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Dietary patterns after prostate cancer diagnosis in relation to disease-specific and total mortality

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Abstract

Men diagnosed with non-metastatic prostate cancer have a long life expectancy and many die of unrelated causes. It is therefore important to know to what extent post-diagnostic diet may impact disease-specific and overall mortality. 926 men participating in the Physicians' Health Study diagnosed with non-metastatic prostate cancer completed diet questionnaires a median of 5.1 years after diagnosis, and were followed thereafter to assess mortality for a median of 9.9 years since questionnaire completion. Two post-diagnostic dietary patterns were identified: a Prudent pattern, characterized by higher intake of vegetables, fruits, fish, legumes, and whole grains; and a Western pattern, characterized by higher intake of processed and red meats, high-fat dairy and refined grains. Cox regression was used to estimate multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs). During 8,093 person-years of follow-up, 333 men died, 56 (17%) of prostate cancer. The Western pattern was significantly related to a higher risk of prostate cancer-specific and all-cause mortality. Comparing men in the highest versus the lowest quartile of the Western pattern, the HRs were 2.53 (95%CI: 1.00-6.42; P_{trend}=0.02) for prostate cancer-specific mortality and 1.67 (95%CI: 1.16-2.42; P_{trend}=0.01) for all-cause mortality. The Prudent pattern was associated with a significantly lower all-cause mortality ($HR_{Quartile\ 4\ vs\ Quartile\ 1}$: 0.64; 95% CI: 0.44-0.93; P_{trend}=0.02); the relationship with prostate cancer-specific mortality was inverse but not statistically significant. Post-diagnostic Western dietary pattern was associated with higher prostate cancer-specific and all-cause mortality, whereas a Prudent dietary pattern was related to lower all-cause mortality after prostate cancer diagnosis.

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Keywords

diet; dietary pattern; prostate cancer; all-cause mortality; Physicians' Health Study

Introduction

Prostate cancer (PCa) is the most commonly diagnosed and second most lethal cancer for men in the U.S.(1), resulting in nearly 3 million U.S. men currently living with PCa (1, 2). Age and tumor characteristics such as grade and stage are well-established risk factors for PCa-specific mortality (2, 3) but are un-modifiable. Increasing evidence suggests that some dietary factors, such as dairy products or fat intake, may have an impact on disease progression, as reflected by associations with biochemical recurrence or disease-specific mortality (4-6). Yet most studies evaluating PCa survival have focused on a single or a group of nutrients or foods without considering dietary patterns. Additionally, research is sparse regarding post-diagnostic diet as a whole (7).

Dietary patterns can provide further insights into the role of nutrition in PCa progression, as they account for interactive or synergistic effects of multiple foods and nutrients (8), and have the advantage of being more readily translatable into clinical and public health recommendations (9). To date, only one study has evaluated the potential role of dietary patterns after PCa diagnosis, concluding that adherence to a Mediterranean dietary pattern was not related to disease-specific mortality (7). The aim of the present study was to prospectively evaluate the relation of data-derived post-diagnostic dietary patterns, with PCa-specific and all-cause mortality among men diagnosed with non-metastatic PCa.

Materials and Methods

Study Population

Men participating in the Physicians' Health Study (PHS) I or II who were diagnosed with non-metastatic PCa and had completed a dietary assessment after PCa diagnosis were included in this study. The PHS I, initiated in 1982, was a randomized trial of aspirin and β-carotene for the primary prevention of cardiovascular disease (CVD) and cancer among 22,071 U.S. male physicians aged 40-84 years (10, 11). The aspirin and β-carotene arms were terminated in 1988 and 1995, respectively (10, 11). The PHS II, initiated in 1997, was a randomized trial of vitamin E, vitamin C, and a multivitamin supplement for the primary prevention of CVD, cancer and age-related eye disease among 14,641 male U.S. physicians, 7,641 of whom had participated in PHS I. The vitamin C and vitamin E arms ended in 2007 and the multivitamin arm ended in 2011. Men who participated in both trials continue to be followed with mailed annual questionnaires to update risk factors and ascertain study endpoints. Follow-up for nonfatal outcomes in PHS is over 97% complete, and for mortality, over 98%. The institutional Review Boards of Partners HealthCare and the Harvard School of Public Health approved this study.

