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Original Contribution

Index-based Dietary Patterns and the Risk of Prostate Cancer in the NIH-AARP Diet and Health Study

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Few studies have investigated the relationship between overall diet and the risk of prostate cancer. We examined the association between 3 diet quality indices—the Healthy Eating Index-2005 (HEI-2005), Alternate Healthy Eating Index-2010 (AHEI-2010), and alternate Mediterranean diet score (aMED)—and prostate cancer risk. At baseline, dietary intake was assessed in a cohort of 293,464 US men in the National Institutes of Health (NIH)-AARP Diet and Health Study. Cox proportional hazards regression was used to estimate hazard ratios. Between 1995 and 2006, we ascertained 23,453 incident cases of prostate cancer, including 2,251 advanced cases and 428 fatal cases. Among men who reported a history of prostate-specific antigen testing, high HEI-2005 and AHEI-2010 scores were associated with lower risk of total prostate cancer (for the highest quintile compared with the lowest, hazard ratio (HR) = 0.92, 95% confidence interval (CI): 0.86, 0.98, *P* for trend = 0.01; and HR = 0.93, 95% CI: 0.88, 0.99, *P* for trend = 0.05, respectively). No significant association was observed between aMED score and total prostate cancer or between any of the indices and advanced or fatal prostate cancer, regardless of prostate-specific antigen testing status. In individual component analyses, the fish component of aMED and ω-3 fatty acids component of AHEI-2010 were inversely associated with fatal prostate cancer (HR = 0.79, 95% CI: 0.65, 0.96, and HR = 0.94, 95% CI: 0.90, 0.98, respectively).

diet; food habits; prostatic neoplasms

Abbreviations: AHEI-2010, Alternate Healthy Eating Index-2010; aMED, alternate Mediterranean Diet Score; CI, confidence interval; HR, hazard ratio; HEI-2005, Healthy Eating Index-2005; NIH, National Institutes of Health; PSA, prostate-specific antigen.

Epidemiologic studies of diet and cancer have traditionally focused on single foods or nutrients (1–3). Rather than examining single-nutrient effects, dietary pattern analyses examine the association between overall diet and disease risk, taking into account the fact that foods are eaten in combination (4). Nutrients consumed in foods may interact with each other and influence absorption and bioavailability (5). Intakes of many nutrients are also highly correlated, making it difficult to examine their individual effects (6). Additionally, the impact of single dietary constituents might be too small to detect, but their additive effects might be large enough to observe (7). Furthermore, dietary recommendations, including the 2010 Dietary Guidelines for Americans (8), are expressed more as patterns rather than as individual foods and nutrients.

Previous studies on dietary patterns and risk of prostate cancer have used different methodological approaches and reported inconsistent findings. Most studies examining this association have used data-driven approaches, such as factor analysis (9–12). In 3 prospective studies, investigators found no significant association between any of the identified dietary patterns and the risk of incident prostate cancer (9–11), but in 1 case-control study, researchers found an increased risk with a western dietary pattern (12). In contrast, index-based methods use a priori approaches, calculating scores based on dietary guidance or recommended diets

(13). A comprehensive review of studies on cancer and the Mediterranean dietary pattern in Mediterranean region concluded that adherence to principles of the Mediterranean diet may significantly reduce prostate cancer incidence (14).

We examined the relationship between diet quality and the risk of prostate cancer in the National Institutes of Health (NIH)-AARP Diet and Health Study cohort using 3 indices defined a priori. High index scores have been associated with a reduced risk of other chronic diseases and premature death in this cohort (15, 16) and in other studies (17–19). The Healthy Eating Index-2005 (HEI-2005) aligns with the 2005 Dietary Guidelines for Americans (20). The alternate Mediterranean Diet Score (aMED) aligns with the principles of the traditional Mediterranean diet. The Alternate Healthy Eating Index-2010 (AHEI-2010) was developed at the Harvard School of Public Health based on dietary predictors of chronic disease.

