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Dietary patterns based on the Mediterranean diet and DASH diet are inversely associated with high aggressive prostate cancer in PCaP

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ABSTRACT

Background: Several foods and nutrients have been linked to the development of prostate cancer, but the association between healthy dietary patterns and prostate cancer aggressiveness is less studied. The aim of this study was to evaluate the relationship between the Mediterranean diet (MED) and Dietary Approaches to Stop Hypertension (DASH) diet scores and prostate cancer aggressiveness by race.
Methods: Data from the population-based, case-only North Carolina–Louisiana Prostate Cancer Project (PCaP) were used to examine the association between diet quality, measured by MED and DASH scores, and prostate cancer aggressiveness in 1899 African American (AA) and European American (EA) research subjects. Dietary intake was assessed using a modified National Cancer Institute Diet History Questionnaire. Logistic regression was used to estimate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for high versus low-intermediate aggressive prostate cancer.
Results: Higher MED scores were inversely associated with high aggressive prostate cancer overall (OR: 0.66; 95% CI: 0.46, 0.95 for high versus low scores); results were similar for AA and EA men. A weaker inverse association between DASH scores and prostate cancer aggressiveness was found (OR: 0.76; 95% CI: 0.55, 1.06).
Conclusions: Higher diet quality, as represented by a Mediterranean-style diet or DASH diet, may reduce the odds of high aggressive prostate cancer.

Introduction

Prostate cancer accounts for the highest number of incident cancer cases and is the second leading cause of cancer death among American men [1]. Diet has been implicated in the development of prostate cancer [2–5]. Fats (particularly animal fats), dairy, and calcium have been linked with an increased risk of prostate cancer [6–8], whereas high intakes of soy, fiber, fruits and vegetables, and tomato products (as a source of lycopene) have been inversely associated with prostate cancer [9–11], although a recent pooled analysis found no association with fruits, vegetables, or mature beans [12]. Patterns of overall dietary intake in relation to prostate cancer risk have been examined because foods and nutrients are not consumed singularly, but with conflicting results; less is known about the relationship between dietary patterns and prostate cancer aggressiveness [13–23].

The Mediterranean diet (MED) and the Dietary Approaches to Stop Hypertension (DASH) diet are two *a priori* dietary patterns that promote high intakes of foods and nutrients beneficial for overall health. High MED scores have been linked to a decreased incidence

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of colorectal, breast, and prostate cancers [23,24]. Although many studies have found no significant association between MED scores and prostate cancer aggressiveness [15,17,20,21,25], recent findings indicate high conformity to a Mediterranean-style diet is associated with lower risk of aggressive prostate cancer [26]. No published study has examined the association between the DASH diet and prostate cancer. In accordance with available evidence, the low intakes of meat, saturated fats, and full-fat dairy, combined with the high fiber, fruit, and vegetable intake characteristics of the MED and DASH diets have a biological basis for decreasing prostate cancer risk, and may confer protection against aggressive forms of prostate cancer [27–30].

Five-year survival rates for local and regional stage diagnoses of prostate cancer remain high, but distant stage prostate cancers have a 28% 5-year survival rate [1]. Mortality rates also vary by race: African American (AA) men are almost twice as likely as European American (EA) or Hispanic men to die of prostate cancer, in part because they are more likely to be diagnosed with more aggressive forms of prostate cancer [31]. Improving diet quality among high-risk men, specifically AAs, may be a means for reducing these disparities. The purpose of this case-only study was to examine the association between dietary patterns, measured using MED and DASH scores, and prostate cancer aggressiveness by race.

Methods

Study population

Data were used from the North Carolina–Louisiana Prostate Cancer Project (PCaP), a cross-sectional, population-based, case-only, incident prostate cancer study designed to investigate racial differences in prostate cancer aggressiveness between AAs and EAs. Men with a first diagnosis of histologically confirmed adenocarcinoma of the prostate between July 1, 2004, and August 31, 2009, were eligible to participate if they met the following criteria: aged 40–79 years at diagnosis, not institutionalized, physically and mentally able to complete the study interview in English, and self-identified as AA/black or white/Caucasian (EA). Of the 2258 men enrolled in PCaP, approximately half were AA ($n = 1128$) and half were EA ($n = 1130$). Written informed consent was obtained from all research subjects. Additional details about the study methods and design were published [32]. Protocols were approved by all institutions enrolling participants and the PCaP funding agency; the present study was approved by the University of South Carolina Institutional Review Board as exempt.

