for measuring lipoproteins were identical at each SHFS examination. TC, TG, LDL-C, HDL-C, ApoA, and Apo B were isolated and measured by ultracentrifugation at baseline, as described previously (19). At the follow-up exam, ApoA and ApoB were unavailable, so outcomes for the prospective analyses include TC, TG, LDL-C, and HDL-C only.

Statistical Analysis

For this report, we were most interested in the association of diet quality and lipoprotein levels among participants with and without diabetes. Generalized estimated equations (GEE) with an independence working correlation and robust standard errors were used to estimate the: (1) cross-sectional associations of diet quality (as determined by AHEI) with TC, TG, LDL-C, HDL-C, ApoA, and ApoB status using data from the baseline examination (primary analyses); and (2) the prospective association of diet quality measured at baseline with TC, TG, LDL-C, and HDL-C measured 4–8 years later at the follow-up examination (secondary analyses). As 91 families comprised the analytic sample, GEE was used to address potential familial correlation within the data. Measures of diet quality were assessed continuously. Lipoprotein levels were also assessed continuously, with log transformations to account for skew, as appropriate. Covariates were selected *a priori* based on their potential association with diet quality and lipoproteins. All analyses were performed using STATA version 13.1 (Stata Corp, College Station, Texas).

Two models were fit to examine the association of diet quality and each lipoprotein—a model that included potential confounders, including age, sex, site, education (years), smoking

(never, former, current), physical activity (steps per day), total caloric intake, lipid-lowering drug use (yes/no), and prevalent diabetes (yes/no), as well as a multiplicative interaction term for the potential interaction of diet quality with diabetes (product of AHEI*diabetes), and a second model that additionally adjusted for BMI. As preliminary analyses indicated that the relationship of diet quality with some lipoprotein levels may differ according to diabetes status (based on Wald test $p < 0.05$ for the multiplicative interaction term), all analyses were presented stratified by diabetes status.

For primary analyses, a Bonferroni correction was used to adjust for multiple comparisons; the significance threshold used for the current analysis was $p = 0.008$ (based on 6 outcomes of interest). We also examined the potential interaction of diet quality (AHEI) with age, sex, and BMI to investigate whether these factors modify the association of diet quality with lipoprotein levels among participants with and without diabetes using Wald tests.

Results

Of the 2 200 SHFS participants who comprised the analytic cohort, 60% were women, and the mean (SD) age at baseline was 40.8 (16.8) years. Mean (SD) BMI was 31.3 (7.4) kg/m^2 , and 18.7% ($n = 162$) of participants had diabetes at the baseline examination. Mean (SD) diet scores were 44.7 (9.1) for the AHEI. Baseline characteristics of study participants stratified by diabetes status are shown in Table 1. Participants with diabetes were older, more likely to be female, less likely to smoke, and accumulated fewer steps per day than participants without diabetes. Additionally, participants with diabetes had higher systolic blood pressure, fibrinogen, TC, TG, ApoB, BMI, and waist circumference, and lower HDL-C than participants without diabetes. Participants with diabetes also reported slightly better diet quality than participants without diabetes. Among participants with diabetes, median duration of diabetes was 5 years (interquartile range: 1, 14 years) for participants in the cross-sectional analyses ($n = 411$) and 5 years (interquartile range: 1, 13 years) for participants in the prospective analysis ($n = 344$).

Cross-sectional associations of diet quality with TC, TG, LDL-C, HDL-C, ApoA, and ApoB are presented in Table 2. For TC, we observed a strong association of diet quality with TC among those with diabetes, while there was no statistically significant association of diet quality with TC among participants without diabetes ($p\text{-interaction} < 0.0001$). For participants with diabetes, TC was 10.6 mg/dL lower among those who reported consuming a healthy diet (90th percentile of AHEI) when compared to participants who reported consuming an unhealthy diet (10th percentile of AHEI) after adjustment for age, sex, site, education, smoking, physical activity, total caloric intake, lipid-lowering drug use, prevalent diabetes and BMI (beta coefficient (95% CI): -10.6 ($-20.4, -0.7$)). Similarly, although we found that higher diet quality was associated with more favorable levels of LDL-C and ApoB among all study participants, the magnitude of the associations was much greater for participants with diabetes compared to those without diabetes ($p\text{-interaction} = 0.005$ for LDL-C; $p\text{-interaction}$ for ApoB = 0.002). We observed no association of AHEI with triglycerides, HDL-C cholesterol, or ApoA.

