

Dietary Patterns and Mediterranean Diet Score and Hazard of Recurrent Coronary Heart Disease Events and All-Cause Mortality in the REGARDS Study

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Background—Previously, we reported on associations between dietary patterns and incident acute coronary heart disease (CHD) in the REGARDS (Reasons for Geographic and Racial Differences in Stroke) study. Here, we investigated the associations of dietary patterns and a dietary index with recurrent CHD events and all-cause mortality in REGARDS participants with existing CHD.

Methods and Results—We included data from 3562 participants with existing CHD in REGARDS. We used Cox proportional hazards regression to examine the hazard of first recurrence of CHD events—definite or probable MI or acute CHD death—and all-cause mortality associated with quartiles of empirically derived dietary patterns (convenience, plant-based, sweets, Southern, and alcohol and salads) and the Mediterranean diet score. Over a median 7.1 years (interquartile range, 4.4, 8.9 years) follow-up, there were 581 recurrent CHD events and 1098 deaths. In multivariable-adjusted models, the Mediterranean diet score was inversely associated with the hazard of recurrent CHD events (hazard ratio for highest score versus lowest score, 0.78; 95% confidence interval, 0.62–0.98; $P_{\text{Trend}}=0.036$). The Southern dietary pattern was adversely associated with the hazard of all-cause mortality (hazard ratio for Q4 versus Q1, 1.57; 95% confidence interval, 1.28–1.91; $P_{\text{Trend}}<0.001$). The Mediterranean diet score was inversely associated with the hazard of all-cause mortality (hazard ratio for highest score versus lowest score, 0.80; 95% confidence interval, 0.67–0.95; $P_{\text{Trend}}=0.014$).

Conclusions—The Southern dietary pattern was associated with a greater hazard of all-cause mortality in REGARDS participants. Greater adherence to the Mediterranean diet was associated with both a lower hazard of recurrent CHD events and all-cause mortality. (*J Am Heart Assoc.* 2018;7:e008078. DOI: 10.1161/JAHA.117.008078.)

Key Words: cardiovascular disease prevention • diet • epidemiology • nutrition

Despite decades of research and improvements in treatment, coronary heart disease (CHD) remains an important cause of death in the United States, accounting for 1 of every 7 deaths in 2014—more than 364 000 deaths in total.¹ Risk factors for CHD are well established and include dyslipidemia, diabetes mellitus, hypertension, overweight/obesity, cigarette smoking, and physical inactivity.² Observational and intervention studies provide evidence that diet also influences risk of CHD, as well as the course of the disease, likely through its documented effects on several of these key risk factors.³

Studies of diet and CHD risk traditionally focus on dietary constituents such as individual foods and nutrients, resulting in important findings such as the adverse associations of red meat and saturated fat with CHD risk.⁴ However, interest in overall diet and CHD risk has increased in the past decade with the understanding—by both researchers and the public—that foods typically are eaten in combination, not in isolation.⁵ Therefore, a comprehensive dietary approach more closely reflects the way most humans actually eat.

Empirically deriving dietary patterns a posteriori has facilitated investigations into the role overall diet may play

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Clinical Perspective

What Is New?

- Greater adherence to a “Southern” dietary pattern, characterized by added fats, fried food, eggs and egg dishes, organ meats, processed meats, and sugar-sweetened beverages, was associated with a greater hazard of all-cause mortality in community-dwelling blacks and whites who were at least 45 years of age.
- Greater adherence to the Southern dietary pattern was not associated with hazard of recurrent coronary heart disease events.
- A higher Mediterranean diet score (indicating greater adherence to the Mediterranean diet) was associated with a lower hazard of both recurrent coronary heart disease events and all-cause mortality.
- Although these are observational data, this study was conducted in a large, population-based, and diverse sample and included a comprehensive assessment of diet and a rigorous method for deriving dietary patterns.

What Are the Clinical Implications?

- Based on these results, it would be reasonable to make recommendations to patients to reduce intakes of the main components of the Southern dietary pattern, and more closely adhere to the principles of the Mediterranean diet.
- There are no known risks associated with these recommendations, and they may favorably influence the hazard of recurrent coronary heart disease and all-cause mortality.

in the etiology of chronic diseases.^{6,7} Factor analysis, a data-driven exploratory method, assesses eating patterns in specified groups without preconceived judgments about which foods commonly are consumed together and has been used in previous studies to derive dietary patterns that subsequently were related to CHD risk.^{8–16} In a previous analysis, we derived dietary patterns with factor analysis within the REGARDS (Reasons for Geographic and Racial Differences in Stroke) study, a national, population-based, longitudinal cohort.¹⁷ We then used Cox proportional hazards regression to examine hazard of incident acute CHD events—nonfatal myocardial infarction and acute CHD death—associated with quartiles of consumption of each pattern in participants free of CHD at baseline.¹⁸ After multivariable adjustment, the highest consumers of the Southern pattern (characterized by added fats, fried food, eggs, organ and processed meats, and sugar-sweetened beverages) experienced a 56% higher hazard of incident acute CHD.

While examining risk factors for incident CHD is critical for primary prevention, individuals who suffer a myocardial infarction (MI) now have greater survival than in previous years.¹⁹ As a result, there is growing interest in examining risk factors for

recurrent events among those with established disease. Therefore, we investigated the association of REGARDS dietary patterns, along with a dietary index—the Mediterranean diet score—with recurrent CHD events and all-cause mortality in REGARDS participants with CHD at baseline.