MATERIALS AND METHODS

Study population

The NIH-AARP Diet and Health Study was initiated in 1995–1996, when AARP members aged 50 to 71 years residing in 6 US states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and 2 metropolitan areas (Atlanta, Georgia, and Detroit, Michigan) responded to a questionnaire eliciting information on their medical history, diet, and demographic characteristics (21). Within 6 months of completing this survey, respondents who did not report colon, breast, or prostate cancer initially were asked to complete a questionnaire inquiring about their history of prostate-specific antigen (PSA) testing and digital rectal examinations over the past 3 years (response rate = 69%).

We excluded participants whose questionnaires were completed by others ($n = 15{,}760$), female participants ($n = 225{,}468$), and participants with cancer other than nonmelanoma skin cancer ($n = 28{,}499$) or self-reported end-stage renal failure ($n = 626$) at baseline. We also excluded those who reported extreme intake of total energy (those more than 2 interquartile ranges above the 75th percentile or below the 25th percentile of Box-Cox log transformed intake, which corresponds to <415 and ≥6,141 kcal/day; $n = 2{,}559$). After these exclusions, data for 293,464 participants were available for analysis.

The NIH-AARP Diet and Health Study was approved by the Special Studies Institutional Review Board of the US National Cancer Institute, and questionnaire return was considered to imply written informed consent.

Dietary assessment

At baseline, participants completed a 124-item food frequency questionnaire that asked about the frequency of intake and portion size over the past 12 months (22). It had 10 predefined response categories ranging from "never" to "≥2 times a day" for solid foods and "never" to "≥6 times per day" for beverages. The food items, portion sizes, and a nutrient database were constructed using the US Department of Agriculture's 1994–1996 Continuous Survey of Food Intake by Individuals (23, 24). The food frequency questionnaire has been validated using 2 nonconsecutive 24-hour recalls in a subset of study participants; correlations for nutrient intake ranged from 0.4 to 0.8 (25). We used food group and nutrient variables to construct individual component scores and total index scores for the HEI-2005, the aMED, and the AHEI-2010 based on previous work and published descriptions of the indices (15). The scoring is briefly described below and summarized in Table 1.

Healthy Eating Index-2005. The HEI-2005 was designed to evaluate concordance with the 2005 dietary guidelines (20). It scores 12 components with points ranging from 0 (nonadherence) to 100 (perfect adherence). Six components (total grains; whole grains; total vegetables; dark-green vegetables, orange vegetables, and legumes; total fruit; and whole fruit) are worth 0 to 5 points; 5 components (milk; meats and beans; oils; saturated fat; and sodium) are worth 0 to 10 points; and 1 component (calories from solid fat, alcohol, and added sugar) is worth 0 to 20 points. Scores are evenly prorated except for saturated fat and sodium; these components are prorated from 0 to 8 and from 8 to 10 points (with 8 and 10 points representing acceptable and optimal levels, respectively). Components and standards for scoring are energy-adjusted on a density basis (per 1,000 calories). Details on HEI-2005 development, evaluation, and scoring have been described previously (20, 26, 27).

Alternate Mediterranean Diet Score. The aMED was based on the Mediterranean diet scale that assesses compliance with a traditional Mediterranean diet (28, 29). The scale was modified by Fung et al. (17) to separate fruit and nuts into 2 groups, include only whole grains, include only red and processed meat, and eliminate dairy. It assesses 9 components with scores ranging from 0 (noncompliance) to 9 points (highest compliance). One point is given for intake above the population median for healthy components (fruits, nuts, vegetables (excluding potatoes), legumes, whole grains, fish, and ratio of monounsaturated to saturated fats) and 1 point is given for intake below the population median for unhealthy components (red and processed meats). For alcohol intake, 1 point is given for moderate alcohol intake (10–25 g/day). Details of the index have been previously described (17, 30).

Alternate Healthy Eating Index-2010. The AHEI-2010 is based on the AHEI (31) and incorporates current evidence on foods and nutrients associated with lower chronic disease risk. Changes include the addition of components for sodium, sugar-sweetened beverages, and ω-3 fatty acids and the exclusion of multivitamin use. The AHEI-2010 is strongly correlated with the AHEI (correlation coefficient = 0.77; $P < 0.001$) (32). It has 11 components, each scored from 0 to 10 for a total score ranging from 0 (least) to 110 (best) points. For 4 components (sugar-sweetened beverages, red and processed meat, sodium, and *trans* fats), higher intakes result in a lower score. Higher intakes of fruits, vegetables, nuts, whole grains, polyunsaturated fatty acids, marine ω-3 fatty acids, and alcohol (within moderate range) result in a higher score. The rationale for the variable selection and the details of the development of the index have been described elsewhere (32).