The prospective associations of diet quality (measured at baseline) with TC, TG, LDL-C, and HDL-C measured an average of 5.4 years later (range of time between baseline and follow-up exams: 2.8–8.5 years) are presented in Table 3. Similar to the results for the cross-sectional analyses, diet quality was associated with more favorable levels of TC (p-interaction: 0.029) and LDL-C (p-interaction: 0.008) among participants with diabetes, but not among participants without diabetes. However, only LDL-C met the significance threshold after consideration of multiple testing. For LDL-C, after adjustment for potential confounders, AHEI score in the 90th percentile was associated with 0.1 mg/dL lower LDL-C (95% CI, -0.2, -0.1) among those with diabetes when compared to those with an AHEI score in the 10th percentile. We observed no association of diet quality with LDL-C among those without diabetes. Similar to cross-sectional analyses, in prospective analyses, diet quality was not associated with TG or HDL-C. There was no statistically significant interaction between AHEI and age, sex, or BMI among participants with or without diabetes. Rerunning analyses using more conservative exclusion criteria cut-points for low or high estimated daily caloric intake (i.e., exclude <500 kcal or >5000 kcal per day for both men and women) did not materially change reported results.

Discussion

In this large study of AIs, healthy diet quality was associated with favorable levels of TC, LDL-C, and ApoB among participants with diabetes independent of other demographic, behavioral, and health factors. Further, findings were similar in both cross-sectional and prospective analyses. The consistency of results across time highlights the importance of targeting diet for lipid management among individuals with diabetes.

This is the first large study that examined the prospective associations of diet quality with lipoprotein levels in a multi-tribal cohort of AIs. A small feeding study that evaluated the effect a healthy diet on lipoproteins among AIs from the southwest (n=14) indicated that a diet high in complex carbohydrates and low in saturated fat (i.e., diet comprised of vegetables, legumes, and cereals) reduced LDL-C, but had no impact on TG (36). The findings reported herein extend previous findings, indicating the importance of diet on lipoproteins among AIs in a non-experimental/population-based setting.

In non-AI populations, results of studies that have examined the associations of diet quality with lipoproteins are mixed—with most published studies using a cross-sectional design (37–39). In one cross-sectional study that assessed the relationship of the AHEI with HDL-C among participants without diabetes, higher levels of the AHEI were associated with higher HDL-C among women, but not men (no other lipids assessed) (37). On the other hand, in a cross-sectional study comprised of nurses, AHEI was not associated with TC, HDL-C, or TG (n=475); in that study, the prevalence of diabetes was low (~5%) and the authors were unable to assess if the association of diet quality with lipoproteins varied according to diabetes status (38).

Few prospective studies have assessed the association of diet quality with lipoproteins. Moreover, most prospective studies have only involved participants free of diabetes or the metabolic syndrome (38, 40), and little is known about the association of diet quality with

lipoprotein levels in individuals with diabetes. Results from a study comprised of individuals without diabetes suggested that higher diet quality (as assessed using an index comprised of saturated fat, polyunsaturated fat, sucrose, fiber, fruits and vegetables, and fish) is associated with lower risk of developing high LDL-C or TG during a 16-year follow-up—although the magnitude of the associations were small (2). Similarly, in the Framingham Offspring Study, a Mediterranean-style diet was associated with lower TG and higher HDL-C among participants without diabetes (40).

In general, SHFS participants had lower mean AHEI than participants in other large cohort studies, such as the Nurses' Health Study (mean AHEI=47.6±10.8) (3), the Health Professionals Follow-Up Study (mean AHEI=52.4±11.5) (3), or the Multiethnic Cohort Study (mean AHEI=64.5±9.2) (37). However, the demographic characteristics of those cohorts are very different than the SHFS. For instance, the Nurses' Health Study, the Health Professionals Follow-Up Study, and the Multiethnic Cohort Study largely comprise participants with high levels of education who reside in urban or suburban communities. Moreover, AIs have experienced major changes in lifestyle over the past 50 years—including the adoption of largely Western diets comprised of processed foods high in saturated fat (15). The findings described in this report complement previous research in the SHFS that indicated that the majority of AIs who participated in the SHFS reported diets that are not optimal for the prevention of cardio-metabolic diseases (16).

