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Dietary patterns and cardiometabolic and endocrine plasma biomarkers in US women[1,2]

*Hala B AlEssa,[3] Vasanti S Malik,[3] Changzheng Yuan,[3] Walter C Willett,[3–5] Tianyi Huang,[4,5] Frank B Hu,[3–5] and Deirdre K Tobias[3,6]**

Departments of [3]Nutrition and [4]Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA; and [5]Channing Division of Network Medicine, Department of Medicine, and [6]Division of Preventive Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

ABSTRACT

Background: Healthful dietary patterns have been associated with lower risks of type 2 diabetes and coronary artery disease, but their relations with intermediate markers of cardiometabolic and endocrine health are less established.

Objective: We evaluated the Dietary Approaches to Stop Hypertension (DASH), the alternate Mediterranean diet (aMED), and the Alternate Healthy Eating Index (aHEI) diet-quality scores with cardiometabolic and endocrine plasma biomarkers in US women.

Design: The trial was a cross-sectional analysis of 775 healthy women in the Women's Lifestyle Validation Study that was conducted within the NHS (Nurses' Health Study) and NHS II longitudinal cohorts. Multiple linear regression models adjusted for potential confounders were used to estimate associations between quartiles of dietary pattern–adherence scores that were derived from a food-frequency questionnaire and plasma biomarker concentrations that were collected simultaneously.

Results: In multivariable models in which highest and lowest quartiles of dietary pattern scores were compared, *1*) DASH was significantly associated with higher concentrations of high-density lipoprotein (9%) and sex-hormone binding globulin (SHBG) (21%), and lower concentrations of leptin (28%), triglycerides (19%), and C-peptide (4%) (all P-trend $\leq$ 0.04); *2*) the aMED was associated with 19% higher SHBG and 16% lower triglycerides (P-trend = 0.02 and 0.003, respectively); and *3*) the aHEI was associated with significantly higher concentrations of insulin (16%) and SHBG (19%) and lower concentrations of leptin (18%) (all P-trend $\leq$ 0.02). Further adjustment for body mass index (BMI) attenuated these associations but remained significant for *1*) DASH with leptin and triglycerides and *2*) the aMED with triglycerides (all P-trend $\leq$ 0.03).

Conclusions: Adherence to healthful dietary patterns is associated with favorable concentrations of many cardiometabolic and endocrine biomarkers. These relations are mediated in part by BMI.
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Keywords: aHEI, alternate Mediterranean diet, cardiometabolic biomarkers, DASH, dietary patterns

INTRODUCTION

Prospective cohort studies have consistently shown that adherence to a variety of healthful dietary patterns is related to lower risks of major chronic diseases and mortality including the Mediterranean diet (1), the Alternate Healthy Eating Index (aHEI)[7] 2010, and Dietary Approaches to Stop Hypertension (DASH) dietary patterns (2). A meta-analysis of randomized controlled trials (RCTs) with durations from 8 to 24 wk showed that the DASH diet can used as a be a successful weight-management strategy (3). An RCT in Spain, with a median duration of 4.8 y, in people at high risk of cardiovascular disease has shown that participants who were randomly assigned to receive the Mediterranean diet supplemented with either extra-virgin olive oil or nuts had 30% and 28% reduced incidences of major cardiovascular events, respectively, compared with the low-fat diet control group (4).

There are multiple biological mechanisms that may serve as underlying etiologic pathways for the observed beneficial relations between healthful dietary patterns and chronic diseases, including inflammatory, cardiometabolic, and endocrine pathways (5–7). However, less is known about the relation between major dietary patterns and cardiometabolic and endocrine biomarkers including adipokines and blood lipids. Therefore, the aim of this study was to comprehensively evaluate the associations between 3 major dietary patterns, i.e., the DASH, the alternate Mediterranean diet (aMED), and the aHEI, with cardiometabolic and endocrine plasma biomarkers including

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[2] Supplemental Figure 1 and Supplemental Tables 1–3 are available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

*To whom correspondence should be addressed. E-mail: dtobias@partners.org.

[7] Abbreviations used: aHEI, Alternate Healthy Eating Index; aMED, alternate Mediterranean diet; DASH, Dietary Approaches to Stop Hypertension; FFQ, food-frequency questionnaire; IGF-1, insulin-like growth factor 1; IGFBP-3, insulin-like growth factor–binding protein 3; NHS, Nurses' Health Study; RCT, randomized controlled trial; SHBG, sex-hormone binding globulin; sR, soluble receptor; T2D, type 2 diabetes; WLVS, Women's Lifestyle Validation Study.

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proinsulin, C-peptide, insulin, insulin-like growth factor–binding protein 3 (IGFBP-3), insulin-like growth factor 1 (IGF-1), adiponectin, leptin, leptin soluble receptor (sR), total cholesterol, HDL cholesterol, triglycerides, folate, and sex-hormone binding globulin (SHBG) in a cross-sectional analysis.

METHODS

Study population

We conducted this analysis in the WLVS (Women's Lifestyle Validation Study), which is 1 of 3 studies in the Multi-Cohort Eating and Activity Study for Understanding Reporting Error and was designed to study the structure of measurement error that is associated with self-reported dietary and physical activity measures (8). The WLVS was conducted from June 2010 to March 2012 in a subset of participants in the NHS (Nurses' Health Study) and the NHS II, which are 2 prospective cohort studies of female registered nurses with biennial follow-up of various lifestyle and disease endpoints (9, 10). Of NHS and NHS II participants who had completed the 2006–2007 questionnaire cycles, had previously provided blood samples in 1989–1990 and 2000–2001, and had no history of coronary artery disease, stroke, cancer, or major neurologic disease, a random sample of 5509 women were invited to participate in the WLVS (**Supplemental Figure 1**). Of these women, 2423 individuals (44%) responded to the invitation, and of these women, 796 individuals (33%) consented to participate in an intensive data-collection protocol that included repeated measures of diet, physical activity, sleep, and biospecimen collections over the course of 1 y. This cross-sectional analysis used a baseline semiquantitative food-frequency questionnaire (FFQ), anthropometric measures, accelerometer measurements, and biospecimen samples. The sample size of participants who were included in our study was between 453 and 775 subjects depending on the biomarker. This study was approved by the Human Subjects Committees of the Harvard T.H. Chan School of Public Health and Brigham and Women's Hospital.