Methods

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Population

Details on the design and methods of REGARDS have been published.²⁰ Briefly, REGARDS is a national, population-based, longitudinal cohort of 30 239 community-dwelling black and white women and men ≥ 45 years of age, identified via mail and telephone using commercially available lists of US residents, and enrolled from 2003 to 2007. The sampling scheme included 30% of participants from the stroke belt (North Carolina, South Carolina, Georgia, Tennessee, Alabama, Mississippi, Arkansas, and Louisiana), 20% from the stroke buckle (the coastal plain of North Carolina, South Carolina, and Georgia), and 50% from elsewhere in the continental United States. The baseline cohort was 42% black and 55% women.

Exclusion criteria included race other than white or black, active treatment for cancer, chronic medical conditions precluding long-term participation, cognitive impairment, current or impending residence in a nursing home, or inability to communicate in English. An initial telephone interview was used to survey participants and establish eligibility. Following verbal consent, demographic information and medical history (including risk factor evaluation) was collected by computer-assisted telephone interviewing. Race was self-classified by participants and included the following options defined by the investigators: white and black/African American. An in-home examination was conducted to perform various physical measurements, medication inventory, ECG, phlebotomy, and urine collection among those eligible. The study was approved by the institutional review boards at all participating institutions, and written informed consent was obtained from all participants.

For this analysis, we included only those REGARDS participants with a history of CHD at baseline ($n=5314$), defined as self-reported history of MI or coronary revascularization procedure, or evidence of MI on the baseline ECG.

Dietary Assessment

Diet was assessed with the Block 98 food frequency questionnaire (FFQ), a validated semiquantitative FFQ that assessed usual dietary intake of 110 food items (NutritionQuest, Berkeley, CA).^{21,22} For each line item on the FFQ,

participants were asked how often, on average, they consumed the food (or group of foods) during the previous year, as well as the quantity of the food consumed. The FFQ included adjustment questions (eg, inquiring about the type of milk consumed—low-fat, nonfat, etc). The FFQ was self-administered after the in-home visit and mailed to the REGARDS Operations Center, where they were checked for completeness, scanned, and forwarded to NutritionQuest for processing and analysis. Amounts of each food on the FFQ consumed by a participant were calculated by multiplying the frequency of consumption of that food by the usual amount consumed. Calculation of the total weight (g) of each line item on the FFQ was provided by NutritionQuest. A total of 56 food groups, on which dietary patterns were based, were derived using the 110 individual food variables on the FFQ using methods described elsewhere.¹⁷

Dietary Patterns

We used split sample replication to (1) derive the dietary patterns using exploratory factor analysis and (2) test the patterns using confirmatory factor analysis.²³ We conducted 3 separate analyses: by sex (male/female), race (black/white), and region (southeastern US stroke belt/nonbelt), and coefficients of congruence were determined for each stratification pair. The final number of factors retained was chosen based on the eigenvalue (scree plot) and the solution providing the optimal congruence across sex, race, and region. As congruence between sex, race, and region was high, we calculated final factor loadings using factor analysis with varimax rotation of 5 factors on the full sample. We named patterns based on the factor loadings that contributed most highly to each pattern. Factor 1 loaded heavily on mixed dishes, pasta dishes, pizza, Mexican food, and Chinese food and was designated the “convenience” pattern. Factor 2 had high factor loadings for vegetables, fruits, fruit juice, cereal, beans, fish, poultry, and yogurt and was named the “plant-based” pattern. Factor 3 loaded on added sugars, desserts, chocolate, candy, and sweetened breakfast foods and was named the “sweets” pattern. Factor 4 loaded heavily on added fats, fried food, eggs and egg dishes, organ meats, processed meats, and sugar-sweetened beverages. This diet reflected a culinary pattern observed in the southeastern US and was named the “Southern” pattern. Factor 5 loaded highly on beer, wine, liquor, green leafy vegetables, tomatoes, and salad dressing. Accordingly, we named it the “alcohol and salads” pattern.

Mediterranean Diet Score

We included the Mediterranean diet score because it has been associated with reduced risk of chronic disease incidence and mortality in various populations.²⁴ The Mediterranean diet

score was derived according to previously published methods used in REGARDS.²⁵ In brief, food group contributors to the Mediterranean diet score included those designated as “beneficial” (vegetables, fruits, legumes, cereals, fish), and those designated as “detrimental” (meat, dairy). One point was assigned for consumption that exceeded the median for the “beneficial” groups or was below the median for “detrimental” food groups. For fat intake (eighth food category) we used the ratio of daily consumption (in grams) of monounsaturated lipids to saturated lipids, and we calculated the median separately for each sex. Individuals with ratios at or above the sex-specific median were assigned a value of 1, and those with ratios below the sex-specific median were assigned a value of 0. Moderate alcohol (ninth food category) consumption was defined as >0 and ≤7 drinks per week for women and >0 and ≤14 drinks per week for men. More-than-moderate consumption was defined as >7 drinks per week for women and >14 drinks per week for men. Individuals were assigned a score of 1 for moderate consumption and a score of 0 for the other 2 categories (0 and more-than-moderate consumption). Summing scores for the 9 food groups resulted in a possible score of 0 to 9, with a higher score reflecting higher adherence to the Mediterranean diet.