In this analysis, SHFS participants with diabetes reported consuming diets of higher quality than those without diabetes. Given Indian Health Services standardization of diabetes care, it is likely that participants with diabetes received nutrition education as part of their care, and participants with diabetes may consume healthier diets as part of diabetes management (41, 42). On the other hand, it is possible that differences in reported diet according to diabetes status may be due to social desirability bias. Nevertheless, the reported difference in diet quality between participants with diabetes and those without diabetes (<3 points for AHEI) is likely too small to have a large impact on blood lipid level outcomes when comparing participants with diabetes to those without diabetes.

This study has several strengths, including the availability of a large, family-based sample, prospective design, validated dietary instruments, and standardized indices for assessing diet quality. This study also has limitations. First, the dietary assessment was based on a FFQ that ascertained information on usual diet over the past year, and some participants might not have accurately recalled dietary information such as specific foods consumed, frequency, or portion sizes, thereby limiting our ability to obtain accurate risk estimates. Although it is possible that diet quality changed during the 4–8 year follow-up, reported dietary intakes of study participants were markedly similar at both the baseline and follow-up exams. This is an observational analysis, and residual confounding by unknown factors is possible. However, results were robust to adjustment for multiple cardio-metabolic risk factors. We utilized a Bonferroni correction to address multiple comparisons; as the lipoproteins of interest are correlated, and a Bonferroni correction is likely conservative. Finally, the cohort comprised AIs from 12 communities, and it is unknown if the findings may be generalizable to other populations.

In summary, this study suggests that diet quality is associated with favorable levels of TC, LDL-C, and ApoB among AIs, particularly in the presence of diabetes. Although it is heartening that individuals with diabetes reported higher diet quality (albeit slight), than those without diabetes, promotion of and opportunity for access to healthy diet may positively influence blood lipoprotein levels among AIs with diabetes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors would like to thank the SHFS participants, the Indian Health Services facilities, and participating tribal communities for their extraordinary cooperation and involvement. The opinions expressed in this paper are those of the author(s) and do not necessarily reflect the views of the Indian Health Service.

Funding

The Strong Heart Study has been funded in whole or in part with federal funds from the National Heart, Lung, and Blood Institute, National Institute of Health, Department of Health and Human Services, under contract numbers 75N92019D00027, 75N92019D00028, 75N92019D00029, & 75N92019D00030. The study was previously supported by research grants: R01HL109315, R01HL109301, R01HL109284, R01HL109282, and R01HL109319 and by cooperative agreements: U01HL41642, U01HL41652, U01HL41654, U01HL65520, and U01HL65521. Dr. Fretts is also supported by 5KL2TR000421.

Abbreviations

SHFS	Strong Heart Family Study
BMI	body mass index
TC	total cholesterol
TG	triglycerides
LDL-C	low density lipoprotein
HDL-C	high density lipoprotein
ApoA	Apolipoprotein A
ApoB	Apolipoprotein B
AI	American Indian
OR	odds ratio
CI	confidence interval
GEE	generalized estimating equations

References

1. Huffman FG, Zarini GG, McNamara E, Nagarajan A. The Healthy Eating Index and the Alternate Healthy Eating Index as predictors of 10-year CHD risk in Cuban Americans with and without type 2 diabetes. *Public Health Nutr* 2011;14(11):2006–14. [PubMed: 21729463]