Table 1. Components and Optimal Quantities for Scoring Standards for Each Component of the Diet Quality Indices,[a] National Institutes of Health-AARP Diet and Health Study, 1995–2006

Dietary Component	HEI-2005 (0–100 Points)		aMED (0–9 Points)		AHEI-2010 (0–110 Points)	
	Optimal Intake	Median Intake	Optimal Intake	Median Intake	Optimal Intake	Median Intake
Grains						
Total	≥3 ounces/1,000 kcal	5.21 ounces				
Whole	≥1.5 ounces/1,000 kcal	0.88 ounces	Median value or higher	1.19 ounces	≥90 g/day	24.98 g
Vegetables						
Total	≥1.1 cups/1,000 kcal	1.80 ounces	Median value or higher	1.85 cups	≥5 servings/day	2.76 servings
Dark, green, and orange vegetables and legumes	≥0.4 cups/1,000 kcal	0.31 cups				
Fruit						
Total	≥0.8 cups/1,000 kcal	1.68 cups	Median value or higher	2.29 cups	≥4 servings/day	1.92 servings
Whole	≥0.4 cups/1,000 kcal	0.96 cups				
Milk	≥1.3 cups/1,000 kcal	1.09 cups				
Meat, fish, legumes, and nuts	≥2.5 ounces/1,000 kcal	4.79 ounces				
Red and processed meat			Less than the median	3.00 ounces	<1 serving/month	0.72 servings
Fish			Median value or higher	0.66 ounces		
Nuts			Median value or higher	0.36 ounces		
Legumes			Median value or higher	0.09 cups		
Nuts, soy, and legumes					>1 serving/day	0.67 servings
Oils	≥12 g/1,000 kcal	14.82 g				
Monounsaturated to saturated fat ratio			Median value or higher	1.24		
Polyunsaturated fats					≥10% kcal	6.62 g
ω-3 fatty acids					≥250 mg/day	80 mg
Fats						
Saturated fat	≤7% of calories	18.88 g				
Trans fats					<0.5% of calories	4.15 g
Sodium	≤700 mg/1,000 kcal	2,799 mg			Lowest decile of intake	2,799 mg
Calories from solid fats, alcohol, and added sugar	≤20% of calories	562.25 kcal				
Sugar-sweetened beverages					<1 drink/day	0.85 drinks
Alcohol			10–25 g/day	5.02 g	0.5–2.0 drinks/day	0.26 drinks

Abbreviations: AHEI-2010, Alternate Healthy Eating Index-2010; aMED, alternate Mediterranean diet score; HEI-2005, Healthy Eating Index-2005.
[a] Higher index scores indicate better diet quality by index scoring standards.

Follow-up and identification of cancer cases

Study participants were followed up from the time of the baseline dietary questionnaire return in 1995–1996 through December 31, 2006. Incident prostate cancer cases were identified through linkage between the NIH-AARP cohort membership and 10 state cancer registry databases (8 original and 2 additional states—Arizona and Texas). The case ascertainment method has been previously described and was certified to be 90% complete within 2 years of cancer occurrence (33). Vital status was ascertained by annual linkage of the cohort to the Social Security Administration Death Master File on deaths in the United States, follow-up searches of the National Death Index Plus for participants who matched to the Social Security Administration Death Master File, cancer registry linkage, questionnaire responses, and responses to other mailings. Details on the cohort design and maintenance have been previously described (21).

Information on prostate cancer stage was also obtained from the registries. Nonadvanced prostate cancer cases were those involving the prostate gland only, with a clinical classification of T1a-T2b, N0, and M0 according to the Joint Committee on Cancer's 1997 Tumor-Node-Metastasis classification system. Advanced prostate cancer cases were those whose cancer had spread beyond the prostate (classified as T3-T4, N1, or M1) or who subsequently died of prostate cancer during follow up. Fatal cases were men with prostate cancer who died of prostate cancer during follow-up.

