Dietary patterns and incident cardiovascular disease in the Multi-Ethnic Study of Atherosclerosis[1–3]

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ABSTRACT

Background: Empirically derived dietary patterns show strong cross-sectional associations with cardiovascular disease (CVD) risk factors in the Multi-Ethnic Study of Atherosclerosis (MESA).

Objective: We investigated associations between dietary patterns and risk of incident CVD in 5316 men and women.

Design: White, black, Hispanic, and Chinese adults aged 45–84 y and free of CVD and diabetes completed food-frequency questionnaires at baseline. Dietary patterns were derived by using principal components analysis. Incident CVD events (n = 207) identified over a median of 4.6 y were verified by death certificates and medical records.

Results: The Fats and Processed Meat dietary pattern was associated with a greater risk (hazard ratio quintile 5 compared with quintile 1: 1.82; 95% CI: 0.99, 3.35), and the Whole Grains and Fruit dietary pattern was associated with a lower risk (0.54; 0.33, 0.91) of CVD after adjustment for demographic and lifestyle confounders. Associations between CVD and the Whole Grains and Fruit dietary pattern remained strong after adjustment for waist circumference, blood pressure, lipids, or inflammatory markers.

Conclusions: Data from this multiethnic cohort reinforce findings from predominantly white cohorts, ie, that "healthy" and "unhealthy" dietary patterns empirically exist and that these patterns are important lifestyle predictors of CVD incidence. *Am J Clin Nutr* 2009;90:647–54.

INTRODUCTION

Dietary pattern research is of considerable interest in nutritional epidemiology. Position statements from the American Heart Association (1), American Diabetes Association (2), and American Cancer Society (3) emphasize the importance of healthful dietary patterns in prolonging life quality and slowing disease rates.

Considering these guidelines, we used data from the Multi-Ethnic Study of Atherosclerosis (MESA) to create empirical dietary pattern scores that globally reflect dietary intake and to characterize their cross-sectional associations with markers of cardiovascular disease (CVD). In MESA, dietary patterns derived by principal components analysis (PCA) showed strong cross-sectional associations with markers of inflammation (4), the ratio of albumin to creatinine (5), and other traditional CVD risk factors (4). The current analysis extends our previous cross-sectional work to study associations between empirical dietary patterns and incident CVD.

On the basis of our previous findings, we hypothesized that our PCA-defined dietary pattern characterized by healthy food intake (greater intakes of whole grains, fruit and vegetables, low-fat dairy products, and nuts and seeds, ie, the Whole Grains and Fruit dietary pattern) would be inversely associated with the risk of CVD, whereas our PCA-defined dietary pattern characterized by unhealthy food intake (greater intakes of red or processed meats, fried foods, desserts, and other refined grains ie, the Fats and Processed Meat dietary pattern) would be positively associated with risk of CVD. We hypothesized that these associations would be independent of demographics and lifestyle factors, but may be partly mediated by hemodynamic, inflammatory, and/or other traditional risk factor pathways.

SUBJECTS AND METHODS

Participants

MESA is a population-based study of 6814 white, African American, Hispanic, and Chinese adults aged 45–84 y and free of clinical CVD. The participants' demographic, lifestyle, and clinical characteristics were collected in 6 field centers: Baltimore City and County, MD; Chicago, IL; Forsyth County, NC; New York, NY; Los Angeles County, CA; and St Paul, MN (6). Each examination cycle spanned ≈2 y, with baseline (2000–2002) and 3 follow-up exams conducted from 2002 to 20003, 2004 to 2005, and 2005 to 2007. Institutional review board approval was obtained, and participants gave informed consent. The current longitudinal investigation includes data from 5316 (2501 men and 2815) women MESA participants (2271 whites,

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1291 blacks, 1091 Hispanics, and 663 Chinese), excluding individuals with prevalent diabetes (n = 764), those whose follow-up time was equal to zero or missing (n = 25), and those who provided insufficient or implausible dietary information (<600 or ≥6000 kcal/d or unusual skip/repeat patterns; n = 630). (For details, *see* reference 4.)

Dietary assessment

At the baseline examination, participants completed a 120-item food-frequency questionnaire (FFQ) quantifying usual intake over the past year (4). The FFQ was previously validated in sample of whites, blacks, and Hispanics and modified to include Chinese dishes (4, 7). Correlation coefficients for validity were statistically significant for most nutrients (mean r = 0.62 for urban non-Hispanic whites, 0.61 for rural non-Hispanic whites, 0.50 for African Americans, and 0.41 for Hispanics) and did not differ between subgroups of obesity or diabetes status. The median correlation coefficient for the total sample was 0.49. For reproducibility, the mean correlation for nutrients evaluated was 0.62 (median r = 0.63) and did not differ between subgroups. Participants recorded the serving size (small, medium, or large) and frequency (times per day, week, or month) of consumption of each FFQ item. Responses were converted to servings per day by multiplying consumption frequency by reported serving size, with weights of 0.5, 1.0, and 1.5 applied to small, medium, and large serving sizes, respectively (7).