2. Sonestedt E, Hellstrand S, Drake I, Schulz CA, Ericson U, Hlebowicz J, et al. Diet Quality and Change in Blood Lipids during 16 Years of Follow-up and Their Interaction with Genetic Risk for Dyslipidemia. *Nutrients* 2016;8(5).
3. Chiuve SE, Fung TT, Rimm EB, Hu FB, McCullough ML, Wang M, et al. Alternative dietary indices both strongly predict risk of chronic disease. *Journal of Nutrition* 2012;142(6):1009–18. [PubMed: 22513989]
4. Howard BV, Knowler WC, Vasquez B, Kennedy AL, Pettitt DJ, Bennett PH. Plasma and lipoprotein cholesterol and triglyceride in the Pima Indian population. Comparison of diabetics and nondiabetics. *Arteriosclerosis* 1984;4(5):462–71. [PubMed: 6477297]
5. Xu J, Eilat-Adar S, Loria C, Goldbourt U, Howard BV, Fabsitz RR, et al. Dietary fat intake and risk of coronary heart disease: the Strong Heart Study. *Am J Clin Nutr* 2006;84(4):894–902. [PubMed: 17023718]
6. Zephier EM, Ballew C, Mokdad A, Mendlein J, Smith C, Yeh JL, et al. Intake of nutrients related to cardiovascular disease risk among three groups of American Indians: the Strong Heart Dietary Study. *Prev Med* 1997;26(4):508–15. [PubMed: 9245673]
7. Rudkowska I, Dewailly E, Hegele RA, Boiteau V, Dubé-Linteau A, Abdous B, et al. Gene-diet interactions on plasma lipid levels in the Inuit population. *Br J Nutr* 2013;109(5):953–61. [PubMed: 23021345]
8. Howard BV. Diabetes and plasma lipoproteins in Native Americans. *Studies of the Pima Indians. Diabetes Care* 1993;16(1):284–91. [PubMed: 8422793]
9. (CDC) CfDCaP. Diagnosed diabetes among American Indians and Alaska Natives aged <35 years--United States, 1994–2004. *MMWR Morb Mortal Wkly Rep* 2006;55(44):1201–3. [PubMed: 17093386]
10. (CDC) CfDCaP. Diabetes prevalence among American Indians and Alaska Natives and the overall population--United States, 1994–2002. *MMWR Morb Mortal Wkly Rep* 2003;52(30):702–4. [PubMed: 12894056]
11. Lee ET, Welty TK, Cowan LD, Wang W, Rhoades DA, Devereux R, et al. Incidence of diabetes in American Indians of three geographic areas: the Strong Heart Study. *Diabetes Care* 2002;25(1):49–54. [PubMed: 11772900]
12. Disparities in premature deaths from heart disease--50 States and the District of Columbia, 2001. *MMWR Morb Mortal Wkly Rep* 2004;53(6):121–5. [PubMed: 14981360]
13. North KE, MacCluer JW, Devereux RB, Howard BV, Welty TK, Best LG, et al. Heritability of carotid artery structure and function: the Strong Heart Family Study. *Arterioscler Thromb Vasc Biol* 2002;22(10):1698–703. [PubMed: 12377752]
14. North KE, Howard BV, Welty TK, Best LG, Lee ET, Yeh JL, et al. Genetic and environmental contributions to cardiovascular disease risk in American Indians: the strong heart family study. *Am J Epidemiol* 2003;157(4):303–14. [PubMed: 12578801]
15. Fretts AM, Howard BV, McKnight B, Duncan GE, Beresford SAA, Mete M, et al. Associations of processed meat and unprocessed red meat intake with incident diabetes: the Strong Heart Family Study. *American Journal of Clinical Nutrition* 2012;95(3):752–758. [PubMed: 22277554]
16. Fretts AM, Howard BV, McKnight B, Duncan GE, Beresford SA, Mete M, et al. Life's Simple 7 and incidence of diabetes among American Indians: the Strong Heart Family Study. *Diabetes Care* 2014;37(8):2240–5. [PubMed: 24804696]
17. Haring B, Wang W, Fretts A, Shimbo D, Lee ET, Howard BV, et al. Red meat consumption and cardiovascular target organ damage (from the Strong Heart Study). *J Hypertens* 2017;35(9):1794–1800. [PubMed: 28399044]
18. Fretts AM, Howard BV, Siscovick DS, Best LG, Beresford SA, Mete M, et al. Processed Meat, but Not Unprocessed Red Meat, Is Inversely Associated with Leukocyte Telomere Length in the Strong Heart Family Study. *J Nutr* 2016;146(10):2013–2018. [PubMed: 27558579]
19. Lee E, Welty T, Fabsitz R, Cowan L, Ngoc A, Oopik A, et al. The Strong Heart Study: A Study of Cardiovascular Disease in American Indians: Design and Methods. *American Journal of Epidemiology* 1990;132:1141–1155. [PubMed: 2260546]
20. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2010;33 Suppl 1:S62–9. [PubMed: 20042775]