Assessment of diet

We estimated dietary intake with the use of the 152-item, self-administered, semiquantitative FFQ at the WLVS baseline. Participants were asked how often, on average, they consumed a specified common portion or serving size of specific foods (answers ranged from never to $\geq$6 times/d). We calculated nutrient intakes by multiplying the frequency of consumption by the nutrient content of the specified portion sizes of each food. We summed across the nutrient content of all food items in a subject's diet to form the individual nutrient variables, which we adjusted for total energy intake. We excluded participants with total daily energy intakes $<$600 kcal or $>$3500 kcal or with $>$70 blank items.

The DASH dietary pattern is based on foods and nutrients that were emphasized or minimized in the DASH diet for the prevention and treatment of hypertension (11). The aMED was based on the original Mediterranean diet scale by Trichopoulou et al. (12) for which it was shown that greater adherence to the traditional Mediterranean diet was associated with a significant reduction in total mortality. Differences between the aMED and the traditional Mediterranean diet scale were that potatoes were removed from the vegetable group, the fruit and nuts group was split into 2 groups, the dairy group was removed, including whole-grain products only, the meat group was limited to processed and red meats only, and alcohol was included whereby alcohol intake between 5 and 15 g/d was assigned 1 point (13). The aHEI 2010 was based on dietary factors that have been consistently associated with lower risk of chronic diseases in both clinical and epidemiologic studies and on the basis of the original aHEI that was developed in 2002 (14, 15). The calculation of individual DASH (16), aMED (17), and aHEI (14) dietary pattern–adherence scores has been described in detail previously. The components, scoring methods, and ranges of each of the 3 dietary patterns are detailed in **Table 1**. For each of the dietary patterns, a higher score was indicative of stronger adherence to that dietary pattern. The possible score range for each of the 3 dietary patterns was 8–39 for the DASH, 0–9 for the aMED, and 0–110 for the aHEI.

Assessment of biomarkers

Participants received a sample-collection kit that contained collection supplies. Blood was drawn by the participant's local laboratory into glass sodium-heparin collection tubes and returned to the processing facility with a cold pack via overnight courier. At the laboratory, the sample was centrifuged for 25 min at 4°C and at 1530 $\times$ *g*, separated into plasma, white blood cell, and red blood cell components, and aliquots were put into cryovials. Postprocessing, aliquots were transferred to vapor-phase liquid-nitrogen freezers for long-term storage.

Total cholesterol, HDL cholesterol, and triglycerides were measured colorimetrically on an automated analyzer (Olympus AU 400, Beckman Coulter Inc.) with the use of kits (Beckman Coulter Inc.) at the Laboratory of Lipid Metabolism and Cardiovascular Signaling in the Molecular Cardiology Research Institute, Tufts University. Folate was determined with the use of a 96-well plate microbial (*Lactobacillus casei*) assay, which was described by Horne and Patterson (18) and included the modifications of Tamura et al. (19), at the Vitamin Metabolism Laboratory at the Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University. SHBG was measured at the Mayo Clinic Medical Laboratories with the use of an ALPCO SHBG ELISA (11-SHBHU-E01; ALPCO). Proinsulin, C-peptide, insulin, IGFBP-3, IGF-1, adiponectin, leptin, and leptin-sR were measured from fasting blood samples with the use of an ELISA at the Cancer Prevention Research Unit of McGill University. Proinsulin was measured with the use of the Mercodia Proinsulin ELISA (Mercodia). C-peptide was measured with the use of the ALPCO C-peptide ELISA (ALPCO). Insulin was measured with the use of the Mercodia Insulin ELISA (Mercodia). Adiponectin was measured with the use of the Quantikine Human Total Adiponectin Immunoassay (DRP300; R&D Systems Europe Ltd.). Leptin was measured with the use of the Quantikine Human Leptin Immunoassay (DLP00; R&D Systems Europe Ltd.). Leptin-sR was measured with the use of the Quantikine Human Leptin-sR Immunoassay (DOBR00; R&D Systems Europe Ltd.). IGFBP-3 was measured with the use of the IDS-iSYS IGFBP-3 Assay (IS-4400; Immunodiagnostic Systems). IGF-1 was measured with the use of IDS-iSYS IGF-1 Assay (IS-3900; Immunodiagnostic Systems). Overall CVs were 5.8–9.3% for total cholesterol, 5.6–8.1% for HDL cholesterol, 6.0–9.9% for

TABLE 1
Components, scoring methods, and ranges of the DASH, aMED, and aHEI dietary patterns[1]

Component	Scoring method	Score range
DASH	In quintiles	
Fruits		1–5
Vegetables		1–5
Red and processed meats		1–5
Whole grains		1–5
Nuts and legumes		1–5
Sugar-sweetened beverages		1–4
Sodium		1–5
Low-fat dairy		1–5
aMED		
Fruit and fruit juices	Less than or greater than the median	0 or 1
Vegetables	Less than or greater than the median	0 or 1
Red and processed meats	Less than or greater than the median	1 or 0
Whole grains	Less than or greater than the median	0 or 1
Legumes	Less than or greater than the median	0 or 1
Nuts	Less than or greater than the median	0 or 1
Fish	Less than or greater than the median	0 or 1
Ratio of monounsaturated fat to saturated fat	Less than or greater than the median	0 or 1
Alcohol	5 ≤ alcohol ≤ 15 g/d or other	1 or 0
aHEI		
Fruit	In deciles, whereby 10 denotes ≥5 servings/d	0–10
Vegetables	In deciles, whereby 10 denotes ≥4 servings/d	0–10
Red and processed meats	In deciles, whereby 10 denotes 0 servings/d	10–0
Whole grains	In deciles, whereby 10 denotes 75 g/d	0–10
Nuts and legumes	In deciles, whereby 10 denotes 1 serving/d	0–10
Sugar-sweetened beverages and fruit juice	In deciles, whereby 10 denotes 0 servings/d	10–0
Long-chain n–3 fats (EPA + DHA)	In deciles, whereby 10 denotes 250 mg/d	0–10
Polyunsaturated fat	In deciles, whereby 10 denotes ≥10 g/d	0–10
trans Fat	In deciles, whereby 10 denotes ≤0.5 g/d	0–10
Alcohol	0 drinks/d = 2.5 0.1 to <0.5 drinks/d = 5 0.5–1.5 drinks/d = 10 1.6 to <2.0 drinks/d = 5 2.0 to <2.5 drinks/d = 2.5 ≥2.5 drinks/d = 0	0–10
Sodium	In deciles	10–0

[1] Inversely scored, thus lower intakes receive higher scores. aHEI, Alternate Healthy Eating Index; aMED, alternate Mediterranean diet; DASH, Dietary Approaches to Stop Hypertension.

triglycerides, 9.2% for folate, 2.1–5.6% for SHBG, 0.2–3.9% for proinsulin, 0.7–4.8% for C-peptide, 0.2–6.0% for insulin, 0.3–5.5% for IGFBP-3, 1.2–4.8% for IGF-1, 0.1–4.1% for adiponectin, 1.8–4.7% for leptin, and 2.5–6.9% for leptin-sR.