Dietary patterns

Dietary patterns were derived from 47 food groups by PCA (SAS PROC FACTOR, with orthogonal varimax rotation) (4). Four dietary patterns were retained as previously described (4). Food groups with the highest factor loads for each dietary pattern were as follows: Fats and Processed Meat dietary pattern (high intake of added fats, processed meat, fried potatoes, and desserts), Vegetables and Fish (several vegetable groups, fish, soup, Chinese foods, red meat, poultry, and soy), Beans, Tomatoes, and Refined Grains (beans, tomatoes, refined grains, high-fat dairy foods, avocado/guacamole, and red meat), and the Whole Grains and Fruit Dietary Pattern (whole grains, fruit, nuts and seeds, green leafy vegetables, and low-fat dairy foods). (*See* **Appendix A** for further details.)

The participants' scores for each dietary pattern were calculated as follows:

$$\Sigma\ [(\text{food group}_i\ \text{servings/d}) \times (\text{food group}_i\ \text{factor loading})] \quad (1)$$

where i = food groups 1–47. A higher score indicates greater conformity with the pattern being calculated. Scores were categorized into quintiles separately for each pattern. By design of the PCA, dietary patterns are mutually independent (ie, uncorrelated) with a mean of 0 and an SD of 1.

Outcome assessment

The main outcome of the current analysis was total incident CVD. Secondary outcomes included incident CVD (hard endpoints only), total incident coronary heart disease (CHD), incident CHD (hard endpoints only), myocardial infarction (fatal and nonfatal), and revascularization (**Table 1**). Participants were followed for incident CVD events from baseline until the participant's follow-up 6 telephone interview. At intervals of 9 to 12 mo, an interviewer contacted the participants to inquire about all hospital admissions, cardiovascular outpatient diagnoses and procedures, and deaths. In addition, MESA occasionally identified medical encounters through cohort clinic visits, participant call-ins, medical record abstractions, or obituaries. To verify self-reported diagnoses, death certificates and medical records for hospitalizations and selected outpatient cardiovascular diagnoses and procedures were reviewed and adjudicated by a medical endpoints committee. Hospital records were obtained for an estimated 98% of hospitalized cardiovascular events and some information on 95% of outpatient diagnostic encounters. CVD events used in these analyses were centrally adjudicated by a physician panel with use of standard diagnostic information abstracted from the medical records for hospitalized events and additionally with use of informant interview data collected for fatal events. Additional details were published previously (8).

TABLE 1
Cardiovascular disease (CVD)–related outcomes and component diseases[1]

Outcome and components (any of the following)
All CVD (n = 207)
Myocardial infarction
Resuscitated cardiac arrest
Definite angina
Probable angina (if followed by revascularization)
Stroke
Stroke death
CHD death
Other atherosclerotic death
Other CVD death
Hard CVD (n = 139)
Myocardial infarction
Resuscitated cardiac arrest
Stroke (not TIA)
CHD death
Stroke death
All CHD (n = 150)
Myocardial infarction
Resuscitated cardiac arrest
Definite angina
Probable angina (if followed by revascularization)
CHD death
Hard CHD (n = 87)
Myocardial infarction
Resuscitated cardiac arrest
CHD death
Myocardial infarction (n = 72)
Revascularization (n = 123)

[1] CHD, coronary heart disease; TIA, transient ischemic attack.

Follow-up

Time (in days) from exam 1 until the follow-up 6 call was calculated for each participant in the cohort (total follow-up time). Separate time to (first) event or last follow-up variable were calculated for each type of event. Participants for whom one or more instances of an event were recorded had the time from exam 1 until the first instance of an event recorded as the time to event value. Participants who were lost-to-follow-up were censored when their status was last known. Participants who missed a follow-up call but who subsequently completed a follow-up call were included.

Assessment of CVD risk factors and other relevant variables

Seated resting blood pressure was measured by using a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon; GE Healthcare, Milwaukee, WI). Three measurements were taken; the average of the last 2 measurements was used in analyses. Body mass index (BMI; in kg/m^2) was calculated from measured weight and height. Waist circumference was measured in centimeters at the umbilicus.