Data collection

Trained research nurses conducted structured, in-person, in-home interviews that collected information on demographics, health history, and lifestyle. Height and weight were measured using standardized protocols. Medical records obtained from diagnosing physicians were used to extract clinical stage, Gleason sum, and prostate-specific antigen (PSA) level at diagnosis. All abstractions were performed by trained personnel to ensure consistency among abstractors.

Dietary assessment

Usual dietary intake for the year before prostate cancer diagnosis was assessed using a modified version of the National Cancer Institute Dietary History Questionnaire; the 144 questions included Southern food items specific to the study catchment areas.

Mediterranean diet score

The MED scores followed the scoring scheme outlined by Trichopoulou et al [24]. A total of nine dietary components were scored: grains and cereals, fatty acids, vegetables, legumes, fruits and nuts, fish, dairy, meat and poultry, and alcohol. Components thought to be representative of traditional MEDs and conferring health benefits (e.g., grains, high ratio of monounsaturated fatty acids [MUFA] to saturated fatty acids [SFA], vegetables, legumes, fruits and nuts, and fish) were scored a 1 for intakes at or above the sample median. Intakes of meat and poultry and dairy were scored 1 if at or below the sample median to reflect their perceived negative health effects and divergence from traditional MEDs. Failure to meet adherence at the median level resulted in a score of 0 for the component. The alcohol component was scored a 1 if average intake was between 10 and 50 grams of alcoholic beverage per day; all other alcohol intakes were scored 0. MED scores ranged from 0 to 9, with higher scores indicating better diet quality according to the MED evidence (Supplemental Table 1).

Dietary Approaches to Stop Hypertension score

DASH scores followed the scoring scheme outlined by Fung et al [33]. Eight components (whole grains, low-fat dairy, vegetables, legumes and nuts, fruit and fruit juices, red and processed meats, sodium, and sweetened beverages) were scored on a 1–5 scale (Supplemental Table 1). Whole grains, low-fat dairy, vegetables, legumes and nuts, and fruit and fruit juices were scored proportionally, with intakes in the highest quintiles receiving the highest component score (5) and the lowest quintiles scoring lowest (1). Red and processed meats, sodium, and sugar sweetened beverages were scored inversely, with the highest quintile of intakes scored lowest (1) and the lowest quintiles of intakes scored highest (5). Scores may range from 8 to 40, with 40 reflecting the healthiest patterns of consumption.

Case definition

Cases were classified as high aggressive if Gleason sum was greater than or equal to 8, or PSA greater than 20 ng/mL, or Gleason sum equal to 7 and stage T3–T4; and as low aggressive if Gleason sum was less than 7 and stage T1–T2 and PSA<10 ng/mL. All other cases were classified as intermediate aggressive. For the purposes of all analyses, aggressiveness was dichotomized into two levels of high aggressive (as defined previously) and combined low-intermediate aggressive to allow for the calculation of the odds of high aggressive prostate cancer.

Statistical analyses

A complete case analysis was used for this study; any research subject with missing values on prostate cancer aggressiveness ($n = 85$) or relevant covariates (body mass index [BMI], $n = 21$; smoking status, $n = 2$; family history, $n = 170$; nonsteroidal anti-inflammatory drugs [NSAIDs] use, $n = 11$; education, $n = 1$; screening history, $n = 1$) was excluded from the sample. Research subjects were also excluded for improbable energy intake values (<500 or ≥6000 kcal/day, $n = 68$).

Descriptive statistics were performed using means and *t*-tests for continuous variables and proportions and χ^2 tests for categorical variables. Dietary pattern scores were evaluated as both continuous and categorical, with MED scores divided into high/intermediate/low levels, and DASH scores categorized into tertiles (T1, T2, T3, ascending conformity) based on the distribution among low-intermediate cases. Multivariable logistic regression was used

to estimate the odds ratios (ORs) and 95% confidence intervals (95% CIs) for high aggressive prostate cancer versus low-intermediate aggressive prostate cancer. The lowest dietary pattern scores served as the referent groups in categorical analyses. Tests for trend were performed by assigning the median value of each category to research subjects in that category and examining the *p*-value for the continuous variable in simple and multivariable models.