Outcome Ascertainment

We defined recurrent CHD events as first occurrence of definite or probable MI or acute CHD death in participants with a history (defined above) of CHD at baseline. Recurrent cases of CHD were captured by participant report and adjudicated by clinicians with appropriate expertise. Participants were contacted by telephone every 6 months to assess vital status. If a suspected heart event was reported, medical records were pursued. MIs were adjudicated based on the presence of signs or symptoms suggestive of ischemia; diagnostic cardiac enzymes (rising and/or falling pattern in cardiac troponin or creatine phosphokinase-MB isoenzyme concentrations over ≥6 hours with a peak concentration greater than twice the upper limit of normal); and ECG changes consistent with ischemia or MI, guided by the Minnesota Code and classified as evolving diagnostic, positive, nonspecific, or not consistent with ischemia.²⁶ In the case of deaths, interviews with family members or other proxies, proximal hospitalizations, baseline medical history, death certificates, and the National Death Index were used to identify CHD as the underlying cause of death for analyses of recurrent CHD events or to identify any death for analyses of all-cause mortality.

Statistical Analysis

Of the participants with a history of CHD at baseline (n=5314), we excluded 1671 participants who were missing FFQ data altogether, had >15% missing data on the FFQ, or

had implausible reported energy intakes (<800 or >5000 kcal/day in men and <500 or >4500 kcal/day in women), precluding derivation of dietary patterns and/or Mediterranean diet score. In addition, we excluded 81 participants who were lost to follow-up. This resulted in a final sample of 3562 (67.0% of the sample with a history of CHD at baseline) (see Figure).

We categorized consumption of the 5 dietary patterns into quartiles, with quartile 1 representing the lowest consumption of each pattern and quartile 4 representing the highest consumption of the pattern. We categorized the Mediterranean diet score into 3 groups representing lowest to highest consumption of the Mediterranean diet. We calculated descriptive statistics (including proportions and measures of central tendency) for demographic, socioeconomic, lifestyle, anthropometric, medical history, and medication variables at the baseline assessment according to these quartiles/groups

using the chi-square test (for proportions) and ANOVA (for continuous variables). We used Cox proportional hazards regression to examine the hazard of recurrent CHD events and all-cause mortality associated with consumption of each of the 5 dietary patterns and Mediterranean diet score, using the lowest quartile/group of consumption (quartile/group 1) as the referent quartile/group throughout. Quartiles proved not to be appropriate for analyses of the Mediterranean diet score. Specifically, attempting to categorize Mediterranean diet scores (originally on a scale of 0–9 to assess adherence) into 4 somewhat uniform groups was not possible because of the distribution of the scores—this would have resulted in at least 1 category with a very small number compared with the other groups. Therefore, 3 more equal groups were created based on the scores 0 to 3, 4 to 5, and 6 to 9. Years since study entry was the time metric, with participants censored at the date of a recurrent CHD event (for the recurrent CHD