C-reactive protein (CRP), interleukin-6 (IL-6), homocysteine, and fibrinogen concentrations were measured in blood samples collected at baseline, processed (9), and stored at −80°C until analyzed. CRP and fibrinogen antigen were measured in plasma with a BNII nephelometer (N High Sensitivity CRP and N Antiserum to Human Fibrinogen; Dade Behring Inc, Deerfield, IL); the average analytic CVs were <6% and <3%, respectively. IL-6 concentrations were measured by ultrasensitive enzyme-linked immunosorbent assay (Qantikine HS Human IL-6 Immunoassay; R&D Systems, Minneapolis, MN; average CV <7%). Plasma homocysteine was measured by polarization immunoassay with an IMx Analyzer (IMx Homocysteine Assay; Axis Biochemicals ASA, Oslo, Norway; average CV <5%).

Total and HDL-cholesterol concentrations were measured directly with reagents from Roche Diagnostics, Indianapolis, IN (analyzed at the Collaborative Studies Clinical Laboratory, Fairview–University Medical Center; Minneapolis, MN; average CVs <2% and <3%, respectively). LDL cholesterol was calculated with the Friedewald equation (10). Information on baseline demographics, education, medication use, smoking history, and physical activity were collected with a combination of self-administered and interviewer-administered questionnaires.

Statistical analysis

Participants' baseline demographic, lifestyle, and clinical characteristics were calculated according to dietary pattern score quintiles 1, 3, and 5 for each of the Fats and Processed Meat and Whole Grains and Fruit dietary patterns. *P* for linear trends across quintiles were calculated with the original dietary pattern score modeled as a continuous variable. With the exception of age, sex, and race-ethnicity, all such values were adjusted for baseline age in years and sex. Cox proportional hazards regression was used to estimate hazard ratios (HRs) and 95% CIs for CVD outcomes across dietary pattern score quintiles. Two multivariable models were used to assess relations between dietary patterns and CVD outcomes. Model 1 adjusted for age (in y, continuous), sex, race-ethnicity (white, black, Hispanic, and Chinese), examination site (CA, MN, NY, IL, NC, and MD), and daily energy intake (continuous). Model 2 included the variables in model 1 plus attained education level (less than, equivalent to, and more than high school), time in active leisure activity [ie, walking for transportation and pleasure; moderate-to-heavy conditioning activities, including running; sports activities (in metabolic equivalent tasks–min/wk); and more sedentary leisure activities (ie, sitting or reclining activities, eg, television watching or reading (in metabolic equivalent tasks–min/wk)], smoking (current, former, or never smoker and pack-years), and dietary supplement use (less than compared with at least weekly frequency; as a proxy for a healthy behavior pattern)]. In the event that associations between a given dietary pattern and outcome were significant, 4 models including collections of variables that possibly mediate associations between dietary patterns and CVD were explored: model 3a included baseline waist circumference (in cm); model 3b included baseline systolic and diastolic blood pressure (mm Hg); model 3c included baseline CRP, IL-6, fibrinogen, and homocysteine (continuous, log values); and model 3d included baseline HDL-cholesterol and LDL-cholesterol concentrations (mg/dL).

Interactions between dietary patterns and sex and race-ethnicity were calculated by adding cross-product terms [eg, dietary pattern score (continuous) × sex] to model 2. All analyses were performed with SAS version 9.1 (SAS Institute Inc, Cary, NC).

RESULTS

Characteristics of the participants according to Fats and Processed Meat and Whole Grains and Fruit dietary patterns are shown in **Table 2**. High scores on the Fats and Processed Meat pattern were associated with male sex, younger age, white race-ethnicity, and age- and sex-adjusted estimates of prevalent current smoking, inactivity during leisure, higher BMI and waist circumference, and higher concentrations of inflammatory markers and LDL cholesterol. High scores on the Whole Grains and Fruit dietary pattern were associated with female sex, older age, white race-ethnicity, and age- and sex-adjusted estimates of prevalent nonsmoking, more time spent in active leisure pursuits, and higher concentrations of HDL cholesterol but lower concentrations of inflammatory markers and LDL cholesterol.

Dietary patterns and total incident CVD

Over an average of 4 y of surveillance, ≈4% of our sample developed some form of CVD (207 events). Higher Fats and Processed Meat dietary pattern scores were associated with a significantly greater relative risk of incident CVD, whereas high Whole Grains and Fruit dietary pattern scores were associated with a lower relative risk of incident CVD (**Table 3**). Incident CVD was not associated with scores on either the Vegetables and Fish or the Beans, Tomatoes, and Refined Grains dietary pattern (Table 3).