Each association was evaluated using both simple models (diet score, age, energy intake, and race) and multivariable-adjusted models. Potential confounders were included in the multivariable-adjusted model based on previous research: study site (North Carolina or Louisiana); family history (yes for prior prostate cancer diagnoses in a first-degree relative or no for all others); education (less than high school diploma, earned high school diploma or completed vocational or technical school, some college or college graduate, or some graduate school or earned graduate/professional degree); screening history (PSA test only, digital rectal exam [DRE] only, PSA and DRE tests, or neither PSA nor DRE test); BMI (<25 kg/m^2, ≥25 kg/m^2 but <30 kg/m^2, or ≥30 kg/m^2); smoking status (current smoker, past smoker, or never smoker); NSAIDs use (yes or no); and comorbidity (Charlson's Comorbidity Index scores categorized into 0, 1–2, or 3 or greater). We conducted sensitivity analyses by omitting BMI from the multivariable analyses because obesity may be a mediator of the association between diet and aggressive prostate cancer. Possible effect modification by race, age, smoking status, or BMI was identified by inclusion of an interaction term of dietary score × covariate in the model. Comparisons of the original models with interaction term models were carried out using likelihood ratio tests. Stratification by possible effect modifiers was performed to examine associations within strata of race, age, smoking, and BMI. All statistical tests were two-sided, and tests were considered significant at the alpha equal to 0.05 level, except for interaction terms, which were evaluated at the 0.10 level. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

The final sample size included 1899 research subjects, with 1567 low-intermediate aggressive cases and 332 high aggressive cases of prostate cancer. Within the sample, 908 of the research subjects identified as AA (47.8%) and 991 identified as EA (52.2%). MED scores had an overall mean and SD of 4.19 ± 1.65. DASH scores had an overall mean and SD of 22.01 ± 4.37. Neither MED nor DASH scores displayed visible departure from normality. Research subjects diagnosed with high aggressive prostate cancer were significantly older, had higher BMI, consumed more calories per day, were more likely AA, had less than a high school education, were current or former smokers, and were less likely to have been screened for prostate cancer previously compared with low-intermediate aggressive cases (Table 1). A higher proportion of AA research subjects scored 1 in all MED components except for vegetables, meat and poultry, and alcohol compared with EA research subjects (Supplemental Table 2). For the DASH diet, a higher proportion of AA research subjects scored in the highest quintile for whole grains, legumes and nuts, and fruit, and in the lowest quintile for red and processed meat and sodium compared with EA research subjects. A higher proportion of EA research subjects scored in the highest quintile for low-fat dairy and vegetables, and in the lowest quintile for sweetened beverages compared with AA research subjects (Supplemental Table 2).

Among research subjects diagnosed with prostate cancer, higher MED and DASH scores were inversely associated with prostate cancer aggressiveness (Table 2). The odds of having high versus having low-intermediate aggressive prostate cancer decreased by 8% for every one point increase in the MED score (OR: 0.92; 95% CI: 0.84, 0.99) (Table 2). In categorical analyses, research subjects with the highest MED scores (6–9) had 34% decreased odds of high versus low-intermediate aggressive prostate cancer compared with research subjects with the lowest MED scores (0–3) after multivariable adjustment. Results for the DASH score were more modest: OR: 0.98 (95% CI: 0.95, 1.01) for the continuous variable and OR: 0.76 (95% CI: 0.55, 1.06) for the highest compared with the lowest tertile. Omitting BMI from the multivariable models in the sensitivity analyses did not change the results (data not shown).