21. Block G, Thompson F, Hartman A. Comparison of Two Dietary Questionnaires Validated Against Multiple Dietary Records Collected During a 1-Year Period. In. *Journal of the American Dietetic Association*; 1992 p. 686–93. [PubMed: 1607564]
22. Caan B, Slattey M, Potter J. Comparison of the Block and Willett Self-Administered Semiquantitative Food Frequency Questionnaires with an Interview-Administered Dietary Food History. In. *American Journal of Epidemiology*; 1998 p. 1137–47. [PubMed: 9867257]
23. Block G, Mandel R, Gold E. On Food Frequency Questionnaires: The Contribution of Open-Ended Questions and Questions on Ethnic Foods. *Epidemiology* 2004;15(2):216–221. [PubMed: 15127915]
24. Block G, Wakimoto P, Block T. A ReVision of the Block Dietary Questionnaire and Database, Based on NHANES III Data. In; 1998 p. available at http://www.nutritionquest.com/products/B98_DEV.pdf.
25. Chiuve SETTF, Rimm EB, Hu FB, McCullough ML, Wang M, Stampfer MJ, and Willett WC. Alternative dietary indices both strongly predict risk of chronic disease. *Journal of Nutrition* 2012(142):1009–1018. [PubMed: 22513989]
26. Schwingshackl L aGH. Diet quality as assessed by the Healthy Eating Index, the Alternate Healthy Eating Index, the Dietary Approaches to Stop Hypertension Score, and health outcomes: a systematic review and meta-analysis of cohort studies.. *Journal of the Academy of Nutrition and Dietetics* 2015;115(5):780–800. [PubMed: 25680825]
27. Wu P CH, Lei W, and Yang S. Alternative healthy Eating Index and the dietary guidelines form American Diabetes Association both may reduce the risk of cardiovascular disease in type 2 diabetes patients. *Journal of Human Nutrition and Dietetics* 2015;29:363–373. [PubMed: 26010198]
28. Onvani S FH, Surkan PJ, Larijani B, and Azadbakht L. Adherence to the Healthy Eating Index and Alternative Healthy Eating Index dietary patterns and mortality from all causes, cardiovascular disease and cancer: a meta-analysis of observational studies. *Journal of Human Nutrition and Dietetics* 2016;30:216–226. [PubMed: 27620213]
29. Neelakantan N NN, Koh W, Yuan J, and Van Dam RM. The Alternative Healthy Eating Index is associated with a lower risk of fatal and nonfatal acute myocardial infarction in a Chinese adult population. 2016;146:1379–1386.
30. Dai LMB Z, van Dam RM, Ang L, Yuan J, and Koh W. Adherence to a vegetable–fruit–soy dietary pattern or the Alternative Health Eating Index is associated with lower hip fracture risk among Singapore Chinese. *Journal of Nutrition* 2014;144:511–518. [PubMed: 24572035]
31. Hagan KA SEC, Stampfer MJ, Kratz JN, and Grodstein F. Greater adherence to the Alternative Healthy Eating index is associated with lower incidence of physical function impairment in the Nurses' Health Study. *Journal of Nutrition* 2016;146:1341–1347. [PubMed: 27170727]
32. Saneei MH P, Keshteli AM, Afshar H, Esmailzadeh A, and Adibi P. Adherence to the Alternative healthy Eating Index in relation to depression and anxiety in Iranian adults. *British Journal of Nutrition* 2016;116:335–342. [PubMed: 27188471]
33. Varraso R SEC, Fung TT, Barr RG, Hu F, Willett W, and Camargo CA. Alternate Healthy Eating Index 2010 and risk of chronic obstructive pulmonary disease among US women and men: prospective study. *BMJ* 2015;3(350):h286.
34. Varraso R, Chiuve SE, Fung TT, Barr RG, Hu FB, Willett WC, et al. Alternate Healthy Eating Index 2010 and risk of chronic obstructive pulmonary disease among US women and men: prospective study. *Bmj* 2015;350:h286. [PubMed: 25649042]
35. Chiuve SE, Fung TT, Rimm EB, Hu FB, McCullough ML, Wang M, et al. Alternative dietary indices both strongly predict risk of chronic disease. *J Nutr* 2012;142(6):1009–18. [PubMed: 22513989]
36. Abbott WG, Swinburn B, Ruotolo G, Hara H, Patti L, Harper I, et al. Effect of a high-carbohydrate, low-saturated-fat diet on apolipoprotein B and triglyceride metabolism in Pima Indians. *J Clin Invest* 1990;86(2):642–50. [PubMed: 2200808]
37. Jacobs S, Boushey CJ, Franke AA, Shvetsov YB, Monroe KR, Haiman CA, et al. A priori-defined diet quality indices, biomarkers and risk for type 2 diabetes in five ethnic groups: the Multiethnic Cohort. *Br J Nutr* 2017;118(4):312–320. [PubMed: 28875870]