After adjustment for demographic characteristics and lifestyle factors, the HRs for CVD across quintiles of the Fats and Processed Meat dietary pattern were attenuated, and the association was no longer statistically significant (HR for quintile 5 compared with quintile 1: 1.82; 95% CI: 0.99, 3.35; *P* for trend = 0.12; model 2, Table 3). When adjusted for baseline systolic and diastolic blood pressure, estimates were similar to those produced from model 3 (HR for quintile 5 compared with quintile 1: 1.81; 95% CI: 0.99, 3.31; *P* for trend = 0.11; model 3b), but were even more strongly attenuated when adjusted for baseline waist circumference (HR for quintile 5 compared with quintile 1: 1.74; 95% CI: 0.94, 3.20; *P* for trend = 0.14; model 3a) or other possible mediating factors, including baseline inflammatory markers (HR for quintile 5 compared with quintile 1:

TABLE 2

Baseline demographic, lifestyle, and clinical characteristics of 5316 men and women from the Multi-Ethnic Study of Atherosclerosis (MESA) according to scores on 2 empirically derived dietary patterns: Fats and Processed Meat and Whole Grains and Fruit[1]

	Factor 1: Fats and Processed Meat pattern				Factor 4: Whole Grains and Fruit pattern			
	Quintile 1	Quintile 3	Quintile 5	*P* for trend	Quintile 1	Quintile 3	Quintile 5	*P* for trend
Sex (% male)[2]	36.4	45.8	57.8	<0.001	59.5	44.8	42.1	<0.001
Age (y)[2]	62.8 ± 0.3[3]	61.8 ± 0.3	59.5 ± 0.3	<0.001	59.2 ± 0.3	61.8 ± 0.3	64.0 ± 0.3	<0.001
Race-ethnicity[2]				<0.001				<0.001
White (%)	24.0	46.9	51.1		15.7	43.2	63.9	
Black (%)	13.5	25.4	35.7		21.7	26.1	21.9	
Hispanic (%)	6.2	20.6	12.0		28.6	23.7	11.4	
Chinese (%)	31.7	7.1	1.3		34.0	7.0	11.4	
>High school education (%)[4]	72.4	84.6	89.6	<0.001	70.1	84.6	92.3	<0.001
Current smoker (%)[4]	5.6	14.1	25.4	<0.001	16.7	14.0	12.3	0.002
Pack-years[4]	5.7 ± 0.7	9.9 ± 0.7	17.9 ± 0.7	<0.001	10.3 ± 0.7	11.8 ± 0.7	10.9 ± 0.7	0.63
Active leisure (MET-min/wk)	2470 ± 94	2476 ± 93	2439 ± 94	0.28	1864 ± 94	2424 ± 92	3017 ± 93	<0.001
Inactive leisure (MET-min/wk)[4]	1390 ± 34	1710 ± 33	1976 ± 34	<0.001	1617 ± 34	1587 ± 34	1722 ± 34	0.07
Weekly supplement use (%)[4]	59.4	58.7	56.7	0.58	58.3	57.6	57.4	0.60
BMI (kg/m^2)[4]	26.3 ± 0.2	28.1 ± 0.2	29.8 ± 0.2	<0.001	27.5 ± 0.2	28.2 ± 0.2	27.8 ± 0.2	0.57
Waist circumference (cm)[4]	92.5 ± 0.4	97.3 ± 0.4	102.2 ± 0.4	<0.001	95.7 ± 0.4	97.6 ± 0.4	96.9 ± 0.4	0.46
Systolic blood pressure (mm Hg)[4]	125.1 ± 0.6	125.3 ± 0.6	127.1 ± 0.6	0.004	127.1 ± 0.6	125.8 ± 0.6	123.2 ± 0.6	<0.001
Diastolic blood pressure (mm Hg)[4]	71.7 ± 0.3	71.8 ± 0.3	72.5 ± 0.3	0.03	72.5 ± 0.3	72.0 ± 0.3	71.0 ± 0.3	0.002
CRP (mg/dL)[4,5]	1.34 (1.25, 1.43)	1.86 (1.74, 1.99)	2.32 (2.17, 2.48)	<0.001	1.82 (1.70, 1.95)	1.87 (1.75, 2.00)	1.66 (1.55, 1.77)	0.01
IL-6 (mg/dL)[4,5]	1.04 (1.00, 1.08)	1.17 (1.13, 1.22)	1.36 (1.30, 1.41)	<0.001	1.24 (1.19, 1.29)	1.18 (1.13, 1.23)	1.14 (1.10, 1.19)	0.01
Fibrinogen (mg/dL)[4,5]	329 (325, 333)	333 (329, 337)	343 (339, 347)	<0.001	339 (335, 343)	334 (330, 338)	330 (326, 334)	0.002
Homocysteine (mg/dL)[4,5]	8.5 (8.4, 8.7)	8.8 (8.7, 9.0)	9.0 (8.9, 9.2)	<0.001	8.9 (8.8, 9.1)	8.7 (8.6, 8.9)	8.6 (8.5, 8.7)	<0.001
HDL cholesterol (mg/dL)[4]	51.0 ± 0.4	51.8 ± 0.4	50.9 ± 0.4	0.38	50.3 ± 0.4	51.7 ± 0.4	53.1 ± 0.4	<0.001
LDL cholesterol (mg/dL)[4]	116.7 ± 1.0	117.9 ± 1.0	119.1 ± 1.0	0.03	118.6 ± 1.0	117.5 ± 1.0	115.4 ± 1.0	0.02