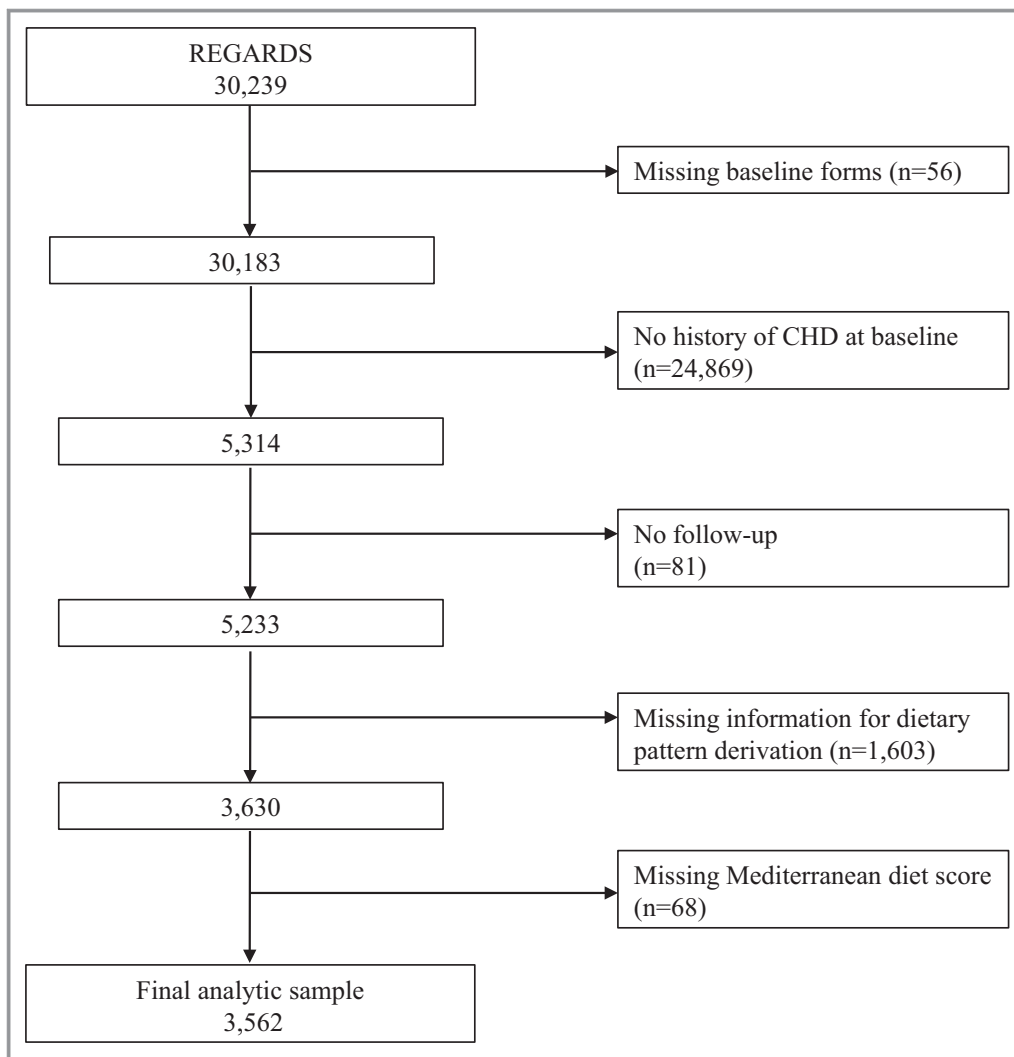


Figure. Participant exclusion cascade. CHD indicates coronary heart disease; REGARDS, Reasons for Geographic and Racial Differences in Stroke.

analysis); date of withdrawal from the study; date of death; or December 31, 2013, whichever came first. We examined Schoenfeld residuals and confirmed that proportional hazards assumptions were met. The base model (model 1) included the demographic variables age, sex, and race. The multivariable-adjusted model (model 2) included factors in model 1 plus socioeconomic factors (education, household income), region, lifestyle factors (smoking, physical activity), total energy intake, anthropometric factors (body mass index [BMI], waist circumference), systolic blood pressure, medical history (hypertension, dyslipidemia, diabetes mellitus), and a physical health summary scale: the Physical Component Summary from the 12-item Short-Form Health Survey.

A Wald test was conducted to assess possible effect modification by sex and race. We conducted a further sensitivity analysis including antihypertensive, antidiabetic, and antidiabetic medications in model 2. To address concerns of collinearity between waist circumference and BMI, we ran all models using residualized variables. In a final sensitivity analysis, we used multiple imputation by chained equations to impute both the main exposure and covariates.

A total of 971 participants (27.3% of the 3562 participants) were missing information for at least 1 covariate of interest. Variables with the largest amount of missing data included income, antihypertensive medication and insulin use, and physical health summary scale. All other characteristics had $\leq 1\%$ missing data. We performed analyses using SAS statistical software, version 9.4 (SAS Institute, Cary, NC) and Stata, version 14.2 (StataCorp, College Station, TX). A *P* value of <0.05 was considered statistically significant. One author (M.M.S.) had full access to all the data in the study and takes responsibility for its integrity and the data analysis.

Results

Over a median 7.1 years follow-up (interquartile range, 4.4, 8.9 years), there were 581 (16.3%) recurrent CHD events and 1098 (30.8%) deaths. Compared with participants without recurrent CHD events, those with recurrent CHD events were older (70.0 ± 9.2 versus 68.3 ± 8.8 years), more likely to be male (70.1% versus 59.4%), more likely to not have graduated from high school (16.2% versus 12.9%), and more likely to be physically inactive (44.9% versus 34.6%) (Table 1). Participants with recurrent CHD events also had higher BMI (29.9 ± 5.7 versus 29.0 ± 5.9 kg/m²), waist circumference (102.2 ± 15.3 versus 98.3 ± 15.4 cm), and systolic blood pressure (132.3 ± 17.9 versus 128.6 ± 16.7 mm Hg); were more likely to have a history of hypertension (77.6% versus 69.3%), dyslipidemia (81.9% versus 77.2%), and diabetes mellitus (42.7% versus 27.3%); were more likely to report antihypertensive medication (72.2% versus 65.9%), regular aspirin (75.0% versus 69.7%), oral antidiabetic medication (30.5% versus

19.5%), and insulin (16.3% versus 8.7%) use; and had a lower physical health summary score (40.2 ± 11.4 versus 43.5 ± 11.4).

In multivariable-adjusted models, the plant-based dietary pattern demonstrated a trend for an increasing hazard of recurrent CHD events, although none of the hazard ratios (HRs) for quartile comparisons were statistically significant (HR for Q4 versus Q1, 1.28; 95% confidence interval [CI], 0.98–1.66; $P_{\text{Trend}}=0.048$) (Table 2). The Southern pattern was adversely associated with the hazard of recurrent CHD events in the minimally adjusted model (HR for Q4 versus Q1, 1.35; 95% CI, 1.05–1.73; $P_{\text{Trend}}=0.011$). However, the Southern pattern was not associated with the hazard of recurrent CHD events in the fully adjusted model (HR for Q4 versus Q1, 1.00; 95% CI, 0.76–1.31; $P_{\text{Trend}}=0.942$). After multivariable adjustment, the alcohol and salads pattern was inversely associated with the hazard of recurrent CHD events (HR for Q4 versus Q1, 0.77; 95% CI, 0.59–1.00; $P_{\text{Trend}}=0.026$). None of the other dietary patterns were significantly associated with hazard of recurrent CHD events. The multivariable-adjusted Mediterranean diet score was inversely associated with the hazard of recurrent CHD events (HR for group 3 versus group 1, 0.78; 95% CI, 0.62–0.98; $P_{\text{Trend}}=0.036$) (Table 3).