Assessment of covariates

We collected demographic and anthropometric data, including age, weight, and height, from the baseline questionnaire and calculated BMI (in kg/m^2) for each participant. Information on lifestyle and reproductive factors such as smoking status, postmenopausal status, postmenopausal hormone use, and multivitamin use was collected from the blood sample–collection questionnaire at baseline. We derived race (1976 and 1989); family history of diabetes (1992 and 1997); family history of myocardial infarction (1984 and 1997); parity and age at first birth (1996 and 2009); and diabetes incidence, diabetes medication use, and statin use (2010 and 2009) from the most-recent biennial NHS and NHS II questionnaires, respectively, that contained these data.

Statistical analysis

We grouped participants into quartiles of dietary pattern scores with the lowest quartile serving as the reference group. This method reduced the influence of outliers and did not assume the linearity of the relation (20). Biomarker measures were standardized for the batch effect as described by Rosner et al. (21). Briefly, the mean β coefficients from a linear regression model for each biomarker with a batch indicator variable was calculated. For each specific batch, the difference between the corresponding β coefficient from the model and the mean coefficient was subtracted from the unadjusted biomarker value to create a continuous measurement that was standardized to the mean batch (22).

We used multiple linear regression to evaluate the associations between dietary patterns and biomarkers. The distributions of biomarkers were assessed for normality and biomarkers with nonnormal distributions, which included all biomarkers in the analysis, were logarithmically transformed to approximate a normal distribution. We estimated the adjusted means of the log-transformed biomarkers as geometric means along with their

95% CIs. We also calculated the percentage difference in geometric means and their respective 95% CIs between quartile 1 and quartiles 2–4. Model 1 was adjusted for age (continuous), Caucasian race (yes or no), postmenopausal status and hormone use (premenopausal; postmenopausal-never use; postmenopausal-past use; or postmenopausal-current use), parity and age at first birth (nulliparous; 1–2 children at <25 y of age at first birth; 1–2 children at ≥25 y of age at first birth; ≥3 children at <25 y of age at first birth; or ≥3 children at ≥25 y of age at first birth), smoking status (never; past; current, 1–14 cigarettes/d; or current, ≥15 cigarettes/d), moderate-to-vigorous physical activity (quartiles), current multivitamin use (yes or no), family history of myocardial infarction (yes or no), family history of diabetes (yes or no), diabetes (yes or no), diabetes medication use (yes or no), and statin use (yes or no). DASH dietary patterns models were further adjusted for alcohol intake (0, 1.0–4.9, 5.0–14.9, or ≥15.0 g/d). Folate models were further adjusted for cold-cereal intake (in quartiles) and alcohol. Because BMI might have been on the causal pathway between dietary patterns and the biomarkers, we present models with and without adjustment for BMI. In a sensitivity analysis to minimize random measurement error in the dietary assessment, we replicated the main analysis with the use of the mean of the baseline FFQ and the FFQ at 1 y of follow-up.

We conducted tests for linear trends with the use of quartiles of dietary pattern variables as a continuous variable by assigning median values of quartiles to the variable. All statistical tests were 2-sided, and we considered $P < 0.05$ to be statistically significant. We conducted the statistical analyses with the use of SAS version 9.3 for UNIX software (SAS Institute Inc.).

RESULTS

The age-adjusted characteristics of the WLVS population by quartiles of the DASH, aMED, and aHEI dietary patterns are displayed in **Table 2**. Women with higher dietary pattern scores, which indicated greater diet quality, on average, were older in age, older at menopause, more likely to be postmenopausal but less likely to use hormone replacement therapy, and more likely to use statins; and had higher levels of moderate-to-vigorous physical activity, higher total energy intake, and lower BMI.

Associations between the DASH dietary pattern and the cardiometabolic and endocrine biomarkers are presented in **Table 3**. The DASH diet was significantly associated with several biomarkers in multivariable model 1 with adjustment for several lifestyle- and health-related characteristics such that participants at the highest quartile of the DASH dietary score had 9% higher HDL cholesterol, 21% higher SHBG, 28% lower leptin, 19% lower triglycerides, and 4% lower C-peptide compared with values of subjects in the lowest quartile (all P-trend ≤ 0.04). However, after further adjustment for BMI in model 2, most of these associations were attenuated but remained significantly lower for quartile 4 than for quartile 1 for leptin (14%) and triglycerides (14%) (P-trend = 0.03 and 0.01, respectively).

Associations between the aMED dietary pattern and the 13 cardiometabolic and endocrine biomarkers are shown in **Table 4**. In multivariable model 1, participants at the highest quartile of the aMED dietary score had 16% lower triglycerides and 19% higher SHBG (P-trend = 0.003 and 0.02, respectively), and after further adjustment for BMI, these comparisons were moderately attenuated but remained significant between the aMED and triglycerides whereby subjects in quartile 4 compared with in quartile 1 had 11% lower triglycerides (P-trend = 0.01). The aMED diet was not significantly associated with the other 11 biomarkers.

Associations between the aHEI dietary pattern and the 13 cardiometabolic and endocrine biomarkers are presented in **Table 5**. In multivariable model 1, the aHEI dietary pattern was significantly associated with several biomarkers whereby participants in the highest quartile of the aHEI dietary score had 18% lower leptin, 19% higher SHBG, and 16% lower insulin (all P-trend ≤ 0.02) compared with values for subjects in the lowest quartile. However, after further adjustment for BMI, most of the associations were no longer significant.

We repeated our main analysis by estimating the pattern scores from the mean of dietary intakes reported on the baseline FFQ and the 1-y follow-up FFQ, and the results are shown in **Supplemental Tables 1–3**. Overall, associations were weaker between the DASH diet and biomarkers but stronger for the AHEI dietary pattern.

DISCUSSION

In this cross-sectional study of 775 women, all 3 healthful dietary patterns were favorably associated with plasma concentrations of various cardiometabolic and endocrine biomarkers independent of numerous potential behavioral and health-related confounders. First, greater adherence to the DASH dietary pattern was associated with higher plasma concentrations of HDL and SHBG and lower concentrations of leptin, triglycerides, and C-peptide. Second, the aMED dietary pattern was associated with higher SHBG and lower triglycerides. Third, the aHEI dietary pattern was associated with higher SHBG and lower insulin and leptin. Last, some of these relations persisted after further adjustment for BMI, which indicated that the majority, but not all, of the associations may have been mediated by body weight.