Statistical analysis

We used Cox proportional hazards regression to estimate hazard ratios and 95% confidence intervals for prostate cancer. Person-years of follow-up were calculated from the date of baseline questionnaire return until diagnosis of first cancer, move out of the cancer registry area, death, or the end of follow-up (December 31, 2006, for total and advanced prostate cancer analysis and December 31, 2005, for fatal prostate cancer analysis). The proportional hazards assumption was tested and confirmed by modeling interaction terms of time and index scores and other covariates.

The multivariate models were adjusted for potential confounding by prostate cancer risk factors previously identified in this cohort and in other studies, including age, race, body mass index (weight (kg)/height $(m)^2$), physical activity level, smoking status, family history of prostate cancer, screening for prostate cancer by PSA, educational level, history of diabetes mellitus, and total energy intake. We included energy intake in the final models to reduce measurement error and to allow for comparability across the indices. We ran models with and without energy and the estimates did not differ appreciably. For covariates with missing responses, we created indicator variables to use in our models. The proportion of missing values was generally less than 4%. To test for linear trend across quintiles of intake, we modeled index scores as continuous variables using the median intake for each quintile. To investigate whether PSA screening influenced our results, we repeated the analysis stratified by PSA screening history (yes vs. no). We also investigated the independent associations of

Table 2. Baseline Characteristics of Male Participants by Quintiles[a] of Diet Quality Index Scores, National Institutes of Health-AARP Diet and Health Study, 1995–2006

Diet Quality Index	No. of Participants	Range of Points	Mean Age,[b] years	White,[b] %	College Education,[b] %	Body Mass Index[b,c]	Never Smoker,[b] %	Physical Activity[b] >5 times/week, %	Energy Intake,[b] kcal	History of PSA Test,[b] %	Family History of Prostate Cancer,[d] %	History of Diabetes,[e] %
HEI-2005												
Quintile 1	58,692	21–55	61.5	93.0	33.5	27.3	20.0	15.6	2368	35.9	8.0	6.1
Quintile 5	58,693	76–97	62.8	92.3	52.6	26.9	36.2	28.2	1787	50.3	8.4	14.7
aMED												
Quintile 1	50,204	0–2	61.5	93.6	33.4	27.6	23.5	15.5	2274	36.7	8.0	9.0
Quintile 5	75,185	6–9	62.6	92.6	54.3	26.7	33.4	27.5	1867	50.2	8.5	9.0
AHEI-2010												
Quintile 1	58,692	11–43	61.7	93.0	32.9	27.7	26.6	15.2	2131	37.6	8.0	9.4
Quintile 5	58,693	61–94	62.4	92.5	56.2	26.7	31.6	30.0	2016	49.6	8.4	9.4

Abbreviations: AHEI-2010, Alternate Healthy Eating Index-2010; aMED, alternate Mediterranean diet Score; HEI-2005, Healthy Eating Index 2005; PSA, prostate-specific antigen.

[a] Quintile 5 indicates a healthier diet by index scoring standards.

[b] Differences between quintile 1 and quintile 5 (t test or χ statistic) are statistically significant at $P < 0.0001$ for all indices.

[c] Weight (kg)/height $(m)^2$.

[d] Differences between quintile 1 and quintile 5 (χ^2 statistic) are statistically significant at $P < 0.005$ for all indices.

[e] Differences between quintile 1 and quintile 5 (χ^2 statistic) are statistically significant at $P < 0.0001$ for HEI-2005.

the individual components in each index by running index-specific models in which we adjusted for all other components in the given index and the covariates specified earlier. We also calculated Spearman correlation of the total scores across the indexes. All statistical tests were 2-sided and $P \leq 0.05$ was considered statistically significant. Analyses were performed using SAS, version 9.1 (SAS institute, Inc., Cary, North Carolina)

RESULTS

Over a mean of 8.9 years of follow-up, 23,453 prostate cancer cases were ascertained, including 2,251 advanced cases and 428 fatal cases. At baseline, compared with men in the lowest quintile for all 3 indices, men in the highest quintile were more physically active, more educated, more likely to have been screened using PSA tests, and more likely to be nonsmokers (Table 2). Men in the highest quintile were also on average slightly older and had slightly lower body mass indexes than did those in the lowest quintile. The AHEI-2010 and the HEI-2005 were positively correlated with the aMED (correlation coefficient = 0.67 and 0.62 respectively, $P < 0.0001$) and with each other (correlation coefficient = 0.55, $P < 0.0001$).