In multivariable-adjusted all-cause mortality analyses, the Southern dietary pattern was adversely associated with the hazard of all-cause mortality (HR for Q4 versus Q1, 1.57; 95% CI, 1.28–1.91; $P_{\text{Trend}}<0.001$) (Table 4). The plant-based pattern was inversely associated with the hazard of all-cause mortality in the minimally adjusted model (HR for Q4 versus Q1, 0.71; 95% CI, 0.59–0.84; $P_{\text{Trend}}<0.001$). While this association was attenuated in the fully adjusted model, evidence of an inverse association of the plant-based pattern with the hazard of all-cause mortality remained (HR for Q4 versus Q1, 0.84; 95% CI, 0.69–1.01; $P_{\text{Trend}}=0.150$). None of the other empirically derived dietary patterns were associated with the hazard of all-cause mortality. The multivariable-adjusted Mediterranean diet score was inversely associated with the hazard of all-cause mortality (HR for group 3 versus group 1, 0.80; 95% CI, 0.67–0.95; $P_{\text{Trend}}=0.014$) (Table 5).

Sensitivity analyses solidified the results above. There was no statistically significant interaction by race or sex. Additionally, estimates were virtually unchanged when antihypertensive, antidiabetic, and antidiabetic medications were added to the final model; waist circumference and BMI were residualized; or the main exposure and covariates were imputed.

Discussion

In this follow-up to our analysis of dietary patterns and incident acute CHD in the REGARDS cohort, a Southern dietary pattern (characterized by added fats, fried food, eggs, organ meats, processed meats, and sugar-sweetened

Table 1. Characteristics of Study Participants Without and With Recurrent CHD Events in the REGARDS Cohort

Characteristic	Total Mean±SD or n (%)	No Recurrent CHD Event Mean±SD or n (%)	Recurrent CHD Event Mean±SD or n (%)	<i>P</i> _{Difference}
	N=3562	n=2981	n=581	
Age, y	68.6±8.9	68.3±8.8	70.0±9.2	<0.001
Sex, male	2179 (61.2)	1772 (59.4)	407 (70.1)	<0.001
Race, black	962 (27.0)	812 (27.2)	150 (25.8)	0.48
Education, did not graduate from high school	477 (13.4)	383 (12.9)	94 (16.2)	0.031
Household income <\$20 000/y	686 (21.7)	557 (21.1)	129 (24.4)	0.092
Resident of stroke belt*	2007 (56.3)	1692 (56.8)	315 (54.2)	0.26
Current smoker	527 (14.9)	434 (14.6)	93 (16.0)	0.38
Physically inactive†	1276 (36.3)	1020 (34.6)	256 (44.9)	<0.001
Total energy intake, kcal/day	1685±688	1684±687	1694±693	0.74
Body mass index, kg/m ²	29.2±5.8	29.0±5.9	29.9±5.7	0.002
Waist circumference, cm	98.9±15.4	98.3±15.4	102.2±15.3	<0.001
Systolic blood pressure, mm Hg	129.2±16.9	128.6±16.7	132.3±17.9	<0.001
Hypertension‡	2506 (70.7)	2058 (69.3)	448 (77.6)	<0.001
Dyslipidemia§	2716 (78.0)	2251 (77.2)	465 (81.9)	0.015
Diabetes mellitus	1030 (29.8)	786 (27.3)	244 (42.7)	<0.001
Antihypertensive use	2298 (66.9)	1887 (65.9)	411 (72.2)	0.003
Statin use	2109 (59.2)	1759 (59.0)	350 (60.2)	0.58
Regular aspirin use	2512 (70.5)	2077 (69.7)	435 (75.0)	0.010
Oral antidiabetic use	759 (21.3)	582 (19.5)	177 (30.5)	<0.001
Insulin use	334 (9.9)	245 (8.7)	89 (16.3)	<0.001
PCS-12	43.0±11.5	43.5±11.4	40.2±11.4	<0.001

CHD indicates coronary heart disease; PCS, Physical Component Summary; REGARDS, Reasons for Geographic and Racial Differences in Stroke study; SD, standard deviation.

*Stroke belt consists of North Carolina, South Carolina, Georgia, Tennessee, Alabama, Mississippi, Arkansas, and Louisiana.

†Physically active defined as ≥4 days of exercise (enough to work up a sweat) per week.

‡Hypertension defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg or self-reported current use of medication to control blood pressure.

§Dyslipidemia defined as total cholesterol ≥6.22 mmol/L (240 mg/dL) and/or low-density lipoprotein cholesterol ≥4.14 mmol/L (160 mg/dL) and/or high-density lipoprotein cholesterol ≤1.04 mmol/L (40 mg/dL) or self-reported current use of medication to control cholesterol.

||Diabetes mellitus defined as fasting glucose ≥6.99 mmol/L (126 mg/dL) and/or nonfasting glucose ≥11.10 mmol/L (200 mg/dL) or self-reported current use of medication to control blood sugar.

beverages) was not associated with the hazard of recurrent CHD events, in contrast to the adverse association of this dietary pattern with the hazard of incident acute CHD.¹⁸ The Southern pattern was adversely associated with the hazard of all-cause mortality in REGARDS participants with existing CHD. Interestingly, greater adherence to the plant-based dietary pattern showed a significant trend of a greater hazard of recurrent CHD events, although none of the HRs for quartile comparisons were statistically significant. Higher consumption of a Mediterranean diet was inversely associated with both hazard of recurrent CHD events and all-cause mortality.