38. AlEsa HB, Malik VS, Yuan C, Willett WC, Huang T, Hu FB, et al. Dietary patterns and cardiometabolic and endocrine plasma biomarkers in US women. *Am J Clin Nutr* 2017;105(2):432–441. [PubMed: 27974312]
39. Fogli-Cawley JJ, Dwyer JT, Saltzman E, McCullough ML, Troy LM, Meigs JB, et al. The 2005 Dietary Guidelines for Americans and risk of the metabolic syndrome. *Am J Clin Nutr* 2007;86(4):1193–201. [PubMed: 17921402]
40. Rumawas ME, Meigs JB, Dwyer JT, McKeown NM, Jacques PF. Mediterranean-style dietary pattern, reduced risk of metabolic syndrome traits, and incidence in the Framingham Offspring Cohort. *Am J Clin Nutr* 2009;90(6):1608–14. [PubMed: 19828705]
41. Lee ET, Howard BV, Savage PJ, Cowan LD, Fabsitz RR, Oopik AJ, et al. Diabetes and impaired glucose tolerance in three American Indian populations aged 45–74 years. The Strong Heart Study. *Diabetes Care* 1995;18(5):599–610. [PubMed: 8585996]
42. Teufel-Shone NI, Jiang L, Beals J, Henderson WG, Acton KJ, Roubideaux Y, et al. Changes in Food Choices of Participants in the Special Diabetes Program for Indians-Diabetes Prevention Demonstration Project, 2006–2010. *Prev Chronic Dis* 2015;12:E193. [PubMed: 26564009]

Table 1:

Baseline characteristics of SHFS participants according to diabetes status

	No Diabetes (N = 1 789)	Diabetes (N = 411)
Age (years) ^a	38.1 (16.2)	52.4 (14.1)
% Female	59.0%	63.0%
Years of Education	12.3 (2.3)	12.3 (2.4)
Smoking ^b		
Never	41.0%	35.0%
Former	22.0%	35.0%
Current	38.0%	30.0%
Waist Circumference (cm) ^a	99.5 (17.0)	113.5 (17.6)
BMI (kg/m ²) ^a	30.5 (7.1)	34.9 (7.7)
Systolic BP (mmHg) ^a	121.4 (15.6)	129.3 (18.4)
Fasting Glucose (mg/dL) ^a	93.9 (10.3)	175.7 (72.1)
Total Cholesterol (mg/dL) ^b	181.8 (35.9)	187.8 (35.8)
HDL-C (mg/dL) ^a	52.7 (14.8)	48.0 (12.4)
LDL-C (mg/dL)	100.2 (30.2)	99.0 (30.6)
Triglycerides (mg/dL) ^a	147.0 (88.9)	214.5 (131.7)
ApoA1 (mg/dL)	138.9 (26.4)	138.6 (25.2)
ApoB (mg/dL) ^a	93.0 (24.0)	102.2 (23.5)
Fibrinogen (mg/dL) ^a	368.0 (82.1)	427.0 (93.6)
% use lipid-lowering medication ^a	2.7%	14.6%
Physical Activity (steps/day) ^a	6231.0 (3965.5)	4044.1 (3132.1)
Total Caloric Intake (calories/day) ^b	2472.9 (1358.6)	2246.7 (1252.2)
AHEI ^a	44.2 (9.1)	47.0 (8.6)
DDI ^a	13.2 (3.8)	15.3 (3.5)

Abbreviations: SHFS, Strong Heart Family Study; BMI, body mass index; HDL-C, high density lipoprotein; LDL-C, low density lipoprotein; Apo, apolipoprotein; BP, blood pressure; AHEI, alternative healthy eating index; DDI, diabetes dietary index

^a p-trend<0.001

^b p-trend<0.05

Table 2.