Associations between the MED score and high aggressive prostate cancer versus low-intermediate aggressive prostate cancer were similar for AAs and EAs, although the effect estimates were not statistically significant for either racial group ($OR_{high\ vs.\ low}$:

Table 1
Dietary and demographic characteristics of PCaP research subjects by high and low-intermediate aggressiveness[†] (after excluding research subjects with missing covariates)

Characteristic	High aggressive (n = 332)		Low-intermediate aggressive (n = 1567)		*P*-value[*]
	Mean	SD	Mean	SD	
MED score	4.0	1.6	4.2	1.7	.06
DASH score	21.6	4.2	22.1	4.4	.06
Age (y)	65	8	63	8	<.0001
Energy intake (kcal/d)	2594.3	1121.3	2458.6	1022.6	.04
Body mass index (kg/m^2)	30.2	6.0	29.1	5.0	<.0001
Physical activity (MET h/wk)	22.3	22.9	24.2	23.6	.18
	n	%	n	%	
Race					.005
AA	182	54.8	726	46.3	
EA	150	45.2	841	53.7	
Site					.35
Louisiana	179	53.9	801	51.1	
North Carolina	153	46.1	766	48.9	
Education level					<.0001
<8th grade/some high school	96	28.9	282	18.0	
High school grad/vo-tech	91	27.4	493	30.8	
Some college/college grad	111	33.4	565	36.1	
Graduate school/prof. degree	34	10.2	237	15.1	
Smoking status					.003
Never	93	28.0	555	35.4	
Former	173	52.1	798	50.9	
Current	66	19.9	214	13.7	
Use of NSAIDs					.70
No	127	38.3	617	39.4	
Yes	205	61.8	950	60.6	
Family history (first-degree relative affected)					.45
No	260	78.3	1144	73.0	
Yes	72	21.7	423	27.0	
Screening history (PSA or DRE)					<.0001
None	73	22.0	164	10.5	
DRE	60	18.1	230	14.7	
PSA	17	5.1	60	3.8	
DRE and PSA	182	54.8	1113	71.0	
Charlson's Comorbidity Index					.33
0	155	46.7	799	51.0	
1-3	152	45.8	669	42.7	
4+	25	7.5	99	6.3	

MET = metabolic equivalent tasks.
[*] *P*-value for differences between high and low-intermediate aggressive cases determined using *t* test for continuous variables and χ^2 test for categorical variables.
[†] Prostate cancer aggressiveness was defined as the severity of the cancer at diagnosis based on combinations of Gleason sum, stage, and PSA as follows: high aggressive, Gleason sum ≥ 8 or PSA > 20 ng/mL or Gleason sum ≥ 7 and stage T3–T4; low aggressive, Gleason sum < 7 and stage T1–T2 and PSA < 10 ng/mL; intermediate aggressiveness, all other cases.

Table 2
Associations between dietary pattern scores and prostate cancer aggressiveness in PCaP

Dietary pattern score	High/low-intermediate aggressive	Simple*		Multivariable-adjusted†	
		OR (95% CI)	*P* (trend)	OR (95% CI)	*P* (trend)
MED					
Continuous	332/1567	0.88 (0.82–0.96)		0.92 (0.84–0.99)	
Low (0–3)	128/544	1.00 (ref)		1.00 (ref)	
Moderate (4–5)	144/668	0.78 (0.60–1.03)		0.85 (0.64–1.14)	
High (6–9)	60/355	0.57 (0.40–0.81)	.007	0.66 (0.46–0.95)	.09
DASH					
Continuous	332/1567	0.96 (0.93–0.99)		0.98 (0.95–1.01)	
T1 (<20)	142/590	1.00 (ref)		1.00 (ref)	
T2 (20–24)	105/512	0.78 (0.58–1.03)		0.83 (0.62–1.21)	
T3 (>25)	85/465	0.65 (0.48–0.89)	.02	0.76 (0.55–1.06)	.23

* Model included dietary score, age, total energy intake, and race.
† Model included dietary score, age, total energy intake, race, BMI, smoking status, family history, NSAIDs use, education, screening history, Charlson's comorbidity score, and site.

0.63; 95% CI: 0.38, 1.04 for AAs, and $OR_{high\ vs.\ low}$: 0.65; 95% CI: 0.37, 1.16 for EAs) (Table 3). The association between the DASH score and high aggressive versus low-intermediate aggressive prostate cancer was relatively stronger for EAs ($OR_{T3vs.T1}$: 0.65; 95% CI: 0.40, 1.06) than for AAs ($OR_{T3vs.T1}$: 0.84; 95% CI: 0.54, 1.30).