Although previous studies have investigated the association of dietary patterns with incident CHD events, CHD risk factors, post-MI prognosis and cardiovascular mortality, and

coronary procedures such as angioplasty or coronary artery bypass graft surgery, ours is among the first to investigate a posteriori-derived dietary patterns and hazard of recurrent CHD events using adjudication, a more rigorous assessment than self-report. This is in contrast to the Mediterranean diet, where clinical trial data from the Lyon Diet Heart Study have shown that patients with a previous MI who were randomized to consume a Mediterranean diet had a lower rate of recurrent MI compared with patients randomized to a prudent-type diet.²⁷ However, because of the relatively small sample size and short duration of follow-up in the Lyon Study, as well as the selective nature of recruitment in this and other clinical trials, observational data from cohorts of community-dwelling people, especially those such as REGARDS, which include a significant proportion of black participants, remain relevant. A

Table 2. Hazard of Recurrent CHD Events by Quartile of Consumption of the Various Dietary Patterns

Dietary Pattern	Model	Quartile 1 (Lowest Consumption), HR (95% CI)	Quartile 2, HR (95% CI)	Quartile 3, HR (95% CI)	Quartile 4 (Highest Consumption), HR (95% CI)	<i>P</i> _{Trend}
Convenience		n=894 (158*)	n=890 (137)	n=888 (138)	n=890 (148)	
		279.4 [†]	237.2	235.8	246.0	
	1 [‡]	1 (referent)	0.87 (0.69–1.09)	0.85 (0.68–1.08)	0.92 (0.73–1.16)	0.472
	2 [§]	1 (referent)	0.83 (0.66–1.05)	0.86 (0.67–1.09)	0.87 (0.67–1.13)	0.296
Plant-based		n=887 (135)	n=894 (146)	n=891 (155)	n=890 (145)	
		238.9	251.0	261.5	245.6	
	1	1 (referent)	0.99 (0.78–1.25)	1.02 (0.81–1.29)	0.97 (0.76–1.23)	0.863
	2	1 (referent)	1.08 (0.85–1.37)	1.19 (0.93–1.51)	1.28 (0.98–1.66)	0.048
Sweets		n=892 (132)	n=888 (152)	n=890 (149)	n=892 (148)	
		226.4	262.9	249.9	258.5	
	1	1 (referent)	1.11 (0.88–1.41)	1.05 (0.83–1.33)	1.10 (0.87–1.39)	0.590
	2	1 (referent)	1.05 (0.83–1.33)	1.00 (0.78–1.28)	1.11 (0.83–1.48)	0.640
Southern		n=895 (134)	n=888 (138)	n=891 (154)	n=888 (155)	
		215.5	236.7	267.9	281.6	
	1	1 (referent)	1.12 (0.88–1.42)	1.26 (1.00–1.60)	1.35 (1.05–1.73)	0.011
	2	1 (referent)	0.99 (0.78–1.27)	1.02 (0.80–1.30)	1.00 (0.76–1.31)	0.942
Alcohol and salads		n=886 (149)	n=887 (158)	n=895 (148)	n=894 (126)	
		263.6	281.0	252.1	204.7	
	1	1 (referent)	1.07 (0.85–1.34)	0.95 (0.75–1.20)	0.75 (0.59–0.96)	0.015
	2	1 (referent)	1.11 (0.89–1.39)	0.93 (0.73–1.17)	0.77 (0.59–1.00)	0.026

CHD indicates coronary heart disease; CI, confidence interval; HR, hazard ratio; PCS, Physical Component Summary.

*Number of events.

[†]Crude rate of recurrent coronary heart disease events per 10 000 person-years.

[‡]Model 1 adjusts for age, sex, and race.

[§]Model 2 adjusts for age, sex, race, education, household income, region, smoking, physical activity, total energy intake, body mass index, waist circumference, systolic blood pressure, history of hypertension, dyslipidemia, diabetes mellitus, and PCS-12.

previous analysis investigating various lifestyle modifications and recurrent CHD events in REGARDS showed an inverse association between the Mediterranean diet score and risk of recurrent CHD events, although this finding was of borderline statistical significance (HR [95% CI] for Q4 versus Q1, 0.77 [0.55–1.06]; *P*_{Trend}=0.084).²⁸ However, that analysis included outcome data through December 31, 2009, while the current analysis includes outcomes occurring over 4 additional years (through December 31, 2013).

Previous studies of dietary patterns and all-cause mortality in various populations have produced mixed results. Western-type diets (high-fat, meat-rich, low-fiber), which have similarities to our Southern dietary pattern, have shown adverse associations with all-cause mortality in several cohorts, including the US Nurse's Health study,²⁹ older British men,³⁰ and Chinese men and women (but only in ever smokers).³¹ However, a Western dietary pattern showed no association with all-cause mortality in a Spanish cohort,³² in English civil service employees in the Whitehall II study,³³ or

in a cohort of Danish men and women.³⁴ There was a surprising *inverse* association of a Western dietary pattern and all-cause mortality in a cohort of Japanese men and women.³⁵ In a recent systematic review and meta-analysis of 13 prospective cohort studies, a Western dietary pattern was not significantly associated with risk of all-cause mortality.³⁶

In contrast to the lack of an association with the plant-based pattern and all-cause mortality in our analysis, a prudent diet (which generally is characterized by high intakes of fruits and vegetables, and low loadings of meats and sweets) was associated with a significantly lower risk of all-cause mortality in the Nurse's Health Study cohort,²⁹ a Chinese population,³¹ Danish men and women,³⁴ and a cohort of Japanese men and women.³⁵ However, there was no association of healthy dietary patterns with all-cause mortality in a study of British men,³⁰ or in the Whitehall II study.³³ In the previously noted systematic review and meta-analysis, a prudent dietary pattern was inversely associated with risk of all-cause mortality.³⁶