[1] MET, metabolic equivalent task (ratio of the calculated metabolic rate to the resting metabolic rate, where one MET is the caloric consumption by an individual while at complete rest); CRP, C-reactive protein; IL-6, interleukin-6. Data and *P* values were derived from linear regression, with the exception of categorical variables (chi-square tests).

[2] Values were unadjusted.

[3] Mean ± SE (all such values).

[4] Values were adjusted for sex and age (in y, continuous).

[5] Because of a skewed distribution, values were log transformed for analysis and are presented as geometric means (95% CIs).

1.62; 95% CI; 0.87, 3.01; *P* for trend = 0.17; model 3c) and baseline HDL and LDL cholesterol (HR for quintile 5 compared with quintile 1: 1.65; 95% CI: 0.89, 3.04; *P* for trend = 0.18; model 3d).

Associations between the Whole Grains and Fruit dietary pattern and incident CVD were robust to multiple adjustments and were similar in magnitude to the estimates across quintiles of the Fats and Processed Meat pattern. For example, after adjustment for differences in demographic characteristics and lifestyle factors, participants scoring above the 80th percentile of the Whole Grains and Fruit pattern had a 46% lower CVD risk compared with those scoring below the 20th percentile (HR for quintile 5 compared with quintile 1: 0.54; 95% CI: 0.33, 0.91; *P* for trend = 0.007; model 2, Table 3). HRs for quintile 5 compared with quintile 1 were virtually unchanged with additional adjustment for possible mediating factors (models 3a-3d), such as waist circumference (0.56; 95% CI: 0.33, 0.94; *P* for trend = 0.01), blood pressure (0.57; 95% CI: 0.34, 0.96; *P* for trend = 0.01), inflammation (0.55; 95% CI: 0.32, 0.93; *P* for trend = 0.06), and lipids (0.56; 95% CI: 0.33, 0.94; *P* for trend = 0.01).;

Participants simultaneously scoring in the lowest Fats and Processed Meat quintile and in the highest Whole Grains and Fruit quintile (*n* = 226) had a 72% lower CVD risk (HR: 0.28; 95% CI: 0.10, 0.80) compared with those scoring simultaneously in the highest Fats and Processed Meat quintile and lowest Whole Grains and Fruit quintile (*n* = 251).

Dietary patterns and other cardiovascular outcomes

Although event numbers were low, Whole Grains and Fruit pattern scores were also significantly associated with hard CVD events [including myocardial infarction (MI), resuscitated cardiac arrest, stroke, CHD death, stroke death; Table 1], hard CHD events (including MI, resuscitated cardiac arrest, and CHD death), and MI alone (**Table 4**). Associations with other outcomes, such

TABLE 3
Rates per person years and hazard ratios (and 95% CIs) for any cardiovascular disease according to quintile (Q) of 4 empirically derived dietary patterns in 5316 men and women from the Multi-Ethnic Study of Atherosclerosis (MESA)[1]

Dietary pattern	Q1	Q2	Q3	Q4	Q5	*P* for trend[2]
Fats and Processed Meat (events/person-years)	32/4877	41/4830	37/4891	46/4833	51/4820	
Model 1[3]	1.00	1.22 (0.76, 1.95)	1.16 (0.70, 1.92)	1.46 (0.87, 2.44)	2.10 (1.16, 3.81)	0.03
Model 2[4]	1.00	1.21 (0.75, 1.94)	1.14 (0.69, 1.89)	1.41 (0.84, 2.37)	1.82 (0.99, 3.35)	0.10
Vegetables and Fish (events/person-years)	39/4802	43/4843	52/4871	49/4850	24/4886	
Model 1[3]	1.00	1.18 (0.76, 1.82)	1.49 (0.98, 2.27)	1.37 (0.88, 2.12)	0.85 (0.47, 1.54)	0.71
Model 2[4]	1.00	1.27 (0.82, 1.97)	1.63 (1.06, 2.49)	1.51 (0.96, 2.36)	0.98 (0.54, 1.79)	0.38
Beans, Tomatoes, and Refined Grains (events/person-years)	46/4849	43/4851	50/4876	39/4877	29/4799	
Model 1[3]	1.00	0.99 (0.65, 1.50)	1.17 (0.78, 1.75)	0.89 (0.56, 1.39)	0.80 (0.45, 1.41)	0.75
Model 2[4]	1.00	0.99 (0.65, 1.50)	1.15 (0.76, 1.72)	0.88 (0.56, 1.39)	0.80 (0.45, 1.42)	0.79
Whole Grains and Fruit (events/person-years)	40/4811	42/4836	46/4841	42/4916	37/4848	
Model 1[3]	1.00	0.78 (0.50, 1.22)	0.77 (0.49, 1.21)	0.62 (0.39, 0.99)	0.51 (0.31, 0.85)	0.002
Model 2[4]	1.00	0.81 (0.52, 1.27)	0.82 (0.52, 1.30)	0.67 (0.41, 1.08)	0.54 (0.33, 0.91)	0.007