Interaction between the MED score and age ("less than 65 years" or "65 years or older") was observed (Table 4). Higher MED scores showed larger inverse associations for research subjects aged 65 years and older than for research subjects younger than 65 years. While significant interactions between MED score and smoking or BMI were not observed, we noted associations for MED score and aggressive prostate cancer were strongest in never and former smokers as compared with current smokers, and among overweight research subjects as compared with normal weight and obese research subjects. No significant interactions between the DASH dietary pattern score and race, age, smoking, or BMI were observed, although the same patterns of decreased odds were observed for older or overweight research subjects, and never/former smokers.

Discussion

In the PCaP study, research subjects who consumed a diet more closely aligned with the Mediterranean or DASH diets had decreased odds of high aggressive versus low-intermediate aggressive prostate cancer at diagnosis. Associations were similar for AAs and EAs, although they appeared to differ by age. Research subjects aged greater than or equal to 65 years had stronger inverse associations between the MED score and high aggressive prostate cancer than younger subjects. We noted patterns of associations between the MED score and high aggressive prostate cancer that were stronger for never or former smokers, as opposed to current smokers, and for overweight, as opposed to normal-weight or obese research subjects.

The differences in the strength of associations found for MED and DASH scores may be related to differences in their composition. All grains are considered beneficial in MED scoring, whereas DASH scoring only considers whole grains as healthy. Conversely, the MED score classifies all dairy as negative, whereas low-fat dairy contributes positively to the DASH score. Fish intake is scored positively for MED, but fish are not considered separately for DASH scoring. The MED considers moderate alcohol and a high monounsaturated to saturated fat intake ratio to be beneficial to health, whereas the DASH does not account for consumption of either, but discounts high sodium and sugary beverage consumption. Vegetable, fruit, nut, and legume consumption in both patterns are considered positively. Given the reported higher risk of prostate cancer aggressiveness for increased dairy intake in previous studies [8], the difference in scoring of dairy products between the two dietary patterns may explain, in part, the stronger associations observed for the MED as compared with the DASH score. Animal models have suggested that fish oil slows prostate tumor growth [34], so counting fish consumption as beneficial in MED, but not DASH, may also contribute to the stronger associations observed. Alcohol consumption is associated with increased risk of other cancers [35], so inclusion of it as a beneficial component of the MED score may attenuate the observed associations. However, the evidence for a positive association between alcohol and overall prostate cancer or aggressive prostate cancer is limited [36].

Only two previous studies [15,20] used the original MED scoring outlined by Trichopoulou et al [24], and neither found a significant

Table 3
Association* between dietary pattern score and prostate cancer aggressiveness by race in PCaP

Dietary pattern score	AA ($n = 908$)			EA ($n = 991$)			$P_{interaction}$
	High/low-intermediate aggressive	OR (95% CI)	P_{trend}	High/low-intermediate aggressive	OR (95% CI)	P_{trend}	
MED							
Continuous	182/726	0.91 (0.81–1.02)	.10	150/841	0.90 (0.80–1.02)	.10	
Low (0–3)	55/191	1.00 (ref)		73/353	1.00 (ref)		
Moderate (4–5)	87/338	0.82 (0.54–1.25)		57/330	0.86 (0.57–1.29)		
High (6–9)	40/197	0.63 (0.38–1.04)	.19	20/158	0.65 (0.37–1.16)	.34	1.0
DASH							
Continuous	182/726	0.99 (0.94–1.03)	.50	150/841	0.96 (0.91–1.00)	.07	
T1 (<20)	80/295	1.00 (ref)		62/295	1.00 (ref)		
T2 (20–24)	54/223	0.87 (0.57–1.32)		51/289	0.75 (0.48–1.16)		
T3 (>25)	48/208	0.84 (0.54–1.30)	.69	37/257	0.65 (0.40–1.06)	.20	.9

* All models included dietary score, age, total energy intake, BMI, smoking status, family history, NSAIDs use, education, screening history, Charlson's comorbidity score, and site.