Table 3. Hazard of Recurrent CHD Events by Mediterranean Diet Score Group

Diet Score	Model	Group 1 (Score 0–3), HR (95% CI)	Group 2 (Score 4, 5), HR (95% CI)	Group 3 (Score 6–9), HR (95% CI)	<i>P</i> _{Trend}
Mediterranean		n=1145 (208*)	n=1500 (248)	n=917 (125)	
		291.2 [†]	252.4	197.4	
	1 [‡]	1 (referent)	0.81 (0.67–0.97)	0.61 (0.49–0.76)	<0.001
	2 [§]	1 (referent)	0.91 (0.76–1.10)	0.78 (0.62–0.98)	0.036

CHD indicates coronary heart disease; CI, confidence interval; HR, hazard ratio; PCS, Physical Component Summary.

*Number of events.

[†]Crude rate of recurrent coronary heart disease events per 10 000 person-years.

[‡]Model 1 adjusts for age, sex, and race.

[§]Model 2 adjusts for age, sex, race, education, household income, region, smoking, physical activity, total energy intake, body mass index, waist circumference, systolic blood pressure, history of hypertension, dyslipidemia, diabetes mellitus, and PCS-12.

In agreement with our results, a Mediterranean dietary pattern was inversely associated with all-cause mortality in the US Multiethnic Cohort,³⁷ the US National Institutes of Health–AARP Diet and Health Study,³⁸ Spanish cohorts,^{32,39} an Italian cohort,⁴⁰ the UK-based EPIC (European Prospective

Investigation of Cancer)–Norfolk study,⁴¹ a Danish cohort,⁴² and a cohort of elderly European men and women.⁴³ However, there was no association of a Mediterranean-type diet with all-cause mortality in the UK-based Whitehall II study.³³ A previous analysis investigating various lifestyle modifications

Table 4. Hazard of All-Cause Mortality by Quartile of Consumption of the Various Dietary Patterns

Dietary Pattern	Model	Quartile 1 (Lowest Consumption), HR (95% CI)	Quartile 2, HR (95% CI)	Quartile 3, HR (95% CI)	Quartile 4 (Highest Consumption), HR (95% CI)	<i>P</i> _{Trend}
Convenience		n=894 (306*)	n=890 (280)	n=888 (261)	n=890 (251)	
		513.3 [†]	461.2	425.6	398.6	
	1 [‡]	1 (referent)	0.95 (0.81–1.12)	0.92 (0.77–1.09)	0.96 (0.80–1.14)	0.527
	2 [§]	1 (referent)	0.92 (0.78–1.09)	0.97 (0.81–1.15)	0.89 (0.74–1.08)	0.342
Plant-based		n=887 (269)	n=894 (282)	n=891 (294)	n=890 (253)	
		454.8	459.5	476.0	405.9	
	1	1 (referent)	0.85 (0.71–1.00)	0.86 (0.73–1.01)	0.71 (0.59–0.84)	<0.001
	2	1 (referent)	0.90 (0.76–1.07)	0.96 (0.81–1.15)	0.84 (0.69–1.01)	0.150
Sweets		n=892 (258)	n=888 (284)	n=890 (275)	n=892 (281)	
		421.2	469.4	440.0	465.6	
	1	1 (referent)	1.00 (0.85–1.19)	0.94 (0.80–1.12)	1.05 (0.88–1.24)	0.781
	2	1 (referent)	0.94 (0.79–1.12)	0.87 (0.72–1.04)	0.94 (0.76–1.16)	0.358
Southern		n=895 (216)	n=888 (262)	n=891 (300)	n=888 (320)	
		330.7	428.3	496.2	554.8	
	1	1 (referent)	1.34 (1.12–1.61)	1.61 (1.35–1.93)	2.01 (1.67–2.41)	<0.001
	2	1 (referent)	1.21 (1.01–1.46)	1.37 (1.15–1.65)	1.57 (1.28–1.91)	<0.001
Alcohol and salads		n=886 (292)	n=887 (291)	n=895 (279)	n=894 (236)	
		489.7	487.0	452.9	370.9	
	1	1 (referent)	1.03 (0.88–1.22)	1.01 (0.85–1.19)	0.82 (0.69–0.98)	0.032
	2	1 (referent)	1.09 (0.92–1.29)	1.03 (0.86–1.22)	0.86 (0.71–1.03)	0.117

CI indicates confidence interval; HR, hazard ratio; PCS, Physical Component Summary.

*Number of events.

[†]Crude rate of all-cause mortality per 10 000 person-years.

[‡]Model 1 adjusts for age, sex, and race.

[§]Model 2 adjusts for age, sex, race, education, household income, region, smoking, physical activity, total energy intake, body mass index, waist circumference, systolic blood pressure, history of hypertension, dyslipidemia, diabetes mellitus, and PCS-12.