Diet assessment

One food frequency questionnaire (FFQ) was sent to all PHS participants to collect information on usual diet between 1999 and 2002. The FFQ was modeled after the one used in the Health Professional Follow-Up Study, which has been previously validated (12). Dietary patterns were derived from FFQs as previously described (9, 13). Briefly, men were asked to report their usual intake over the previous year of foods and beverages included in the FFQ. Food items were classified into 39 pre-defined food groups to minimize within-person variation in intakes of individual foods (9) (Supplemental Table S1). Dietary patterns were subsequently derived from these food groups through principal component analysis. Specifically, orthogonal transformations were used to obtain uncorrelated factors (dietary patterns) with simpler structures and greater interpretability (13). Eigenvalues (>1; the amount of variance explained by the factor), the Scree plot (a plot of all the eigenvalues for the derived factors in descending order), and the substantive meanings of the rotated factors and consistency with prior literature (9) were considered to determine the number of factors retained. Individual scores were calculated for each factor as the sum of the frequency of consumption multiplied by factor loadings across all food items. Thus, each participant was given a score for the ‘Prudent’ and ‘Western’ patterns.

Disease confirmation and death ascertainment

Participants were asked to report newly diagnosed PCa in the yearly follow-up questionnaires. We obtained medical records and pathology reports to confirm the diagnosis and abstract information on date of diagnosis, tumor clinical stage (TNM staging system) (14), grade (Gleason), prostate-specific antigen (PSA) values, initial treatments, and clinical presentation (PSA screening, abnormal digital rectal examination, clinical symptoms or other). Among 1,002 men diagnosed with PCa and complete diet information, we excluded men with metastatic disease (T4/N1/M1; n=23) or missing data on clinical stage (n=53) thus restricting the study to men with confirmed non-metastatic disease. Deaths were identified by reports from family members and postal authorities, and systematic searches of the National Death Index. Deaths were confirmed through review of death certificates and medical records to determine cause of death, assigned by the Endpoints Committee of three physicians. When medical records cannot be obtained, cause of death is assigned upon reviews of all other available data by the Endpoints Committee. A death was attributed to PCa if PCa metastases were present and no more plausible cause of death was mentioned.

Statistical analysis

Men were classified into quartiles of the “Prudent” and “Western” dietary patterns. χ^2 test and analysis of variance were used to test the associations of baseline characteristics across quartiles of dietary patterns. Cox proportional hazards regression models were used to examine post-diagnostic dietary patterns in relation to PCa-specific and all-cause mortality, using the lowest quartile of dietary pattern as the reference group. For analyses of PCa-specific mortality, men were followed from the date of FFQ completion until death due to PCa, death due to other cause or end of follow-up, whichever came first. For all-cause mortality, men were followed from the date of FFQ completion until death or end of follow-up. We initially fit models adjusted for age at diagnosis (years; continuous) and total energy

intake (kcal; continuous). The multivariable models included additional terms for body mass index (BMI; kg/m^2; <25, 25-30, >30), smoking status (never, past, current), vigorous exercise (days/week, continuous), time interval between diagnosis and FFQ completion (years, continuous), Gleason score (<7, 7, >7), clinical stage (T1/T2, T3), PSA levels (ng/ml; <4, 4-9.9, 10-19.9, 20+), initial treatment (radiation, prostatectomy, others, unspecified or missing), and family history of PCa (yes, no). Adjustment for randomization arm modified Charlson comorbidity index (15, 16), aspirin use, cholesterol medication, and personal history of diabetes did not change the results, and therefore, these variables were not included in the main analysis. In addition, we utilized multivariable competing-risk regression model (17) to obtain sub-distribution estimates, taking into account non-PCa mortality risk.

To test the robustness of our results, we conducted sensitivity analyses excluding men who died within two years of completing the FFQ (n=35), men with PCa death classified as "unrefuted" (n=6), and men who developed distant metastases between diagnosis and completion of FFQ (n=9). P values for trend were calculated by the Wald statistics of a score variable that contained median values of each quartile of dietary pattern. The proportional hazards assumption was assessed by creating an interaction term of pattern and follow-up time, and no violation was observed. Effect modification by age at diagnosis and BMI was evaluated by including cross-product terms to the multivariable model. All the statistical analyses were two-sided and carried out using SAS 9.2 (SAS Institute, Inc., Cary, NC). P-values < 0.05 were considered statistically significant.