Beta (95% CI) for cross-sectional association of AHEI with lipoprotein levels among SHFS participants with (n=411) and without diabetes (n=1789) in 2001-2003^a

	Diabetes	No Diabetes	P-interaction
Total Cholesterol			
Model 1 ^b	-10.0 (-20.0, 0.0)	-1.1 (-4.8, 2.7)	<0.0001
Model 2 ^c	-10.6 (-20.4, -0.7)	-1.2 (-4.9, 2.6)	<0.0001
Triglycerides			
Model 1 ^b	0.1 (-0.1, 0.2)	0.0 (0.0, 0.1)	0.081
Model 2 ^c	0.0 (-0.1, 0.2)	0.0 (0.0, 0.1)	0.233
HDL-C cholesterol			
Model 1 ^b	0.0 (-0.1, 0.1)	0.0 (0.0, 0.0)	0.433
Model 2 ^c	0.0 (-0.1, 0.1)	0.0 (0.0, 0.1)	0.127
LDL-C cholesterol			
Model 1 ^b	-10.4 (-18.6, -2.3)	-3.5 (-6.6, -0.5)	0.003
Model 2 ^c	-10.2 (-18.2, -2.3)	-3.7 (-6.7, -0.6)	0.005
Apo A			
Model 1 ^b	1.6 (-4.9, 8.1)	2.0 (-1.0, 4.9)	0.745
Model 2 ^c	0.9 (-5.5, 7.3)	2.2 (-0.8, 5.2)	0.385
Apo B			
Model 1 ^b	-4.5 (-10.4, 1.4)	-1.0 (-3.3, 1.4)	0.001
Model 2 ^c	-4.9 (-10.7, 1.0)	-1.1 (-3.4, 1.1)	0.002

^aBeta (95% CI) compares the difference in each lipid associated with a 23 point difference in AHEI (i.e., difference between the 10th & 90th percentiles)

^bModel 1 adjusts for age, sex, site, education (years), smoking (never, former, current), physical activity (steps per day), total caloric intake, lipid-lowering drug use, and prevalent diabetes (yes/no)

^cModel 2 adjusted for all model 1 covariates and BMI. Abbreviations: SHFS, Strong Heart Family Study; AHEI, alternative healthy eating index; HDL-C, high density lipoprotein; LDL-C, low density lipoprotein; Apo A, apolipoprotein

Table 3.

Beta (95% CI) for prospective associations of AHEI with lipoprotein levels among SHFS participants with prevalent diabetes (n=344) and without prevalent diabetes (n=1555)^a

	Diabetes	No Diabetes	P-interaction
Total Cholesterol			
Model 1 ^b	-3.9 (-14.0, 6.1)	4.5 (1.3, 7.7)	0.074
Model 2 ^c	-5.3 (-15.7, 5.0)	4.7 (1.4, 7.9)	0.029
Triglycerides			
Model 1 ^b	0.1 (0.0, 0.2)	0.00 (-0.1, 0.1)	0.439
Model 2 ^c	0.1 (0.0, 0.2)	0.00 (-0.1, 0.1)	0.414
HDL-C cholesterol			
Model 1 ^b	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	0.245
Model 2 ^c	0.0 (-0.1, 0.1)	0.0 (0.0, 0.1)	0.087
LDL-C cholesterol			
Model 1 ^b	-0.1 (-0.2, 0.0)	0.0 (0.0, 0.1)	0.014
Model 2 ^c	-0.1 (-0.2, -0.1)	0.0 (0.0, 0.1)	0.008

^aBeta (95% CI) compares the difference in each lipid associated with a 23 point difference in AHEI (i.e., difference between the 10th & 90th percentiles)

^bModel 1 adjusts for age, sex, site, education (years), smoking (never, former, current), physical activity (steps per day), total caloric intake, lipid-lowering drug use, and prevalent diabetes (yes/no)

^cModel 2 adjusted for all model 1 covariates and BMI. Abbreviations: SHFS, Strong Heart Family Study; AHEI, alternative healthy eating index; HDL-C, high density lipoprotein; LDL-C, low density lipoprotein.