In the multivariate models, the HEI-2005 and the AHEI-2010 were inversely associated with total prostate cancer (comparing highest quintile with the lowest, for HEI-2005, HR = 0.94, 95% confidence interval (CI): 0.90, 0.98, *P* for trend = 0.01; for the AHEI-2010, HR = 0.96, 95% CI: 0.92, 1.00, *P* for trend = 0.009). There was no association between total prostate cancer and the aMED score (HR = 0.97, 95% CI: 0.91, 1.03; *P* for trend = 0.09). When associations were examined stratified by recent screening for prostate cancer by PSA, the weak inverse association was seen only among men who reported PSA screening in the preceding 3 years (comparing the highest quintile with the lowest, for HEI-2005, HR = 0.92, 95% CI: 0.86, 0.98, *P* for trend = 0.01; for the AHEI-2010, HR = 0.93, 95% CI: 0.88, 0.99, *P* for trend = 0.05) (Table 3). There was no significant association between the HEI-2005, the aMED, or the

Table 3. Hazard Ratios for Total Prostate Cancer by Quintile[a] of Diet Quality Indices Stratified by Baseline Prostate-specific Antigen Screening History, National Institutes of Health-AARP Diet and Health Study, 1995–2006

PSA Screening in Past 3 Years	Quintile of Diet Quality Scores									*P* for trend
	1	2		3		4		5[b]		
	HR	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	
PSA Screening (n = 128,736)										
HEI-2005										
Age-adjusted	1.00	0.95	0.89, 1.01	0.99	0.93, 1.05	0.95	0.89, 1.01	0.93	0.88, 0.99	0.03
Multivariate[c]	1.00	0.94	0.88, 1.00	0.97	0.91, 1.03	0.93	0.88, 1.00	0.92	0.86, 0.98	0.01
aMED										
Age-adjusted	1.00	1.03	0.96, 1.10	1.04	0.98, 1.11	1.03	0.97, 1.10	1.01	0.95, 1.07	0.98
Multivariate[c]	1.00	1.02	0.96, 1.09	1.02	0.96, 1.09	1.01	0.95, 1.08	0.97	0.91, 1.03	0.09
AHEI-2010										
Age-adjusted	1.00	0.97	0.92, 1.03	0.98	0.92, 1.04	1.01	0.95, 1.07	0.97	0.91, 1.02	0.41
Multivariate[c]	1.00	0.97	0.91, 1.03	0.97	0.91, 1.03	0.99	0.93, 1.05	0.93	0.88, 0.99	0.05
No PSA Screening (n = 37,015)										
HEI-2005										
Age-adjusted	1.00	1.00	0.89, 1.12	0.94	0.83, 1.07	1.06	0.94, 1.20	0.98	0.86, 1.12	0.93
Multivariate[c]	1.00	0.98	0.87, 1.10	0.92	0.81, 1.04	1.03	0.90, 1.17	0.95	0.83, 1.09	0.65
aMED										
Age-adjusted	1.00	1.08	0.95, 1.22	0.95	0.83, 1.08	1.04	0.91, 1.19	1.04	0.62, 1.17	0.78
Multivariate[c]	1.00	1.06	0.93, 1.20	0.92	0.81, 1.05	1.00	0.87, 1.14	0.98	0.86, 1.11	0.51
AHEI-2010										
Age-adjusted	1.00	1.10	0.98, 1.24	1.02	0.90, 1.16	1.07	0.95, 1.22	1.02	0.89, 1.16	0.86
Multivariate[c]	1.00	1.10	0.97, 1.24	1.01	0.89, 1.15	1.05	0.93, 1.19	0.98	0.86, 1.13	0.72

Abbreviations: AHEI-2010, Alternate Healthy Eating Index-2010; aMED, alternate Mediterranean diet score; CI, confidence interval; HR, hazard ratio; HEI-2005, Healthy Eating Index 2005; PSA, prostate-specific antigen.