Results

We identified 333 deaths, 56 (17%) due to PCa, during 8,093 person-years of follow-up among 926 men with non-metastatic PCa. Two dietary patterns were identified. The Prudent pattern was characterized by higher intake of legumes, vegetables, fruits, whole grains, garlic, soy products, fish, and oil and vinegar dressing. The Western pattern was characterized by higher intake of processed and red meats, eggs, potatoes, high-fat dairy products, butter, refined grains, snacks, sweets and desserts (Table 1). Men with higher Prudent pattern score were more likely to be never smokers, and consume less fat from animal sources and alcohol (Table 2). Men with higher Western pattern scores were older at PCa diagnosis and more likely to be Caucasian and smokers. They had higher intake of animal fats and lower intake of calcium and vitamin D.

Post-diagnostic Prudent pattern score was associated with lower PCa-specific mortality but this association did not reach statistical significance (Table 3). On the other hand, we found a positive association between adherence to the Western dietary pattern and disease-specific mortality. Men in the highest quartile of the Western pattern had a 2.5-fold higher risk of PCa-specific death compared to men in the lowest quartile (Hazard ratio [HR] $_{\text{Quartile 4 vs Quartile 1}}$: 2.53; 95% Confidence Interval [95%CI]: 1.00 - 6.42; $P_{\text{linear-trend}}$= 0.02) (Table 3). Results were similar using competing-risk regression models (Supplemental Table S2).

The Prudent pattern score was inversely associated with all-cause mortality. Men in the highest quartile of this pattern had a 36% lower risk (95% CI: 7% - 56%) of death compared to men in the lowest quartile (Table 4). Conversely, greater adherence to the Western pattern was associated with a 67% higher risk of overall mortality (95% CI: 16% - 142%) after full adjustment of potential confounders.

The relation of the Western pattern with PCa-specific mortality appeared to be predominantly driven by intake of processed meats. In the adjusted model, the HRs for PCa death was 1.32 (95% CI: 1.06 - 1.64; $P = 0.01$) for each one-ounce increase in daily intake of processed meats (Supplemental Table S3). Additionally, the inverse relation of the Prudent pattern with all-cause mortality appeared to be driven by oil and vinegar-dressing intake ($HR_{1std\ increase}$=0.84, 95%CI: 0.74 - 0.95; $P = 0.005$), whereas the positive relation between the Western pattern and total deaths was driven by processed meat ($HR_{1std\ increase}$ =1.17, 95%CI: 1.06 - 1.30; $P = 0.003$) and high-fat dairy intake ($HR_{1std\ increase}$ =1.18, 95%CI: 1.07 - 1.30; $P = 0.001$) (Supplemental Table S3).

We further mutually adjusted for dietary patterns in multivariable models. The linear trends remained similar although the associations were slightly attenuated. Specifically, the HRs (95% CI) comparing top to bottom quartiles of Western pattern scores were 2.18 (0.81 - 5.89) for disease-specific mortality and 1.50 (1.01 - 2.24) for all-cause mortality. In sensitivity analyses, excluding deaths within two years of the diet assessment (35 deaths; 8 due to PCa) attenuated the association of Western pattern with PCa-specific mortality ($HR_{Quartile4\ vs\ Quartile1}$= 1.66; 95% CI: 0.61 - 4.52), while the relationship with all-cause mortality remained similar ($HR_{Quartile4\ vs\ Quartile1}$= 1.69; 95% CI: 1.15 - 2.49). Excluding unrefuted deaths or men who reported distant metastases between diagnosis and diet assessment did not appreciatively alter the results. In addition, the associations of the Western and Prudent patterns with disease-specific mortality were not modified by age at diagnosis (<65y vs. ≥65y) and BMI (<25 kg/m^2 vs. ≥25 kg/m^2).

Discussion

In a cohort of men diagnosed with non-metastatic PCa, greater post-diagnostic adherence to a Western dietary pattern was associated with higher risk of disease-specific and all-cause mortality, while a Prudent dietary pattern was inversely related to mortality risks. The associations of the Western pattern appeared to be driven by intake of processed meats whereas the Prudent pattern association with all-cause mortality appeared to be driven by intake of oil and vinegar-dressing. These findings add to the growing literature suggesting that dietary choices after PCa diagnosis may have an impact on disease progression and survivorship.