[1] Hazard ratios (and 95% CIs) generated by Cox proportional hazards regression, with Q1 as the referent.
[2] *P* for linear trend across quintiles was calculated with the dietary pattern score variable modeled as a continuous variable.
[3] Adjusted for study center, age, sex, race-ethnicity, and energy intake (kcal/d).
[4] Adjusted for the variables in model 1 plus education, physical activity, smoking status, pack-years, and weekly dietary supplement use.

as total CHD (which includes definite and probable angina in addition to outcomes listed for hard CHD) and coronary revascularization were not statistically significant, but suggested relations similar to those observed for all CVD (Table 4). The Fats and Processed Meat pattern was not associated with these additional outcomes (data not shown).

Interactions

Interactions between dietary patterns and sex and race-ethnicity were not statistically significant ($P \geq 0.17$). For example, although stratum-specific estimates were not always formally significant, the magnitude of HRs were similar in men and women for the Fats and Processed Meat dietary pattern [HR for quintile 5 compared with quintile 1 for men (1.61; 95% CI: 0.76, 3.42) and for women (2.57; 95% CI: 0.91, 7.23); model 2; *P* for interaction = 0.49] and for the Whole Grains and Fruit dietary pattern (HR for quintile 5 compared with quintile 1 for men: 0.51; 95% CI: 0.27, 0.97) and for women (0.58; 95% CI: 0.21, 1.60); model 2; *P* for interaction = 0.17]. Estimates were also similar between the 4 race-ethnicity groups, although the CIs were wide, especially in the Chinese, in whom there were only 2 cases in quintile 5 of the Fats and Processed Meat pattern and 1 case in quintile 5 of the Whole Grains and Fruit pattern (model 2): quintile 5 compared with quintile 1 of the Fats and Processed Meat pattern: 1.82 (95% CI: 0.70, 4.71) for whites, 27.2 (95% CI: 2.76, 267) for the Chinese, 4.80 (95% CI: 0.80, 24.1) for blacks, and 1.49 (95% CI: 0.38, 5.80) for Hispanics (*P* for interaction = 0.23); quintile 5 compared with quintile 1 for the Whole Grains and Fruit pattern: 0.67 (95% CI: 0.30, 1.49) for whites, 0.66 (95% CI:

TABLE 4
Hazard ratios (and 95% CIs) for select cardiovascular outcomes according to quintile (Q) of the Whole Grains and Fruit dietary pattern in 5316 men and women from the Multi-Ethnic Study of Atherosclerosis (MESA)[1]

	Whole Grains and Fruit dietary pattern score					
	Q1	Q2	Q3	Q4	Q5	*P* for trend[2]
Hard CVD (events/person-years)	27/4844	28/4865	37/4860	29/4940	18/4900	
Model 2[3]	1.00	0.75 (0.43, 1.30)	0.93 (0.54, 1.58)	0.64 (0.36, 1.14)	0.37 (0.19, 0.72)	0.002
CHD all (events/person-years)	28/4837	33/4852	32/4863	29/4945	28/4871	
Model 2[3]	1.00	0.92 (0.55, 1.56)	0.83 (0.48, 1.42)	0.68 (0.38, 1.21)	0.63 (0.34, 1.16)	0.05
Hard CHD (events/person-years)	16/4870	20/4882	24/4883	18/4969	9/4923	
Model 2[3]	1.00	0.91 (0.46, 1.81)	1.02 (0.52, 2.00)	0.70 (0.33, 1.46)	0.35 (0.14, 0.85)	0.01
Myocardial infarction (events/ person years)	13/4871	17/4882	22/4882	13/4969	7/4923	
Model 2[3]	1.00	0.98 (0.46, 2.10)	1.18 (0.56, 2.48)	0.65 (0.28, 1.52)	0.34 (0.12, 0.94)	0.03
Revascularization (events/person-years)	21/4848	26/4864	28/4864	23/4950	25/4884	
Model 2[3]	1.00	1.02 (0.56, 1.85)	1.03 (0.56, 1.88)	0.76 (0.40, 1.47)	0.79 (0.40, 1.55)	0.36

[1] Hazard ratios (and 95% CIs) generated by Cox proportional hazards regression, with Q1 as the referent. CVD, cardiovascular disease; CHD, coronary heart disease.
[2] *P* for linear trend across quintiles was calculated with the dietary pattern score variable modeled as a continuous variable.
[3] Adjusted for study center, age, sex, race-ethnicity, energy intake (kcal/d), education, physical activity, smoking status, pack-years, and weekly dietary supplement use.