The association between healthful dietary patterns and adipokines was inconclusive. Unlike our study, in an previous cross-sectional analysis of 1922 women in the NHS, adherence to the DASH and aHEI dietary patterns was positively associated with adiponectin before adjusting for BMI (23). In a cross-sectional study of 813 women in the NHS II, the aHEI was associated with lower leptin and insulin and higher leptin-sR and adiponectin before and after BMI adjustment (24). However, unlike in the current analysis, there was no adjustment for family history of disease or additional reproductive factors in the study. We did not find any associations between the aMED and adipokines in our study in contrast with previous studies. A meta-analysis of RCTs that compared the Mediterranean diet with control diets showed that the Mediterranean diet was associated with a significant increase in adiponectin (6). However, in a more recent meta-analysis of 16 RCTs with durations that ranged from 1 to 24 mo, healthy dietary pattern consumption (12 Mediterranean diet, one DASH diet, 2 Nordic diets, and one Tibetan diet) was associated with decreased CRP but was not associated with leptin, adiponectin, and other biomarkers (7). These results were likely due to the limited number of studies that have assessed non-CRP biomarkers as well as to the short durations and small sample sizes of many of the RCTs (7). Meta-analyses of prospective cohort studies have shown a clear inverse dose-response relation between adiponectin and risk of type 2 diabetes (T2D), but the associations with coronary artery disease,

TABLE 2
Age-adjusted characteristics of the WLVS population by quartiles of the DASH, aMED, and aHEI dietary patterns with the use of the baseline FFQ (n = 475)[1]

	DASH, quartiles				aMED, quartiles				aHEI, quartiles			
	1	2	3	4	1	2	3	4	1	2	3	4
n	107	103	122	98	97	152	77	107	124	122	121	108
Median score	18	22	25	29	2	3	5	6	48	56	65	74
Age,[2] y	60 ± 9[3]	63 ± 10	65 ± 9	67 ± 9	61 ± 10	63 ± 9	65 ± 9	67 ± 8	61 ± 10	64 ± 10	66 ± 9	65 ± 8
BMI, kg/m^2	28.3 ± 5.9	26.8 ± 5	26.2 ± 5.1	25.4 ± 5.1	28.1 ± 5.5	26.4 ± 5.3	26.9 ± 5.6	25.1 ± 4.9	27.9 ± 5.8	26.9 ± 6.1	26.5 ± 4.8	25.8 ± 5
Age at menopause,[2] y	48 ± 8	49 ± 6	49 ± 7	50 ± 5	48 ± 8	48 ± 7	50 ± 6	50 ± 5	47 ± 8	49 ± 6	50 ± 7	49 ± 6
Postmenopausal, %	84	79	83	82	83	84	83	80	86	82	83	82
Current PMH use, %	8	3	2	5	7	2	3	6	6	5	2	3
Caucasian, %	91	93	93	90	94	89	91	90	87	91	95	96
Diabetes, %	4	4	6	8	5	5	5	5	7	3	4	6
Diabetes medication use, %	3	5	4	6	5	3	5	7	5	4	4	5
Statin use, %	45	33	30	25	45	28	31	32	39	33	31	26
Current smoker, %	3	0	2	1	1	2	0	2	5	0	2	2
Moderate-to-vigorous physical activity, min/d	11 ± 14	17 ± 20	17 ± 22	23 ± 27	11 ± 14	16 ± 18	17 ± 23	28 ± 31	13 ± 17	16 ± 19	21 ± 27	19 ± 21
Total energy, kcal/d	1898 ± 523	1889 ± 551	2008 ± 554	2016 ± 578	1746 ± 485	1839 ± 561	2062 ± 556	2294 ± 504	1869 ± 533	1830 ± 545	1980 ± 537	2119 ± 578
Alcohol, g/d	12 ± 18	8 ± 11	10 ± 12	11 ± 14	8 ± 14	11 ± 14	12 ± 17	11 ± 12	8 ± 16	8 ± 11	12 ± 14	13 ± 14
Multivitamin use, %	64	59	61	64	57	63	62	62	65	67	56	60
Sodium, mg/d	2254 ± 734	2182 ± 693	2214 ± 716	2126 ± 796	2062 ± 625	2067 ± 729	2246 ± 772	2537 ± 761	2192 ± 718	2119 ± 717	2159 ± 690	2226 ± 782
Omega 3, mg/d	0.4 ± 0.3	0.4 ± 0.4	0.5 ± 0.4	0.6 ± 0.4	0.4 ± 0.4	0.4 ± 0.4	0.5 ± 0.4	0.6 ± 0.4	0.3 ± 0.4	0.5 ± 0.4	0.5 ± 0.4	0.6 ± 0.4
Whole grains, g/d	30 ± 16	37 ± 18	42 ± 16	40 ± 15	31 ± 17	37 ± 17	37 ± 14	41 ± 15	31 ± 16	41 ± 17	39 ± 17	40 ± 15
Foods, servings/d												
Fruit	1.1 ± 1.5	2 ± 2.2	2.8 ± 2.5	4.1 ± 2.9	1.5 ± 2.3	2.3 ± 2.6	2.8 ± 2.6	3.5 ± 2.6	1.3 ± 1.7	2.1 ± 2.2	3 ± 2.6	3.7 ± 2.9
Vegetables	0.9 ± 0.7	1.3 ± 1.3	1.8 ± 1.9	3.1 ± 3	0.9 ± 1	1.4 ± 1.7	1.9 ± 2	2.9 ± 2.6	1.1 ± 1.2	1.2 ± 1.1	1.8 ± 1.7	3.1 ± 3.1
Fish	0 ± 0.1	0.2 ± 1	0.1 ± 0.6	0.1 ± 0.5	0 ± 0	0.2 ± 0.9	0.1 ± 0.1	0.2 ± 0.8	0.1 ± 0.6	0.1 ± 0.1	0.1 ± 0.7	0.2 ± 0.8
Red meat	1.6 ± 2.7	1.5 ± 2.9	1.4 ± 2.9	1.1 ± 2.6	1.6 ± 2.7	1.6 ± 3.2	1.2 ± 2.8	0.8 ± 2.1	1.9 ± 3.2	1.6 ± 2.8	1.1 ± 2.5	1 ± 2.8
Processed meat	0.3 ± 1.1	0.1 ± 0.5	0.4 ± 1.4	0.2 ± 1.2	0.3 ± 1.1	0.3 ± 1.3	0.2 ± 1.1	0.1 ± 0.8	0.4 ± 1.4	0.2 ± 1.1	0.2 ± 0.9	0.3 ± 1.2
Nuts	0.2 ± 0.3	0.2 ± 0.3	0.3 ± 0.6	0.5 ± 0.8	0.1 ± 0.2	0.2 ± 0.3	0.4 ± 0.5	0.6 ± 1	0.1 ± 0.2	0.2 ± 0.2	0.3 ± 0.4	0.6 ± 0.9
Legumes	0.2 ± 0.8	0.5 ± 1.5	1 ± 2.1	2.2 ± 2.9	0.2 ± 1	1.1 ± 2.2	1.1 ± 2.2	1.1 ± 2.2	0.3 ± 1.2	0.8 ± 2	1 ± 2.1	1.6 ± 2.6
Low-fat dairy	0.8 ± 1.9	1.5 ± 2.8	2.3 ± 3.1	4.3 ± 4.5	1.4 ± 2.9	2.2 ± 3.3	2.4 ± 3.8	2.6 ± 3.5	1.9 ± 3	2.2 ± 3.3	2 ± 3.7	2.6 ± 3.5
Whole grains	0.5 ± 0.9	1.4 ± 2.2	1.2 ± 1.9	2.6 ± 3.1	0.8 ± 1.6	1.6 ± 2.6	1.1 ± 1.4	1.9 ± 2.5	1.6 ± 2.7	1.5 ± 2.4	1.3 ± 1.9	1.4 ± 2
Sugar-sweetened beverages, including fruit juices	0.7 ± 1.5	0.7 ± 1.8	1.5 ± 2.4	2 ± 3	1.1 ± 2.1	1.2 ± 2.3	1.1 ± 2.1	1.6 ± 2.8	2 ± 2.6	1.5 ± 2.6	1.4 ± 2.5	0.3 ± 1.5