Prospective studies investigating the relation of dietary pattern and PCa incidence have reported inconsistent results (8, 18-21). Three cohorts evaluating dietary patterns using principal component analysis (as we did in this study) found no association between the data-derived patterns and PCa risk (8, 19, 20). Using index-based methods, studies indicated that alternate or modified Mediterranean Diet Score were not appreciatively associated with risk of PCa (18, 21), whereas the Healthy Eating Index-2005 and Alternate Healthy Eating

Index-2000 were significantly associated with lower risk of developing incident PCa (18, 21). However, studies on risk of total PCa are expected to differ from those that focus on disease-specific mortality, due to the high incidence of indolent PCa in populations with PSA screening.

Data on post-diagnostic dietary patterns in relation to disease-specific and overall survival are scarce. In the Health Professionals Follow-up Study (HPFS), greater post-diagnostic adherence to a Mediterranean diet, which overlapped considerably with our Prudent dietary pattern, was completely unrelated to disease-specific survival (7). While we did not find a statistically significant association between the Prudent pattern and disease-specific mortality, our results suggest an inverse relation with this outcome. Despite similarity between two studies, reasons for the divergent findings may include different cutoffs of dietary patterns (Mediterranean diet score of 0-3, 4-5, and 6-9 in HPFS vs. quartiles of Prudent diet in PHS), differences in follow-up time after diagnosis (a median 7.6 years in HPFS vs. a median of 13.8 years in this report), calendar year of disease diagnosis (diagnosis date of 1986 to 2006 in HPFS vs diagnosis date of 1982 to 2000 in PHS), and lower statistical power in the current study relative to the previous report. The positive association between the Western pattern and greater risk of PCa-specific mortality in our study is consistent with previous studies which indicated that higher intake of saturated fat, primarily from animal sources, may be related to disease progression. Strom *et al.* (22) documented a 2-fold greater risk of biochemical failure with high saturated fat intake in a cohort of 390 Caucasian men with localized PCa treated with prostatectomy. Meyer *et al.* (23) found a 3-fold greater risk of PCa-specific death among Canadian men in the upper tertile of saturated fat intake compared to those in the lowest tertile (HR: 3.13; 95% CI: 1.28-7.67) and Epstein *et al.* (24) reported that Swedish men in the highest quartile of myristic acid and short-chain saturated fatty acids had more than 2-fold higher risk of disease-specific death than those in the lowest quartile (HR for myristic acid: 2.39; 95% CI: 1.06, 5.38; HR for short-chain saturated fat: 2.88; 95% CI: 1.24 - 6.67). Nevertheless, these relations of saturated fat with PCa-specific mortality were not replicated in HPFS (6). Clearly, whether diet after PCa diagnosis influences disease progression deserves further investigation.

We also documented significant relations of the Prudent and Western patterns after PCa diagnosis with all-cause mortality. Specifically, the Prudent diet was related to a lower risk whereas the Western was related to a higher risk of all-cause mortality. These findings are consistent with results from the HPFS where a greater adherence to Mediterranean diet after diagnosis of PCa was associated with 22% reduction in overall mortality (7). Moreover, because CVD was the leading cause of death among men with localized PCa in this cohort (21% of deaths), the results of this study can also be interpreted in light of the wider literature on the relation between diet patterns and CVD mortality (7, 25-29). Interestingly, oil and vinegar-dressing, processed meats and high-fat dairy appeared to be the main drivers of the associations of all-cause mortality with Prudent and Western diets, respectively. The oil and vinegar-dressing result is in agreement with previous findings of an inverse relation between vegetable oil intake with all-cause mortality among men with localized PCa (6), and with results of the PREDIMED trial, where individuals randomized to a Mediterranean

diet supplemented with olive oil had significantly lower risk of CVD than the control group (29). Furthermore, in a recent meta-analysis composed of nine prospective studies, the highest consumption of processed meat increased the risk of all-cause mortality by 23%, compared to lowest consumption (30). High-fat dairy was reported to be associated with increased CVD mortality (31), though not in all studies (32). Although these food groups were identified as major drivers, admittedly, the highly-correlated matrix obtained by principal component analysis indicated a collective effect on mortality risks from grouped food items in Prudent or Western patterns. Our findings suggest that adherence to a heart-healthy diet could increase survival among men with non-metastatic PCa - a highly relevant finding given that most men with non-metastatic PCa die of unrelated causes.