Table 4
Effect modification of association[†] between dietary pattern score and prostate cancer aggressiveness by age, smoking status, and BMI in PCaP[‡]

Dietary pattern score	Age (y)		*P*-value[§]	Smoking status			*P*-value[§]	BMI (kg/m^2)			*P*-value[§]
	<65	≥65		Never	Former	Current		<25	25 ≤ 30	≥30	
High/low-intermediate aggressive (n)	159/900	173/667		93/555	173/798	66/214		56/295	126/693	150/579	
MED											
Low (0–3)	1.00 (ref)	1.00 (ref)		1.00 (ref)	1.00 (ref)	1.00 (ref)		1.00 (ref)	1.00 (ref)	1.00 (ref)	
Moderate (4–5)	1.05 (0.69–1.59)	0.70 (0.47–1.04)		0.96 (0.56–1.62)	0.72 (0.48–1.07)	1.14 (0.53–2.45)		1.94 (0.91–4.14)	0.53 (0.33–0.85)	0.96 (0.62–1.48)	
High (6–9)	0.99 (0.60–1.65)	0.43 (0.25–0.75)	.09[*]	0.69 (0.23–1.44)	0.60 (0.37–0.99)	0.84 (0.33–2.14)	.20	1.41 (0.56–3.56)	0.44 (0.25–0.79)	0.76 (0.42–1.37)	.10
DASH											
T1 (<20)	1.00 (ref)	1.00 (ref)		1.00 (ref)	1.00 (ref)	1.00 (ref)		1.00 (ref)	1.00 (ref)	1.00 (ref)	
T2 (20–24)	1.05 (0.68–1.62)	0.75 (0.50–1.12)		0.64 (0.36–1.08)	0.84 (0.56–1.27)	0.85 (0.40–1.80)		0.82 (0.38–1.76)	0.80 (0.50–1.28)	0.88 (0.55–1.39)	
T3 (>25)	1.02 (0.65–1.60)	0.62 (0.39–0.99)	.30	0.58 (0.32–1.08)	0.70 (0.44–1.10)	1.23 (0.55–2.72)	.20	1.11 (0.51–2.43)	0.43 (0.25–0.75)	1.07 (0.65–1.77)	.20

[*] *P*-value <0.10 considered statistically significant interaction.
[†] All models included dietary score, total energy intake, family history, NSAIDs use, education, screening history, Charlson's comorbidity score, and site. Age, smoking, and BMI were included except in their respective stratified models.
[‡] Table values reported as OR (95% CI) unless otherwise noted.
[§] *P*-value for likelihood ratio test comparing no interaction model with interaction model.

association with this index and prostate cancer risk independent of tumor aggressiveness. No previous studies on the association between prostate cancer and the DASH diet exist, but some authors also report an absence of association between the alternative MED score and prostate cancer [16,19]. This index separates fruits and nuts into two groups, disregards dairy, and only includes whole grains and red/processed meats, which makes alternative MED score components more similar to DASH components. However, previous work has found inverse associations between the DASH diet and risk for other cancers, such as lung cancer [37] and colorectal cancer in men [38,39]. Americans with the highest DASH scores had lower cancer mortality than those with the lowest scores in multiple studies [40,41]. Finally, two studies identified dietary patterns using data-driven approaches that were labeled as "Mediterranean" [20,26]. One study found no association with prostate cancer [20] but the other found significant inverse associations with aggressive prostate cancer [26].

Differences in study design and sample composition may contribute to explaining why this study found an association between adherence to a MED and prostate cancer aggressiveness where others did not. PCaP is a case-only study, where the comparison group consisted of research subjects diagnosed with low or intermediate aggressive prostate cancers, whereas control groups in previous studies comprised cancer-free individuals. It is possible that certain foods or dietary patterns are associated with slower progression or decreased mortality of prostate cancer, while not being associated with overall prostate cancer incidence. For example, a meta-analysis of fish consumption reported no association with prostate cancer incidence, but a significant reduction in risk of metastatic prostate cancer or prostate cancer–specific mortality [42]. Similarly, previous studies on the association between dietary fat and prostate cancer incidence have reported mixed results, while there are more consistent data for advanced or fatal prostate cancer [43,44].