0.06, 7.37) for the Chinese, 0.26 (95% CI: 0.05, 1.38) for blacks, and 0.59 (95% CI: 0.20, 1.77) for Hispanics (*P* for interaction = 0.61).

DISCUSSION

An empirically defined dietary pattern characterized by high consumption of whole grains, fruit, and nuts and seeds was significantly associated with a lower risk of CVD over 5 y of follow-up in individuals free of CVD at baseline. HRs for CVD according to Whole Grains and Fruit dietary pattern scores were only modestly attenuated by adjustment for waist circumference or biomarkers of CVD risk. The dietary pattern characterized by high consumption of added fats, processed meats, and fried potatoes was associated with a greater risk of incident CVD, although the association was largely explained by lifestyle and clinical characteristics. Associations of dietary pattern with CVD were similar across sex or race-ethnicity strata. The other 2 dietary patterns (Vegetables and Fish and Beans and Tomatoes and Refined Grains) were not associated with incident CVD outcomes, consistent with the results of our previous investigations in which consistent cross-sectional associations with CVD risk factors were observed for only the Fats and Processed Meat and Whole Grains and Fruit dietary patterns (4, 5). In total, these results underscore the concept that a constellation of dietary behaviors determines an individual's risk of CVD. As was shown many years ago in the Lyon Diet Heart Study (11), a dietary pattern structured similarly to the Whole Grains and Fruit pattern can be successfully applied in high-risk populations to reduce CVD recurrence. The data presented here suggest that similar benefit could be realized in a lower risk population free of clinical CVD.

An individual's dietary pattern is represented by his or her scores on multiple PCA dietary patterns, not just a single PCA dietary pattern score. Thus, to more fully characterize participants' dietary patterns, we created categories based on scores for both the Fats and Processed Meat and Whole Grains and Fruit patterns. We found a substantial (72%) reduction in relative risk—greater in magnitude than observed for either dietary pattern alone, although admittedly, the CI associated with this estimate was large. Results of the present study are consistent with other studies evaluating the relation between dietary patterns and CVD (12, 13). Accumulating evidence suggests that, whereas dietary patterns vary to some degree across populations, there are more commonalities than discrepancies. In composite, dietary patterns characterized by high intakes of whole grains, fruit and vegetables, low-fat dairy foods, and rich sources of polyunsaturated fatty acids and low intakes of red or processed meats, refined grains, and processed snack foods show beneficial associations with multiple health outcomes (13). These generalities were true also in this unique, ethnically diverse cohort of healthy adults.

The associations between Whole Grains and Fruit dietary pattern scores and HRs for CVD were also only modestly attenuated when adjusted for a variety of CVD risk factors, such as blood pressure, lipids, and inflammation. These results are not entirely surprising given our incomplete understanding of CVD pathogenesis. Notwithstanding the possibility of residual confounding by imperfect reflections of the disease process (biomarker limitations) or the fact that risk factors were measured as a single point in time, our findings suggest that the dietary factors reflected by the Whole Grains and Fruit pattern reduce CVD risk through a combination of pathways, including traditional CVD risk factors and perhaps those yet-to-be identified. In contrast, HRs for CVD across Fats and Processed Meats dietary pattern scores were attenuated when adjusted for lifestyle characteristics and CVD risk factors. Together these observations may point to differences in the pathways that mediate the observed associations between dietary patterns and CVD.

Whereas the Fats and Processed Meat and Whole Grains and Fruit dietary patterns were strongly associated with all CVD events, HRs for other secondary outcomes were more modest (Table 1). The Whole Grains and Fruit dietary pattern showed suggestive favorable associations with secondary outcomes, but event numbers were small in comparison with total CVD. We anticipate that associations will strengthen when additional events accrue and the long-term effects of dietary choices become more evident.

The limitations of our study (and others of similar design) deserve discussion. Inherent in most diet-disease analyses are 2 sources of biases with anticipated contradictory effects on HRs. On the one hand is the potential for residual confounding by nondietary factors to exaggerate HRs [eg, healthy diets are generally paralleled by other healthy lifestyle factors (which may be unmeasured or measured imperfectly) showing favorable relations with CVD]. On the other hand, HRs may be attenuated because of imprecise measurement of dietary intake, which, in prospective studies, is likely random (not systematically related to the outcome of interest). However, in the present study, HRs were fairly large in magnitude, robust to multiple adjustments, and consistent with previous investigations. Taken together, these observations indicate that diet does influence the relative risk of CVD in this cohort.