Strengths and limitations of this study are worth careful weighing. On one hand, the study had high follow-up rates and a long follow-up time, which allowed us to study mortality rather than surrogate outcomes such as biochemical recurrence. Nevertheless, the study had a small number of disease-specific deaths resulting in wide confidence intervals and unstable estimates in some sensitivity analyses, and suggesting caution in the interpretation of the results. In addition, because we did not collect data on pre-diagnostic diet, we cannot evaluate its potential confounding effects on post-diagnostic diet. However, studies where both pre- and post-diagnostic diets were assessed have found that adjustment for pre-diagnostic diet had little influence on post-diagnostic diet effect estimates (7). In addition, we relied on a single prospective measure of post-diagnostic diet and lacked detail on certain potential confounders such as physical activity (e.g., time in non-vigorous activity), history of PSA screening, and treatment combinations. Furthermore, most men in the cohort are Caucasian physicians, which may limit the generalizability of the results to men with different socioeconomic backgrounds or from racial or ethnic minorities. Although the study setting may potentially minimize residual confounding by socioeconomic status, our results need to be replicated in independent populations with a larger number of disease specific-endpoints, pre-diagnostic exposure data, repeated dietary assessments, more detailed covariate assessment and more diverse socioeconomic and racial/ethnic backgrounds.

In conclusion, among men diagnosed with non-metastatic PCa, greater post-diagnostic adherence to a Western dietary pattern may increase risk of all-cause mortality, whereas a Prudent dietary pattern may lower mortality risks after PCa diagnosis. These findings suggest that modifications to diet after PCa diagnosis may influence survival and have a direct clinical translation. These diet choices are informative to clinicians and PCa survivors who are highly motivated to seek informing treatment and lifestyle decisions in order to reduce the suffering and improve the overall survival of men living with PCa. Nevertheless, given the scarcity of literature on the relation between post-diagnostic diet and PCa progression, and the small number of disease-specific deaths in the current study, these associations, particularly those for disease-specific mortality, merit caution in their interpretation as well as further evaluation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Factor-loading matrix for two dietary patterns identified from post-diagnostic food-frequency questionnaire among men with prostate cancer (n=926) in the Physicians' Health Study[a]

Food group	Prudent Dietary Pattern	Western Dietary Pattern
Legumes	0.55	-
Dark-yellow vegetables	0.55	-
Green, leafy vegetables	0.54	-
Other vegetables	0.54	-
Fruit	0.51	-
Cruciferous vegetables	0.51	-
Tomatoes	0.49	-
Whole grains	0.44	-
Garlic	0.40	-
Soy products	0.36	-
Fish	0.32	-
Oil and vinegar dressing	0.31	-
Processed meats	-	0.66
Red meats	-	0.60
Eggs	-	0.48
Snacks	-	0.46
High-fat dairy products	-	0.45
Potatoes	-	0.44
French fries	-	0.42
Butter	-	0.39
Sweets and desserts	-	0.35
Refined grains	-	0.33

[a]Food groups with loading factors less than 0.3 for both dietary patterns were not listed in the table, and included fruit juice, poultry, condiments, nuts, tea, low-fat dairy products, pizza, organ, cold breakfast cereal, wine, margarine, mayonnaise, low-energy drink, beer, coffee, high-energy drink, and liquor.

Table 2

Demographic and post-diagnostic dietary characteristics according to quartiles of dietary pattern scores among 926 men with non-metastatic prostate cancer in Physicians' Health Study (n=926)

	Total population	Prudent Dietary Pattern			Western Dietary Pattern		
		Quartile 1	Quartile 4	P value[a]	Quartile 1	Quartile 4	P value[a]
n	926	231	231		231	231	
Subject characteristics							
Age at diagnosis, y, mean (SD)	68.6 (6.9)	69.4 (7.2)	67.8 (6.5)	0.08	68.2 (7.1)	69.9 (6.5)	0.01
Caucasian, %	95.68	95.7	96.1	0.98	93.5	97	0.01
BMI, kg/m2, %				0.04			0.24
<25	46.7	39.4	48.9		52.8	40.7	
25-30	47.3	56.7	42.9		42.9	52	
>30	6.1	3.9	8.2		4.3	7.4	
Smoking status, %				0.009			<0.001
Never	47.1	42.4	54.1		48.1	37.7	
Past	50.4	53.3	43.7		51.2	57.6	
Current	2.5	4.3	2.2		0.4	4.8	
Days per week of vigorous exercise[b]				0.04			0.04
None	33.7	37.2	29.0		27.3	28.5	
<1 day/week	2.5	3.0	1.7		2.6	2.6	
1-2 day/week	17.7	16.0	14.3		20.4	13.0	
3-4 day/week	29.5	26.8	36.8		30.3	24.7	
5-7 day/week	16.6	16.9	18.2		19.5	21.2	
Family history of prostate cancer, %[c]	16.9	11.7	19.1	0.07	20.4	15.2	0.35
Clinical Stage, %				0.97			0.97
T1/T2	95.1	94.8	95.2		95.7	95.2	
T3	4.9	5.2	4.8		4.3	4.8	
Gleason score, %				0.86			0.54
<7	69.1	71.9	69.3		73.6	64.9	
7	21.5	19.1	20.8		17.3	24.2	