In addition, the sample population of PCaP is unique in that AA and EA research subjects were enrolled in equal proportion. Previous research conducted in the United States using data from the NIH-AARP and HPFS cohorts comprised mostly EA men [15,17], and other studies on MED dietary patterns and prostate cancer outcomes were based on Swedish populations [16,20]. While neither dietary pattern showed significant differences in associations by race in PCaP, further research is needed to corroborate these findings.

Associations with MED score were modified by age, with a significantly greater benefit seen in research subjects 65 years or older compared with research subjects younger than 65 years. Dietary benefits may accumulate over time, or the effect of diet may be magnified as risk of high aggressive prostate cancer increases with age. Additional studies are needed to explore these modifying relationships.

Strengths and weaknesses

The National Cancer Institute Dietary History Questionnaire, modified to include regional dishes of North Carolina and Louisiana, was used to assess research subjects' diet for the year before diagnosis. Food frequency questionnaires can be inaccurate and are innately subject to recall bias; however, the effect of differential recall bias is likely minimized in this study because all research subjects were diagnosed with prostate cancer [45]. Even assuming accuracy of dietary information, only food intakes for the year before diagnosis were assessed, although the most relevant period of dietary exposure for prostate cancer is unknown and diets are likely to be relatively stable in adulthood [46,47]. Owing to missing outcome, exposure, and covariate data, 359 research subjects were

excluded from analysis. When these research subjects were compared with the final sample, excluded research subjects (with diagnostic measurements) were more likely to have high aggressive prostate cancer than included subjects, although mean dietary pattern scores were similar between the groups (Supplemental Table 3). It is difficult to predict how exclusion of these research subjects would have affected the results of this analysis (i.e., whether biased toward or away from the null value), although the inclusion of a larger sample size of high aggressive cases would likely have increased power, particularly in the stratified analyses.

Despite these weaknesses, this study also has a number of strengths. The sample population was optimized for studying population-based racial differences in prostate cancer aggressiveness because recruitment was based on race with similar numbers of AAs and EAs enrolled. Enrolling only men with confirmed prostate cancer and using low-intermediate aggressive cases as the comparison group may have minimized outcome misclassification due to the high prevalence of indolent prostate cancer in the American population. In traditional case-control studies, some "controls" may be erroneously assumed to be disease-free because they had not been screened previously. Data on a large number of potential confounders and effect modifiers were collected from research subjects and used in the analyses. However, residual or unmeasured confounding cannot be ruled out in any observational study.

Conclusions

The results of this study suggest a protective effect of consuming a Mediterranean-style diet, and possibly the DASH diet, against aggressive prostate cancer diagnosis. Further research is needed to corroborate these findings and to better understand how diet may influence racial disparities in prostate cancer aggressiveness.

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Appendix A

Supplemental Table 1
Scoring schema for MED and DASH dietary pattern scores

Dietary component	Criteria for maximum score	Score range
MED[a]		
Grains/cereals	≥ median g/d	0–1
Dairy	≤ median g/d	0–1
Fatty acids (MUFA/SFA)	≥ median g/d	0–1
Vegetables	≥ median g/d	0–1
Legumes	≥ median g/d	0–1
Fruits and nuts	≥ median g/d	0–1
Fish	≥ median g/d	0–1
Meat and poultry	≤ median g/d	0–1
Alcoholic drinks	10–50 g/d	0–1
DASH[b]		
Whole grains	Highest quintile	1–5
Low-fat dairy	Highest quintile	1–5
Vegetables	Highest quintile	1–5
Legumes and nuts	Highest quintile	1–5
Fruit (including juices)	Highest quintile	1–5
Red and processed meat	Lowest quintile	1–5
Sodium	Lowest quintile	1–5
Sweetened beverages	Lowest quintile	1–5

[a] Sample median calculated for each dietary component, then each research subject scored based on their individual intake.
[b] Sample quintiles calculated for each dietary component, then each research subject scored based on their individual intake.