[a] Range of scores by index quintiles 1–5: HEI-2005: <54.7, 54.7–63.2, 63.3–69.6, 69.7–75.5, and >75.5; aMED: ≤2, 3, 4, 5, and ≥6; and AHEI-2010: <43.1, 43.1–49.1, 49.2–54.5, 54.6–60.9, and >60.9.

[b] Quintile 5 indicates a healthier diet by index scoring standards.

[c] Multivariate hazard ratios were adjusted for age, ethnicity, educational level, body mass index, smoking, physical activity, family history of prostate cancer, diabetes, and energy.

Table 4. Hazard Ratios for Advanced and Fatal Prostate Cancer by Quintile[a] of Diet Quality Indices in the National Institutes of Health-AARP Diet and Health Study, 1995–2006

Dietary Quality Index	Quintile of Diet Quality Scores									*P* for trend
	1	2		3		4		5[b]		
	HR	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	
Advanced Prostate Cancer										
HEI-2005										
Age-adjusted	1.00	1.01	0.89, 1.15	0.99	0.87, 1.13	1.05	0.92, 1.20	0.99	0.86, 1.12	0.94
Multivariate[c]	1.00	1.00	0.87, 1.14	0.97	0.85, 1.12	1.03	0.90, 1.18	0.97	0.84, 1.12	0.88
aMED										
Age-adjusted	1.00	1.03	0.89, 1.19	1.05	0.91, 1.20	1.12	0.98, 1.29	1.07	0.94, 1.22	0.17
Multivariate[c]	1.00	1.01	0.87, 1.17	1.02	0.88, 1.17	1.07	0.93, 1.24	1.00	0.87, 1.15	0.82
AHEI-2010										
Age-adjusted	1.00	1.08	0.95, 1.24	1.03	0.89, 1.18	1.16	1.02, 1.32	1.15	1.01, 1.32	0.25
Multivariate[c]	1.00	1.07	0.93, 1.22	1.00	0.87, 1.15	1.12	0.98, 1.28	1.10	0.96, 1.26	0.54
Fatal Prostate Cancer										
HEI-2005										
Age-adjusted	1.00	1.11	0.83, 1.48	0.85	0.63, 1.16	0.89	0.66, 1.21	0.76	0.56, 1.04	0.03
Multivariate[c]	1.00	1.26	0.94, 1.69	1.26	0.94, 1.69	1.17	0.85, 1.60	1.06	0.76, 1.48	0.83
aMED										
Age-adjusted	1.00	0.97	0.72, 1.31	0.95	0.83, 1.08	0.90	0.67, 1.21	0.65	0.48, 0.67	0.01
Multivariate[c]	1.00	1.04	0.76, 1.41	0.81	0.59, 1.11	1.05	0.78, 1.43	0.80	0.59, 1.10	0.23
AHEI-2010										
Age-adjusted	1.00	0.81	0.60, 1.08	0.76	0.56, 1.02	0.78	0.58, 1.04	0.77	0.57, 1.03	0.14
Multivariate[c]	1.00	0.87	0.65, 1.17	0.86	0.64, 1.16	0.91	0.68, 1.23	0.96	0.71, 1.30	0.59

Abbreviations: AHEI-2010, Alternate Healthy Eating Index-2010; aMED, alternate Mediterranean diet score; CI, confidence interval; HR, hazard ratio; HEI-2005, Healthy Eating Index 2005;.

[a] Range of scores by index quintiles 1–5: HEI-2005: <54.7, 54.7–63.2, 63.3–69.6, 69.7–75.5, and >75.5; aMED: ≤2, 3, 4, 5, and ≥6; and AHEI-2010: <43.1, 43.1–49.1, 49.2–54.5, 54.6–60.9, and >60.9.

[b] Quintile 5 indicates a healthier diet by index scoring standards.

[c] Multivariate hazard ratios are adjusted for age, ethnicity, educational level, body mass index, smoking, physical activity, family history of prostate cancer, diabetes, energy, and history of prostate-specific antigen screening.