Table 5. Hazard of All-Cause Mortality by Mediterranean Diet Score Group

Diet Score	Model	Group 1 (Score 0–3), HR (95% CI)	Group 2 (Score 4, 5), HR (95% CI)	Group 3 (Score 6–9), HR (95% CI)	<i>P</i> _{Trend}
Mediterranean		n=1145 (379*)	n=1500 (481)	n=917 (238)	
		499.9 [†]	468.7	359.6	
	1 [‡]	1 (referent)	0.84 (0.73–0.96)	0.60 (0.51–0.71)	<0.001
	2 [§]	1 (referent)	0.98 (0.85–1.13)	0.80 (0.67–0.95)	0.014

CI indicates confidence interval; HR, hazard ratio; PCS, Physical Component Summary.

*Number of events.

[†]Crude rate of all-cause mortality per 10 000 person-years.

[‡]Model 1 adjusts for age, sex, and race.

[§]Model 2 adjusts for age, sex, race, education, household income, region, smoking, physical activity, total energy intake, body mass index, waist circumference, systolic blood pressure, history of hypertension, dyslipidemia, diabetes mellitus, and PCS-12.

and recurrent CHD events in REGARDS showed an inverse association between the Mediterranean diet score and risk of all-cause mortality, although this finding was of borderline statistical significance (HR [95% CI] for Q4 versus Q1, 0.84 [0.66–1.07]; *P*_{Trend}=0.061).²⁸ This analysis included outcome data through December 31, 2009, while the current analysis includes outcomes occurring over 4 additional years (through December 31, 2013). In another recent analysis from REGARDS, the Mediterranean diet pattern was inversely associated with all-cause mortality⁴⁴; however, this analysis was not restricted to participants with CHD at baseline, as in the current analysis.

There are several mechanisms potentially contributing to an association between greater consumption of the Southern dietary pattern and increased hazard of CHD. Examples include the high sodium content of processed meats that can contribute to hypertension, a risk factor for CHD; nitrite preservatives in processed meats, which have been shown experimentally to promote atherosclerosis and vascular dysfunction⁴⁵; and the high sugar-sweetened beverage consumption characteristic of the Southern pattern, which not only negatively impacts BMI but also increases glycemic load, resulting in insulin resistance, β -cell dysfunction, and inflammation, all setting the stage for atherosclerosis.⁴⁶ However, while the Southern pattern was adversely associated with the hazard of incident CHD events in our previous analysis,¹⁸ it was not associated with the hazard of recurrent CHD events in the current analysis. There are several possible explanations for this. First, those participants who experienced a recurrent CHD event may be different in important ways from those who did not, including having different susceptibilities to recognized CHD risk factors, including diet. Second, it is conceivable that risk factors and/or strength of associations vary between incident and recurrent events, such that while an adverse dietary pattern plays an important role in the initiation of CHD, once CHD is established, its importance in the risk factor profile is diminished relative to other

concomitant factors. Under either scenario, different covariates would be declared statistically significant between the 2 analyses. Finally, those at greatest risk may have changed their diet to a healthier pattern after their initial CHD event with the intent of reducing the risk of recurrent disease. If this were to occur in a sizable segment of the study population, the risk of recurrent CHD in those adhering to a Southern pattern at baseline might have been underestimated. It is important to note that dietary assessment was conducted only at baseline, so we were unable to assess whether participants changed their dietary patterns between their incident and recurrent CHD events. Changing dietary habits from what are perceived as less healthy to healthier in response to a major life event, such as the diagnosis of an incident CHD event, potentially could have resulted in misclassification of the exposure (dietary intake) in reference to recurrent events, which could have attenuated the results. Unfortunately, we were unable to address this directly in the current study because dietary assessment was not repeated in REGARDS participants.

Possible reasons for disagreement in the results among previous studies noted above include differences in critical study elements such as sample size and population characteristics, dietary assessment instrument and methodology utilized, dietary pattern derivation and selection, and rigorosity of end point determination. The strengths of this study included the large, population-based sample with sociodemographic and regional diversity, including a sizable proportion of black participants, which distinguishes it from most previous studies; a comprehensive assessment of diet with a recognized instrument; derivation of dietary patterns using a rigorous method—factor analysis—based on the actual dietary data collected in the population of interest rather than dietary patterns created a priori based on the authors’ opinions on what defines various dietary patterns; and expert adjudication of study end points. Limitations include the recognized potential for measurement error with

any dietary assessment instrument that relies on recall of dietary intake, as is the case with FFQs, which could result in misclassification of dietary intake. However, if random, this would tend to bias results toward the null, potentially reducing the magnitude of the associations between dietary patterns/score and recurrent CHD events and all-cause mortality observed in this analysis. Additionally, those who did not provide a completed FFQ showed no differences in sex or race compared with those who completed the FFQ but were more likely to be black, less educated, and have a lower income. Noncompleters also were slightly more likely to be current smokers and inactive, and had a slightly lower BMI, compared with those who completed the FFQ. In order to reduce potential bias and increase the power of our sample tests, we multiply imputed those who did not complete the FFQ in a sensitivity analysis. Finally, the results observed may not be generalizable to groups other than whites and blacks in the United States.

In summary, the Mediterranean diet score was inversely associated with the hazard of recurrent CHD events and all-cause mortality, while the Southern dietary pattern was associated with the hazard of all-cause mortality but not recurrent CHD events in this diverse sample of white and black adults. Because diet is a modifiable factor, identifying dietary patterns that may contribute to mortality or recurrent CHD events may pave the way for the development of specific nutritional health messages aimed at changing dietary choices made by individuals who have survived CHD.

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Disclosures

None.

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Dietary Patterns and Mediterranean Diet Score and Hazard of Recurrent Coronary Heart Disease Events and All-Cause Mortality in the REGARDS Study

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