[1] Characteristics in the table are given for the n = 475 women for whom the nonlipid biomarkers were assayed. Values were standardized to the age distribution of the study population unless otherwise indicated. aHEI, Alternate Healthy Eating Index; aMED, alternate Mediterranean diet; DASH, Dietary Approaches to Stop Hypertension; FFQ, food-frequency questionnaire; PMH, postmenopausal hormone; WLVS, Women's Lifestyle Validation Study.

[2] Values were not age adjusted.

[3] Mean ± SD (all such values).

TABLE 3
Plasma biomarkers by quartiles of the DASH dietary pattern in the WLVS population with the use of the baseline FFQ[1]

	Quartile				
	1	2	3	4	*P*-trend[2]
Score					—
Median	18	22	25	29	
Range	13–20	21–23	24–26	27–37	
Proinsulin (n = 437), pmol/L					
Model 1	18.4 (16.5, 20.4)[3]	18.4 (16.6, 20.5)	18.8 (17.2, 20.7)	17.9 (16.0, 19.9)	0.80
Model 2	17.8 (16.1, 19.7)	18.5 (16.7, 20.4)	18.9 (17.4, 20.7)	18.3 (16.6, 20.3)	0.62
C-peptide (n = 487), ng/mL					
Model 1	6.61 (6.44, 6.79)	6.45 (6.28, 6.62)	6.50 (6.35, 6.65)	6.33 (6.17, 6.49)	0.04
Model 2	6.54 (6.38, 6.71)	6.45 (6.30, 6.61)	6.51 (6.38, 6.65)	6.39 (6.24, 6.54)	0.26
Insulin (n = 417), mU/mL					
Model 1	7.53 (6.50, 8.72)	6.66 (5.75, 7.70)	7.30 (6.46, 8.24)	6.87 (5.93, 7.95)	0.56
Model 2	7.06 (6.18, 8.07)	6.67 (5.85, 7.61)	7.45 (6.67, 8.31)	7.13 (6.24, 8.14)	0.68
IGFBP-3 (n = 487), ng/mL					
Model 1	3.66 (3.49, 3.85)	3.74 (3.57, 3.93)	3.71 (3.56, 3.87)	3.82 (3.65, 4.00)	0.28
Model 2	3.67 (3.49, 3.86)	3.75 (3.57, 3.93)	3.71 (3.56, 3.87)	3.81 (3.64, 3.99)	0.34
IGF-1 (n = 487), ng/mL					
Model 1	103 (96, 111)	102 (95, 109)	108 (102, 114)	106 (99, 113)	0.43
Model 2	104 (97, 112)	102 (95, 109)	108 (102, 114)	105 (98, 112)	0.64
Adiponectin (n = 488), μg/mL					
Model 1	12.2 (10.9, 13.8)	13.0 (11.6, 14.6)	12.0 (10.8, 13.2)	14.6 (13.0, 16.3)	0.09
Model 2	12.8 (11.4, 14.3)	13.0 (11.7, 14.5)	11.9 (10.8, 13.0)	14.1 (12.7, 15.7)	0.39
Leptin (n = 487), ng/mL					
Model 1	35.9 (31.6, 40.8)	31.0 (27.3, 35.1)	30.2 (27.1, 33.6)	26.0 (23.0, 29.4)	0.001
Model 2	32.7 (29.8, 35.8)	31.0 (28.4, 33.9)	30.5 (28.3, 32.9)	28.1 (25.8, 30.7)	0.03
Leptin-sR (n = 487), ng/mL					
Model 1	29.6 (27.9, 31.3)	31.1 (29.4, 32.8)	29.1 (27.7, 30.5)	32.1 (30.4, 33.9)	0.14
Model 2	30.4 (28.9, 32.0)	31.1 (29.6, 32.7)	28.9 (27.7, 30.2)	31.4 (29.9, 33.0)	0.72
Total cholesterol (n = 775), mg/dL					
Model 1	209 (203, 216)	214 (207, 221)	205 (199, 211)	212 (206, 219)	0.95
Model 2	210 (203, 217)	214 (207, 221)	205 (199, 211)	212 (206, 219)	0.94
HDL cholesterol (n = 775), mg/dL					
Model 1	66 (63, 69)	70 (67, 73)	67 (65, 70)	72 (69, 75)	0.01
Model 2	67 (65, 70)	70 (68, 73)	67 (65, 69)	71 (69, 74)	0.14
Triglycerides (n = 488), mg/dL					
Model 1	104 (95, 113)	100 (92, 108)	94 (88, 101)	84 (78, 91)	0.0003
Model 2	100 (93, 109)	100 (92, 108)	95 (88, 102)	86 (80, 93)	0.01
Total folate (n = 493), ng/mL					
Model 1	10.1 (7.6, 13.4)	11.3 (8.6, 14.9)	8.5 (6.6, 10.9)	8.2 (6.3, 10.6)	0.16
Model 2	10.0 (7.5, 13.4)	11.3 (8.6, 14.9)	8.5 (6.6, 10.9)	8.2 (6.3, 10.7)	0.17
SHBG (n = 488), nmol/L					
Model 1	44.5 (40.0, 49.5)	47.7 (43.0, 52.9)	46.3 (42.4, 50.7)	53.7 (48.5, 59.4)	0.02
Model 2	46.5 (42.1, 51.4)	47.7 (43.3, 52.5)	46.0 (42.3, 50.0)	52.0 (47.3, 57.1)	0.17