In conclusion, a dietary pattern characterized by a high intake of whole grains, fruit and vegetables, low-fat dairy foods, and rich sources of polyunsaturated fats was associated with a lower risk of CVD, an association that was already evident and robust to multiple adjustments within a relatively short period of follow-up. Associations of dietary pattern with CVD were in the same direction in each of the ethnic groups represented in MESA, despite limited power within some strata. Although causality remains an issue of debate, until large scale, primary prevention trials focused on dietary patterns are executed, observational data such as these are key to determining the best dietary counseling practices and advocating within industry and government for healthy food choices for all, regardless of race-ethnicity.

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The authors' responsibilities were as follows—JAN and DRJ: study concept and design and analysis and interpretation of the data; DRJ and GLB: acquisition of data; JAN, JFP, RT, GLB, and DRF: critical revision of the manuscript for important intellectual content; and JAN: draft of the manuscript, full access to all of the data in the study, and responsibility for the integrity of the data and the accuracy of the data analysis. None of the authors had any conflicts of interest to report.

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APPENDIX A

Food group factor loadings on the Fats and Processed Meat and Whole Grains and Fruit dietary patterns in 5316 men and women from the Multi-Ethnic Study of Atherosclerosis (MESA)

	Empirically derived dietary patterns			
Food groups	Fats and Processed Meats	Vegetables and Fish	Beans, Tomatoes, and Refined Grains	Whole Grains and Fruit
Added fats and oils	0.65	−0.01	0.05	0.18
Processed meat	0.63	0.02	0.04	−0.12
Fried potatoes	0.60	0.004	0.14	−0.09
Salty snacks	0.50	−0.01	0.02	0.08
Desserts	0.48	−0.09	0.04	0.10
High-fat cheese/cream sauce	0.42	−0.05	0.57	0.16
Red meat	0.42	0.42	0.46	−0.13
Pizza	0.42	−0.07	0.14	0.08
Sweet breads	0.41	0.08	−0.02	0.11
Pasta or potato salad	0.41	0.12	0.01	0.29
Ice cream	0.40	−0.07	−0.01	0.15
White potatoes	0.37	0.14	0.02	0.04
Poultry	0.36	0.38	0.32	0.01
Sugar-sweetened soda	0.36	−0.04	0.11	−0.16
Sweets	0.36	−0.07	0.06	0.13
Eggs/omelets	0.34	0.14	0.10	−0.08
Chicken, tuna, or egg salad	0.30	0.16	−0.03	0.30
Coffee	0.29	−0.08	0.05	0.16
Cream-based soup	0.28	0.13	0.05	0.11
Refined grain bread, rice, cereal, pasta	0.28	0.30	0.60	−0.19
Cream in coffee or tea	0.23	−0.08	−0.05	0.08
Beer	0.19	−0.09	0.05	−0.03
Fish	0.14	0.60	−0.03	0.13
Whole milk	0.13	−0.03	0.20	−0.07
Seeds or nuts	0.13	0.14	0.02	0.46
Cottage or ricotta cheese	0.12	−0.04	0.14	0.30
Tomatoes	0.12	0.06	0.73	0.25
Other alcohol	0.11	−0.09	−0.03	0.16
Diet soda	0.10	−0.06	0.11	0.10
Other soups	0.09	0.58	0.10	−0.09
Hot chocolate	0.09	−0.02	0.10	0.08
High-fat Chinese dishes	0.05	0.42	0.22	−0.21
Fruit juice	0.05	0.002	0.15	0.24
Low-fat dairy desserts	0.04	0.10	−0.08	0.28
Other vegetables	0.04	0.62	0.18	0.27
Meal-replacement drinks	0.03	0.02	−0.004	0.10
Green, leafy vegetables	0.01	0.13	0.01	0.38
Low-fat milk	0.01	−0.04	0.03	0.33
Yogurt	0.01	−0.02	0.16	0.21
Whole grain bread, rice, cereal, pasta	0.01	0.01	−0.001	0.59
Tea	−0.03	0.25	−0.12	0.09
Beans	−0.04	0.02	0.76	0.09
Dark-yellow vegetables	−0.15	0.77	0.07	0.21
Soyfoods/soy milk	−0.15	0.37	−0.11	0.05
Avocados or guacamole	−0.15	0.004	0.53	0.10
Fruit	−0.17	0.21	0.10	0.55
Cruciferous vegetables	−0.18	0.75	−0.05	0.13