	Total population	Prudent Dietary Pattern			Western Dietary Pattern		
		Quartile 1	Quartile 4	P value[a]	Quartile 1	Quartile 4	P value[a]
>7	6.9	5.6	7.8		6.9	7.4	
Missing	2.5	3.5	2.2		2.2	3.5	
PSA at diagnosis, ng/ml, %				0.19			0.007
<4	10.5	10.8	13		11.7	13.4	
4-9.9	46.0	41.9	48.5		50.7	39.4	
10-19.9	19.7	21.2	18.2		17.3	20.4	
≥20	10.8	7.4	9.5		10.8	8.2	
Missing	13.1	17.8	10.8		9.5	18.6	
Primary treatment, %[d]				0.60			0.72
Radiation	10.4	12.6	7.4		10.0	10.8	
Prostatectomy	43.7	44.2	46.8		48.5	39.8	
Chemo or hormone therapy	7.1	5.19	7.36		6.9	7.8	
Others	1.8	2.16	1.73		0.9	3.0	
Unspecified or missing	36.9	35.9	36.8		33.8	38.5	
Daily dietary nutrients (energy-adjusted)							
Carbohydrate, g, mean (SD)	217.4 (40.9)	203.3 (43.8)	232.4 (36.0)	<0.001	242.7 (38.9)	192.7 (32.7)	<0.001
Protein, g, mean (SD)	76.9 (13.6)	74.3 (15.6)	78.7 (12.6)	<0.001	76.9 (14.0)	78.4 (12.7)	0.28
Fat, g, mean (SD)	50.5 (11.9)	55.3 (12.8)	45.6 (10.8)	<0.001	41.3 (9.4)	59.1 (9.8)	<0.001
Vegetable fat, g, mean (SD)	20.2 (7.3)	19.5 (7.9)	20.5 (7.3)	0.27	19.2 (7.2)	20.5 (7.3)	0.08
Animal fat, g, mean (SD)	30.3 (11.6)	35.7 (12.6)	25.1 (10.4)	<0.001	22.1 (8.9)	38.6 (10.5)	<0.001
Cholesterol, mg, mean (SD)	211 (95)	238 (119)	187 (85)	<0.001	162 (68)	269 (110)	<0.001
Caffeine, mg, mean (SD)	165 (135)	180 (149)	159 (124)	0.21	150 (135)	185 (142)	0.05
Alcohol, g, mean (SD)	13.2 (15.3)	17.6 (20.1)	9.5 (10.1)	<0.001	13.8 (17.0)	12.2 (12.6)	0.64
Calcium, mg, mean (SD)	989 (559)	917 (576)	1023 (527)	0.12	1162 (670)	841 (376)	<0.001
Vitamin D, IU, mean (SD)	379 (283)	363 (300)	363 (219)	0.32	459 (320)	321 (220)	<0.001

y = years; BMI = body mass index; PSA = prostate-specific antigen; IU = international unit.

[a] Chi-square test was used for categorical variables; Analysis of Variance was used for continuous variables. All statistical tests were two- sided.

[b] If a patient reported to engage in a regular program of exercise vigorous enough to work up a sweat then vigorous exercise, additional information on the frequency of engagement was collected.

[c] If a patient reported he had a brother or father was ever diagnosed with prostate cancer without including half siblings.

[d] Others include orchiectomy, watchful waiting, and other treatments.