[1] Geometric means and 95% CIs were calculated with the use of multiple linear regression models. Model 1 was adjusted for age (continuous), Caucasian race (yes or no), postmenopausal status and postmenopausal hormone use (premenopausal, never, past, or current use), parity and age at first birth (nulliparous; 1–2 children at <25 y of age at first birth; 1–2 children at ≥25 y of age at first birth; ≥3 children at <25 y of age at first birth; or ≥3 children at ≥25 y of age at first birth), family history of myocardial infarction (yes or no), family history of diabetes (yes or no), diabetes (yes or no), diabetes medication use (yes or no), statin use (yes or no), smoking status (never; past; current, 1–14 cigarettes/d; or current, ≥15 cigarettes/d), moderate-to-vigorous physical activity (min/d; quartiles), multivitamin use (yes or no), and alcohol intake (0, 1.0–4.9, 5.0–14.9, or ≥15.0 g/d). Models for folate were further adjusted for cold-cereal intake (quartiles). Model 2 was adjusted as for model 1 and for BMI (kg/m^2; continuous). DASH, Dietary Approaches to Stop Hypertension; FFQ, food-frequency questionnaire; IGF-1, insulin-like growth factor 1; IGFBP-3, insulin-like growth factor–binding protein 3; SHBG, sex-hormone binding globulin; sR, soluble receptor; WLVS, Women's Lifestyle Validation Study.

[2] Test for trend was based on a variable containing the median value for each quartile.

[3] Geometric mean; 95% CI in parentheses (all such values).

stroke, and hypertension were not as evident (25–28). Meanwhile, in obese persons, leptin may stimulate vascular inflammation, oxidative stress, and vascular smooth-muscle hypertrophy, which may contribute to the development of T2D, hypertension, and atherosclerosis (29).

Several studies have explored the association between dietary patterns and blood lipids. In our study, both DASH and aMED dietary patterns were associated with lower concentrations of triglycerides, and the DASH diet was associated with higher concentrations of HDL in models that were not adjusted for BMI.

TABLE 4
Plasma biomarkers by quartiles of the aMED dietary pattern in the WLVS population with the use of the baseline FFQ[1]

	Quartiles				
	1	2	3	4	*P*-trend[2]
Score					—
Median	2	3	5	6	
Range	0–2	3–4	5–5	6–9	
Proinsulin (n = 437), pmol/L					
Model 1	20.3 (18.3, 22.6)[3]	16.7 (15.3, 18.2)	20.3 (18.1, 22.9)	18.1 (16.4, 20.0)	0.36
Model 2	19.8 (17.9, 21.9)	16.9 (15.5, 18.3)	19.7 (17.7, 22.1)	18.6 (16.9, 20.4)	0.70
C-peptide (n = 487), ng/mL					
Model 1	6.65 (6.47, 6.83)	6.36 (6.22, 6.49)	6.57 (6.39, 6.76)	6.39 (6.23, 6.54)	0.10
Model 2	6.60 (6.43, 6.77)	6.38 (6.25, 6.50)	6.53 (6.36, 6.71)	6.43 (6.29, 6.58)	0.31
Insulin (n = 417), mU/mL					
Model 1	8.02 (6.91, 9.29)	6.13 (5.43, 6.92)	8.16 (6.95, 9.58)	7.06 (6.15, 8.09)	0.60
Model 2	7.72 (6.76, 8.83)	6.24 (5.59, 6.96)	7.85 (6.79, 9.07)	7.33 (6.48, 8.29)	0.92
IGFBP-3 (n = 487), ng/mL					
Model 1	3.60 (3.43, 3.79)	3.73 (3.59, 3.88)	3.78 (3.59, 3.98)	3.81 (3.64, 3.98)	0.11
Model 2	3.62 (3.44, 3.80)	3.73 (3.59, 3.88)	3.79 (3.60, 3.99)	3.80 (3.63, 3.97)	0.14
IGF-1 (n = 487), ng/mL					
Model 1	100 (93, 107)	105 (100, 111)	106 (99, 114)	109 (102, 116)	0.08
Model 2	100 (94, 108)	105 (100, 111)	107 (99, 115)	108 (101, 115)	0.13
Adiponectin (n = 488), μg/mL					
Model 1	11.7 (10.3, 13.2)	13.3 (12.1, 14.7)	13.1 (11.5, 14.9)	13.2 (11.8, 14.7)	0.22
Model 2	12.1 (10.7, 13.6)	13.1 (12.0, 14.4)	13.4 (11.9, 15.2)	12.8 (11.5, 14.2)	0.52
Leptin (n = 487), ng/mL					
Model 1	34.4 (30.2, 39.1)	28.7 (25.9, 31.8)	32.9 (28.7, 37.7)	28.3 (25.2, 31.9)	0.09
Model 2	32.1 (29.2, 35.2)	29.4 (27.3, 31.6)	31.0 (28.1, 34.2)	30.3 (27.9, 33.0)	0.56
Leptin-sR (n = 487), ng/mL					
Model 1	30.4 (28.7, 32.2)	30.3 (29.0, 31.8)	30.1 (28.3, 32.0)	30.5 (29.0, 32.2)	0.93
Model 2	31.0 (29.5, 32.7)	30.1 (28.9, 31.3)	30.7 (29.0, 32.4)	30.0 (28.6, 31.4)	0.42
Total cholesterol (n = 775), mg/dL					
Model 1	209 (202, 216)	213 (208, 219)	208 (201, 215)	208 (202, 215)	0.68
Model 2	209 (202, 217)	213 (207, 219)	208 (201, 215)	208 (202, 214)	0.58
HDL cholesterol (n = 775), mg/dL					
Model 1	67 (64, 70)	69 (66, 71)	69 (66, 72)	71 (68, 74)	0.09
Model 2	68 (65, 71)	68 (66, 71)	69 (66, 72)	70 (68, 73)	0.29
Triglycerides (n = 488), mg/dL					
Model 1	103 (94, 112)	99 (92, 105)	90 (82, 99)	87 (81, 94)	0.003
Model 2	100 (92, 109)	99 (93, 106)	89 (82, 97)	89 (83, 95)	0.01
Total folate (n = 493), ng/mL					
Model 1	9.5 (7.0, 12.9)	11 (8.7, 13.8)	9.2 (6.8, 12.4)	7.7 (6.0, 10.0)	0.20
Model 2	9.4 (6.9, 12.8)	11 (8.8, 13.9)	9.2 (6.8, 12.4)	7.8 (6.0, 10.1)	0.22
SHBG (n = 488), nmol/L					
Model 1	44.7 (40.1, 49.8)	46.6 (42.8, 50.8)	47.9 (42.7, 53.7)	53.0 (48.1, 58.5)	0.02
Model 2	46.2 (41.8, 51.0)	46.0 (42.5, 49.8)	49.3 (44.3, 54.8)	51.5 (47.0, 56.4)	0.07