AHEI-2010 and either advanced or fatal prostate cancer, regardless of PSA screening status (Table 4).

Estimates of the independent risk associated with index-specific components are shown in Table 5. Within the aMED, higher scores for the fish component were associated with a lower risk of fatal prostate cancer (HR = 0.79, 95% CI: 0.65, 0.96). Higher scores for the ω-3 fatty acid component of the AHEI-2010 were also associated with a slightly lower risk of fatal prostate cancer (HR = 0.94, 95% CI: 0.90, 0.98). The legume component of the aMED was associated with a higher risk of fatal prostate cancer (HR = 1.26, 95% CI: 1.03, 1.53). There were no other significant associations observed between individual components and the risk of total, advanced, or fatal prostate cancer.

DISCUSSION

The higher HEI-2005 and AHEI-2010 index scores were associated with a lower risk of total prostate cancer only among men who reported PSA testing over the preceding 3 years (comparing the highest quintiles with the lowest). Men in the highest quintiles of both indices were more likely to report recent PSA screening, so it is likely that a greater proportion of nonadvanced disease was detected in men in the highest quintiles. More intense PSA testing among men with the highest level of adherence likely led to depletion of the pool of prevalent localized cancer, yielding a spurious reduction in apparent incidence of those cancers. It is also possible that adherence to these 2 indices is associated with a lower risk of indolent prostate cancer cases, as no association was found with advanced or fatal prostate cancer.

Past studies of dietary patterns and prostate cancer risk have reported inconsistent findings (9–12, 14). A comprehensive review by Trichopoulou et al. (14) used effect estimates from studies of dietary intake and cancer in the Mediterranean region, incidence rates of prostate cancer, and food consumption patterns to calculate the fraction of prostate cancer incidence that could be avoided by

Table 5. Index-specific Multivariate Hazard Ratios[a] for Fatal Prostate Cancer for Components of the Diet Quality Indices, National Institutes of Health-AARP Diet and Health Study, 1995–2006

	Diet Quality Index					
	HEI-2005		aMED		AHEI-2010	
	HR	95% CI	HR	95% CI	HR	95% CI
Grains						
Total grains	0.98	0.86, 1.11				
Whole grains	1.01	0.92, 1.11	1.04	0.85, 1.26	1.01	0.96, 1.05
Vegetables						
Total vegetables	1.06	0.94, 1.20	1.04	0.85, 1.27	1.02	0.97, 1.07
Dark green, orange vegetables and legumes	0.98	0.90, 1.07				
Fruit						
Total fruit	1.04	0.93, 1.16	1.10	0.90, 1.35	1.01	0.98, 1.05
Whole fruit	0.95	0.86, 1.05				
Milk	0.98	0.95, 1.02				
Meat, fish, legumes, and nuts	0.99	0.93, 1.06				
Red and processed meat			0.82	0.67, 1.00	0.97	0.92, 1.01
Fish			0.79	0.65, 0.96		
Legumes			1.26	1.03, 1.53		
Nuts			0.88	0.73, 1.07		
Nuts, soy and legumes					0.99	0.96, 1.03
Oils	0.97	0.93, 1.01				
Monounsaturated to saturated fat ratio			0.84	0.69, 1.03		
Polyunsaturated fats					0.99	0.93, 1.06
ω-3 fatty acids					0.94	0.90, 0.98
Fats						
Saturated fats	0.97	0.93, 1.00				
Trans fats					1.01	0.95, 1.06
Sodium	1.02	0.96, 1.09			1.02	0.95, 1.09
Calories from Solid Fat, Alcohol and Added sugar	1.02	0.99, 1.04				
Sugar-sweetened Beverages					0.99	0.96, 1.02
Alcohol			0.92	0.74, 1.15	1.01	0.99, 1.03

Abbreviations: AHEI-2010, Alternate Healthy Eating Index-2010; aMED, alternate Mediterranean diet score; CI, confidence interval; HR, hazard ratio; HEI-2005, Healthy Eating Index-2005.