Table 3

Relative risk of prostate cancer-specific mortality among 926 men diagnosed with non-metastatic prostate cancer by post-diagnostic dietary patterns

	Quartile of Prudent Dietary Pattern				
	1	**2**	**3**	**4**	P_{trend}[a]
n	231	232	232	231	
Events	16	16	14	10	
Follow-up time, py	1923	2014	2079	2077	
Incidence rate, #/10,000py	83	79	67	48	
Model 1 HR (95% CI)[b]	1.00 (Ref)	0.91 (0.45 - 1.83)	0.72 (0.34 -1.53)	0.48 (0.19 - 1.18)	0.09
Model 2 HR (95% CI)[c]	1.00 (Ref)	0.87 (0.41 - 1.82)	0.73 (0.33 - 1.63)	0.46 (0.17 - 1.24)	0.11

	Quartile of Western Dietary Pattern				
	1	**2**	**3**	**4**	P_{trend}[a]
n	231	232	232	231	
Events	9	11	15	21	
Follow-up time, py	2096	2035	2065	1897	
Incidence rate, #/10,000py	43	54	73	111	
Model 1 HR (95% CI)[b]	1.00 (Ref)	1.31 (0.54 - 3.18)	1.92 (0.82 - 4.49)	3.20 (1.32 - 7.75)	0.005
Model 2 HR (95% CI)[c]	1.00 (Ref)	0.95 (0.38 - 2.34)	1.81 (0.76 - 4.33)	2.53 (1.00, 6.42)	0.02

Abbreviation: py, person years; HR, hazard ratio; CI, confidence interval.

[a] P_{trend} calculated by modeling the median of each category as a continuous term. All statistical tests were two-sided.

[b] Cox proportional hazards regression model adjusted for age at diagnosis (years, continuous) and total energy intake (kcal, continuous).

[c] Cox proportional hazards regression model adjusted for variables in Model 1 plus body mass index (kg/m^2, <25, 25-30, >30), smoking status (never, past, current), vigorous exercise (days/week, continuous), Gleason score (<7, 7, >7), clinical stage (T1/T2, T3), prostate-specific antigen level (ng/ml, <4, 4-9.9, 10-19.9, ≥20), time interval between diagnosis and FFQ completion (years, continuous), initial treatment after diagnosis (radiation, prostatectomy, others, unspecified or missing), and family history of prostate cancer (yes, no).

Table 4

Relative risk of all-cause mortality among 926 men diagnosed with non-metastatic prostate cancer by post-diagnostic dietary patterns

	Quartile of Prudent Dietary Pattern				
	1	**2**	**3**	**4**	P_{trend}[a]
n	231	232	232	231	
Events	97	86	82	68	
Follow-up time, py	1923	2014	2079	2077	
Incidence rate, #/10,000py	504	427	394	327	
Model 1 HR (95% CI)[b]	1.00 (Ref)	0.84 (0.62 - 1.13)	0.72 (0.53 - 0.99)	0.59 (0.41 - 0.84)	0.003
Model 2 HR (95% CI)[c]	1.00 (Ref)	0.88 (0.64 - 1.20)	0.83 (0.60 - 1.14)	0.64 (0.44 - 0.93)	0.02

	Quartile of Western Dietary Pattern				
	1	**2**	**3**	**4**	P_{trend}[a]
n	231	232	232	231	
Events	59	88	76	110	
Follow-up time, py	2096	2035	2065	1897	
Incidence rate, #/10,000py	281	432	368	580	
Model 1 HR (95% CI)[b]	1.00 (Ref)	1.65 (1.18 - 2.30)	1.43 (1.01 - 2.02)	2.06 (1.44 - 2.95)	<0.001
Model 2 HR (95% CI)[c]	1.00 (Ref)	1.40 (0.99 - 1.97)	1.33 (0.93 - 1.90)	1.67 (1.16 - 2.42)	0.01

Abbreviation: py, person years; HR, hazard ratio; CI, confidence interval.

[a] P_{trend} calculated by modeling the median of each category as a continuous term. All statistical tests were two-sided.

[b] Cox proportional hazards regression model adjusted for age at diagnosis (years, continuous) and total energy intake (kcal, continuous).

[c] Cox proportional hazards regression model adjusted for variables in Model 1 plus body mass index (kg/m^2, <25, 25-30, >30), smoking status (never, past, current), vigorous exercise (days/week, continuous), Gleason score (<7, 7, >7), clinical stage (T1/T2, T3), prostate-specific antigen level (ng/ml, <4, 4-9.9, 10-19.9, ≥20), time interval between diagnosis and FFQ completion (years, continuous), initial treatment after diagnosis (radiation, prostatectomy, others, unspecified or missing), and family history of prostate cancer (yes, no).