[1] Geometric means and 95% CIs were calculated with the use of multiple linear regression models. Model 1 was adjusted for age (continuous), Caucasian race (yes or no), postmenopausal status and postmenopausal hormone use (premenopausal, never, past, or current use), parity and age at first birth (nulliparous; 1–2 children at <25 y of age at first birth; 1–2 children at ≥25 y of age at first birth; ≥3 children at <25 y of age at first birth; or ≥3 children at ≥25 y of age at first birth), family history of myocardial infarction (yes or no), family history of diabetes (yes or no), diabetes (yes or no), diabetes medication use (yes or no), statin use (yes or no), smoking status (never; past; current, 1–14 cigarettes/d; or current, ≥15 cigarettes/d), moderate-to-vigorous physical activity (min/d; quartiles), and multivitamin use (yes or no). Models for folate were further adjusted for cold-cereal intake (quartiles). Model 2 was adjusted as for model 1 and for BMI (kg/m^2; continuous). aMED, alternate Mediterranean diet; FFQ, food-frequency questionnaire; IGF-1, insulin-like growth factor 1; IGFBP-3, insulin-like growth factor–binding protein 3; SHBG, sex-hormone binding globulin; sR, soluble receptor; WLVS, Women's Lifestyle Validation Study.

[2] Test for trend was based on a variable containing the median value for each quartile.

[3] Geometric mean; 95% CI in parentheses (all such values).

A meta-analysis of RCTs with durations that ranged from 2 to 24 wk showed that, overall, the DASH diet was associated with a significant decrease of plasma cholesterol and LDL but was not significantly associated with fasting plasma glucose (30) compared with the effects of control diets. An 8-wk RCT in 48 women with polycystic ovary syndrome in Iran showed that adherence to the DASH diet than to a control diet resulted in a significant decrease in serum triglycerides and VLDLs (31). An RCT in 144 overweight or obese, unmedicated, hypertensive adults showed that the DASH diet with aerobic exercise and caloric restriction compared with the DASH diet alone and with usual diet controls was associated with significant decreases in

TABLE 5
Plasma biomarkers by quartiles of the aHEI dietary pattern in the WLVS population with the use of the baseline FFQ[1]

	Quartiles				
	1	2	3	4	*P*-trend[2]
Score					—
Median	48	56	65	74	
Range	28–53	53–60	60–69	69–99	
Proinsulin (n = 437), pmol/L					
Model 1	19.2 (17.4, 21.1)[3]	18.9 (17.1, 20.8)	18.4 (16.8, 20.3)	17.2 (15.6, 18.9)	0.11
Model 2	18.5 (16.9, 20.2)	19.0 (17.3, 20.8)	18.8 (17.1, 20.5)	17.4 (15.9, 19.1)	0.34
C-peptide (n = 487), ng/mL					
Model 1	6.50 (6.35, 6.66)	6.50 (6.34, 6.66)	6.51 (6.36, 6.66)	6.33 (6.18, 6.48)	0.12
Model 2	6.44 (6.30, 6.59)	6.50 (6.36, 6.65)	6.54 (6.40, 6.68)	6.36 (6.22, 6.50)	0.43
Insulin (n = 417), mU/mL					
Model 1	7.88 (6.93, 8.97)	7.77 (6.77, 8.92)	6.39 (5.64, 7.23)	6.60 (5.78, 7.55)	0.02
Model 2	7.44 (6.62, 8.36)	7.76 (6.86, 8.78)	6.63 (5.93, 7.42)	6.76 (6.00, 7.63)	0.12
IGFBP-3 (n = 487), ng/mL					
Model 1	3.65 (3.49, 3.80)	3.72 (3.57, 3.89)	3.78 (3.63, 3.94)	3.76 (3.61, 3.92)	0.28
Model 2	3.66 (3.50, 3.82)	3.72 (3.57, 3.89)	3.77 (3.62, 3.93)	3.76 (3.60, 3.92)	0.36
IGF-1 (n = 487), ng/mL					
Model 1	102 (96, 108)	106 (100, 112)	106 (100, 112)	106 (100, 112)	0.46
Model 2	103 (97, 109)	106 (100, 112)	106 (100, 112)	105 (99, 112)	0.63
Adiponectin (n = 488), μg/mL					
Model 1	11.8 (10.6, 13.1)	14.0 (12.6, 15.6)	12.6 (11.4, 14.0)	13.3 (12.0, 14.8)	0.28
Model 2	12.2 (11.0, 13.5)	14.0 (12.7, 15.5)	12.4 (11.3, 13.7)	13.1 (11.9, 14.5)	0.69
Leptin (n = 487), ng/mL					
Model 1	33.5 (29.9, 37.5)	30.7 (27.3, 34.4)	30.1 (26.9, 33.6)	27.6 (24.7, 30.9)	0.02
Model 2	31.0 (28.6, 33.5)	30.4 (28.1, 33.0)	31.4 (29, 33.9)	28.9 (26.7, 31.3)	0.30
Leptin-sR (n = 487), ng/mL					
Model 1	29.8 (28.4, 31.4)	29.8 (28.4, 31.4)	30.6 (29.2, 32.1)	31 (29.5, 32.5)	0.22
Model 2	30.5 (29.2, 31.9)	29.8 (28.5, 31.2)	30.2 (29.0, 31.6)	30.6 (29.3, 32.0)	0.78
Total cholesterol (n = 775), mg/dL					
Model 1	205 (199, 212)	212 (206, 219)	211 (205, 217)	213 (207, 220)	0.12
Model 2	206 (200, 212)	212 (206, 219)	211 (205, 217)	213 (207, 219)	0.15
HDL cholesterol (n = 775), mg/dL					
Model 1	68 (65, 71)	68 (65, 71)	70 (68, 73)	70 (68, 73)	0.13
Model 2	69 (66, 71)	68 (66, 71)	70 (68, 72)	70 (67, 72)	0.40
Triglycerides (n = 488), mg/dL					
Model 1	92 (85, 99)	97 (90, 105)	98 (91, 105)	89 (83, 96)	0.56
Model 2	90 (84, 97)	97 (90, 105)	98 (92, 106)	90 (84, 97)	0.94
Total folate (n = 493), ng/mL					
Model 1	8.2 (6.3, 10.6)	10.9 (8.4, 14.1)	11.1 (8.7, 14.1)	8.0 (6.2, 10.3)	0.81
Model 2	8.2 (6.3, 10.6)	10.9 (8.4, 14.1)	11.1 (8.7, 14.2)	8.0 (6.2, 10.3)	0.82
SHBG (n = 488), nmol/L					
Model 1	43.8 (39.9, 48.2)	49.0 (44.5, 54.0)	47.7 (43.5, 52.3)	52.2 (47.5, 57.3)	0.02
Model 2	45.5 (41.7, 49.7)	49.0 (44.9, 53.5)	46.8 (43.0, 50.9)	51.2 (46.9, 55.7)	0.13