[a] Hazard ratios are adjusted for age, ethnicity, educational level, body mass index, smoking, physical activity, family history of prostate cancer, diabetes, energy, history prostate-specific antigen screening, and all other components in the specific index.

adherence to the principles of the Mediterranean diet. They estimated that approximately 10% of prostate cancer cases in the United States could be prevented by adherence to the traditional healthy Mediterranean diet. The risk estimate was based on 9 components of the Mediterranean diet pattern, which were scored based on population distribution of intake. The median intake is considerably higher in a Greek population than in an American one, which may explain the different findings. Other studies have used data-driven techniques, such as factor analysis, to examine this relationship. In 3 prospective studies, investigators found no significant association between identified dietary patterns and the risk of incidence prostate cancer (9–11) or advanced prostate cancer (9). A case-control study with 546 cases found a positive association between a western dietary pattern and prostate cancer (12). However, case-control studies are prone to selection and recall bias, which may limit the comparability of these findings to ours.

The ability of a diet quality index score to predict prostate cancer risk depends on how well the index measures dietary risk factors for prostate cancer. Though these indices have been associated with other chronic disease outcomes (15, 16, 19), they were not created specifically for prostate cancer.

In the individual component analyses, we found a significant inverse association between the fish component of the aMED and fatal prostate cancer. We evaluated the possibility that some or all of this association could be explained by differential early detection and treatment due to increased PSA screening among men who ate more fish. This is not likely because 46% of the men with a fish intake above the median reported PSA screening compared with 43% whose intakes were below the median.

Other studies have also reported an inverse association between fish intake and fatal prostate cancer risk (34–37). A Swedish prospective cohort study conducted before PSA screening was widespread (34) reported a 3-fold higher risk of fatal prostate cancer for nonconsumption of fish compared with a high consumption. In the Health Professionals Follow-up Study, Augustsson et al. (35) reported a 44% lower risk of metastatic prostate cancer among men who ate fish 3 or more times per week versus those who ate it less than 2 times per month. Similarly, Chavarro et al. (36) found an inverse association for consumption of fish 5 or more times per week versus less than once per week. Several studies have also reported an inverse association with the intake of marine ω-3 fatty acids (35, 36, 38), a marker of fish intake and with biomarkers of the fatty acids (2). A proposed mechanism for the effect of fish could be through the long-chained ω-3 fatty acids (39–41) found mainly in fish. These fatty acids have been shown to inhibit the biologic activity of eicosanoids and androgens, which may stimulate the growth of cancer cells (39, 42, 43).

The aMED is the only index of the 3 that we examined that has an individual fish construct. In the AHEI-2010, fish intake is captured by the marine ω-3 fatty acids component, which was associated with a lower risk of fatal prostate cancer. The HEI-2005 scores all meats and major protein sources (meat, fish, legumes, and nuts) as one construct. Fish may be protective, but the portion of the component contributed by red meat and legumes may dilute this effect. Evidence suggests that men who consume high amounts of fish are likely to consume less red and processed meat (34), but the HEI-2005 scoring algorithm does not take this into account. The 2010 dietary guidelines encourage intake of 8 or more ounces of seafood per week as part of protein intake (8). It would be of interest to see how these guidelines influence the index's scoring and whether any changes affect the index-disease relationship.

Unexpectedly, the legume construct of the aMED was positively associated with increased risk of fatal prostate cancer. No previous studies have reported similar findings, and we found no plausible explanation for this association. It is possible that consumption of legumes in our population is associated with higher intake of other foods, for example, red and processed meat. The finding could also be due to chance. Additional research is needed to examine this association further.

Our study was strengthened by the prospective design and the large number of prostate cancer cases that enabled us to examine risk by disease stage. A limitation of our study is that dietary intake was self-reported and assessed using a single baseline food frequency questionnaire; thus, there is potential for nondifferential measurement error. Also, with only a single measure, we could not account for changes in consumption over time. Exposure would therefore be misclassified in individuals who change their dietary intake in the follow-up period. This misclassification would likely be nondifferential and may have resulted in underestimating the true effect. Another potential limitation is the misclassification of cause of death in using the National Death Index to ascertain vital status.

In summary, our findings suggest that diet quality patterns are not associated with the risk for advanced and fatal prostate cancer. The individual component analyses support findings from previous studies that reported an inverse association between fish and ω-3 fatty acids intake and the risk of fatal prostate cancer.

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