Supplemental Table 2
Frequency of healthiest score for MED and DASH diet components by race

Dietary components	AA (n = 908)		EA (n = 991)		p-value*
	n	%	n	%	
MED					
Grains/cereals (≥median g/d)	571	62.9	383	38.9	<.0001
Dairy (≤median g/d)	503	55.4	409	41.3	<.0001
Fatty acids (MUFAs/SFA ≥ median g/d)	492	54.2	462	46.6	0.001
Vegetables (≥median g/d)	435	47.9	493	49.8	0.4
Legumes (≥median g/d)	464	51.1	452	45.6	0.02
Fruits and nuts (≥median g/d)	502	55.3	436	44.0	<.0001
Fish (≥median g/d)	489	53.9	437	44.1	<.0001
Meat and poultry (≤median g/d)	440	48.5	557	56.2	0.0007
Alcohol (10–50 g/d)	175	19.3	258	26.0	0.0005
DASH					
Whole grains (highest quintile)	179	23.4	172	17.4	0.0003
Low-fat dairy (highest quintile)	108	11.9	285	28.8	<.0001
Vegetables (highest quintile)	169	18.6	189	19.1	0.02
Legumes and nuts (highest quintile)	195	21.5	162	16.4	0.002
Fruit (highest quintile)	238	26.2	132	13.3	<.0001
Red and processed meat (lowest quintile)	217	23.9	179	18.1	<.0001
Sodium (lowest quintile)	214	23.6	173	17.5	<.0001
Sweetened beverages (lowest quintile)	172	18.9	237	23.9	0.0001

* P-value for differences between AA and EA research subjects determined using χ^2 test.

Supplemental Table 3
Comparison of research subjects included in final analyses to those excluded due to missing data or energy intake outliers

Characteristic	Research subjects included in analyses (n = 1899)		Research subjects excluded due to missing data or energy intake outliers (n = 359)		P-value*
	Mean	SD	Mean	SD	
MED score	4.2	1.6	4.3	1.6	0.11
DASH score	22.0	4.4	22.3	4.2	0.23
Age	63	8	63	8	0.92
Body mass index	29.3	5.2	28.9	5.9	0.31
MET hours per week	23.9	23.5	20.3	18.0	0.0069
Total energy intake (kcal)	2482.3	1041.5	3341.7	2456.8	<0.0001
	n	%	n	%	
Aggressiveness[†]					0.041
High	332	17.5	64	23.4	
Low-intermediate	1567	82.5	210	76.6	
Race					<0.0001
AA	908	47.8	222	61.8	
EA	991	52.2	137	38.2	
Site					<0.0001
LA	980	51.6	247	68.8	
NC	919	48.4	112	31.2	
Education					<0.0001
Less than high School	378	19.9	114	32.0	
High school graduate/vo-tech school	574	30.2	113	31.7	
Some college/college graduate	676	35.6	27.53	27.5	
Graduate/professional training or degree	271	14.3	31	8.7	
Smoking status					<0.0001
Never	648	34.1	91	25.5	
Former	971	51.1	185	51.8	
Current	280	14.7	81	22.7	
NSAIDs use					0.43
No	744	39.2	127	36.9	
Yes	1155	60.8	217	63.1	
Family history in first degree relative					0.92
No	1404	73.9	128	73.6	
Yes	495	26.1	46	26.4	
Screening history					<.0001
None	237	12.5	74	20.7	
DRE only	290	15.3	85	23.7	
PSA only	77	4.1	15	4.2	
DRE & PSA	1295	68.2	184	51.4	
Charlson's Comorbidity Index					0.57
0	954	50.2	167	47.7	
1-3	821	43.2	162	46.3	
4+	124	6.5	21	6.0	

MET = metabolic equivalent tasks.
* P-value for differences between included and excluded research subjects determined using t test for continuous variables and χ^2 test for categorical variables.
† Prostate cancer aggressiveness was defined as the severity of the cancer at diagnosis based on combinations of Gleason sum, stage, and PSA as follows: high aggressive, Gleason sum ≥ 8 OR PSA > 20 ng/mL OR Gleason sum ≥ 7 and stage T3–T4; low aggressive, Gleason sum < 7 and stage T1–T2 and PSA < 10 ng/mL; intermediate aggressiveness, all other cases.