[1] Geometric means and 95% CIs were calculated with the use of multiple linear regression models. Model 1 was adjusted for age (continuous), Caucasian race (yes or no), postmenopausal status and postmenopausal hormone use (premenopausal, never, past, or current use), parity and age at first birth (nulliparous; 1–2 children at <25 y of age at first birth; 1–2 children at ≥25 y of age at first birth; ≥3 children at <25 y of age at first birth; or ≥3 children at ≥25 y of age at first birth), family history of myocardial infarction (yes or no), family history of diabetes (yes or no), diabetes (yes or no), diabetes medication use (yes or no), statin use (yes or no), smoking status (never; past; current, 1–14 cigarettes/d; or current, ≥15 cigarettes/d), moderate-to-vigorous physical activity (min/d; quartiles), and multivitamin use (yes or no). Models for folate were further adjusted for cold-cereal intake (quartiles). Model 2 was adjusted as for model 1 and for BMI (kg/m^2; continuous). aHEI, Alternate Healthy Eating Index; FFQ, food-frequency questionnaire; IGF-1, insulin-like growth factor 1; IGFBP-3, insulin-like growth factor–binding protein 3; SHBG, sex-hormone binding globulin; sR, soluble receptor; WLVS, Women's Lifestyle Validation Study.

[2] Test for trend was based on a variable containing the median value for each quartile.

[3] Geometric mean; 95% CI in parentheses (all such values).

total cholesterol, triglycerides, and glucose concentrations and improved insulin sensitivity (32). The DASH diet with aerobic exercise and caloric restriction was also associated with lower LDL cholesterol and fasting glucose compared with the effect of usual diet controls (32). Atherogenic dyslipidemia, which is characterized by high-LDL, low-HDL, and high-triglyceride concentrations, is a feature of obesity, insulin resistance, and TD2 and is a precursor of cardiovascular disease (33). In addition, high triglyceride and low-HDL concentrations are metabolic risk factors that are part of the metabolic syndrome, which is positively associated with risks of cardiovascular disease and diabetes (34, 35).

We showed associations between some dietary patterns and endocrine biomarkers. The aHEI dietary pattern was associated with lower insulin, the DASH diet was associated with lower C-peptide, and all 3 dietary patterns were associated with higher SHBG. In a cross-sectional study in the NHS and Health Professionals Follow-up Study, the prudent dietary pattern, which is characterized by higher intakes of fruit, vegetables, whole grains, and poultry, was positively associated with plasma folate and inversely associated with insulin and homocysteine (36). Meanwhile, the Western dietary pattern, which is characterized by higher intakes of red meats, refined grains, and high-fat dairy, was positively associated with insulin, C-peptide, leptin, and homocysteine (36). A meta-analysis of 20 short-term RCTs has shown that the DASH diet could significantly reduce fasting insulin but not fasting blood glucose and HOMA-IR (37). Elevated C-peptide and insulin are markers of insulin resistance, which is implicated in the development of T2D and CVD (38). Fasting insulin has been associated with the incidence of cardiovascular disease (39, 40), and elevated C-peptide has been associated with the incidence of coronary artery disease and with cardiovascular and total mortality in individuals without diabetes (41, 42). In addition, lower SHBG was consistently associated with the incidence of T2D in epidemiologic studies (43).

Note that, although the dietary components of the 3 dietary patterns are similar, there are a few exceptions and additions to each individual dietary pattern. In addition, the scoring methods are slightly different, which might explain some of the differences that were shown in these associations. In addition, overall, associations between the 3 dietary patterns and biomarkers were similar when we calculated the dietary patterns on the basis of the mean of baseline and 1-y FFQs, which could have been due to the minimal change in diet over the 1-y period.

There are several strengths to our study. First, the large number of biomarkers that were available enabled a more thorough look into the associations between dietary patterns and cardiometabolic and endocrine risks. Second, diets were measured with the use of FFQs that were validated against multiple-day diet records; however, a potential misclassification may still have been a concern (44, 45). Third, because the WLVS was performed in a subset of NHS and NHS II participants, a wealth of data that have been available from several decades of previous data collection enabled adjustment for potential confounders. There are also some limitations to our study, including the cross-sectional design, which did not allow for any temporal causal inference. In addition, most participants were Caucasian nurses, which increased the internal validity but may have limited generalizability to other populations. Last, the single measure of biomarkers may have introduced some measurement error, and such nondifferential misclassification may have attenuated the results.

In conclusion, accumulating evidence supports a role for adherence to an overall healthful dietary pattern with numerous chronic disease and mortality endpoints although the precise mediators that underlie these benefits are largely unknown. We observed that 3 healthful dietary patterns are associated with some cardiometabolic and endocrine biomarkers, which may partly mediate previously reported relations with disease outcomes. Most associations may be partially mediated by BMI. Adherence to these dietary patterns can have a favorable impact on an individual's cardiometabolic and endocrine risk and subsequent chronic disease risk.

The authors' responsibilities were as follows—HBA: conducted the analysis, interpreted the data, and wrote the manuscript; HBA, FBH, and DKT: designed the analysis; HBA and DKT: had primary responsibility for the final content of the manuscript; VSM, CY, WCW, TH, FBH, and DKT: assisted in the interpretation of the data and edited the manuscript; WCW and FBH: obtained funding and managed and conducted the WLVS; and all authors: critically reviewed the manuscript for important intellectual content and read and approved the final manuscript. None of the authors reported a conflict of interest related to the study.

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