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Vegetable and fruit intake after diagnosis and risk of prostate cancer progression

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Abstract

Cruciferous vegetables, tomato sauce, and legumes have been associated with reduced risk of incident advanced prostate cancer. *In vitro* and animal studies suggest these foods may inhibit progression of prostate cancer, but there are limited data in men. Therefore, we prospectively examined whether intake of total vegetables, and specifically cruciferous vegetables, tomato sauce, and legumes, after diagnosis reduce risk of prostate cancer progression among 1,560 men diagnosed with non-metastatic prostate cancer and participating in the Cancer of the Prostate Strategic Urologic Research Endeavor, a United States prostate cancer registry. As a secondary analysis, we also examined other vegetable sub-groups, total fruit, and subgroups of fruits. The participants were diagnosed primarily at community-based clinics and followed from 2004–2009. We assessed vegetable and fruit intake via a semi-quantitative food frequency questionnaire, and ascertained prostate cancer outcomes via urologist report and medical records. We observed 134 events of progression (53 biochemical recurrences, 71 secondary treatments likely due to recurrence, six bone metastases, four prostate cancer deaths) during 3,171 person-yrs. Men in the fourth quartile of post-diagnostic cruciferous vegetable intake had a statistically significant 59% decreased risk of prostate cancer progression compared to men in the lowest quartile (hazard ratio (HR): 0.41; 95% confidence interval (CI): 0.22, 0.76; p-trend: 0.003). No other vegetable or fruit group was statistically significantly associated with risk of prostate cancer progression. In conclusion, cruciferous vegetable intake after diagnosis may reduce risk of prostate cancer progression.

Keywords

prostate cancer; vegetables; fruit; cruciferous; survivorship

INTRODUCTION

More than 2.2 million men currently live with prostate cancer in the United States (US).[1] Cruciferous vegetables, tomato sauce, and legumes have been linked to a lower risk of

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incident prostate cancer and, in some cases, reduced risk of advanced or aggressive disease at diagnosis.[2–6] However, there are limited data on the chemotherapeutic effects of diet after diagnosis of prostate cancer. Among 1,202 men with non-metastatic prostate cancer in the Health Professionals' Follow-up Study (HPFS), post-diagnostic intake of tomato sauce and fish were associated with reduced risk of prostate cancer progression.[7] In the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE™), intakes of poultry with skin and eggs after diagnosis were associated with elevated risk of prostate cancer progression.[8] Saturated fat intake has also been reported to increase risk of prostate cancer progression,[9, 10] and small clinical trials conducted in men with prostate cancer and examining biomarker outcomes support a role of diet in prostate cancer progression.[11–14]

Thus, we prospectively examined post-diagnostic intake of vegetables and fruits in relation to risk of prostate cancer progression among men with non-metastatic prostate cancer at diagnosis. We hypothesized that total vegetables, and specifically cruciferous vegetables, tomato sauce, and legumes, would be inversely associated with risk of prostate cancer progression.

MATERIAL AND METHODS

Study population

CaPSURE is a US prostate cancer registry study initiated in 1995.[15, 16] Forty sites (34 community-based clinics, three academic institutions, three Veterans Administration hospitals) have enrolled men with biopsy-verified prostate cancer. CaPSURE participants complete surveys at baseline and every 6 mos. thereafter, and urologists provide clinical data at baseline and subsequent clinic visits. The base population for this study included 2,134 participants in CaPSURE who completed a semi-quantitative food frequency questionnaire (FFQ) during 2004–2005. The Institutional Review Boards of the University of California, San Francisco and collaborating institutions approved this study.

Dietary Assessment

Vegetable and fruit groups of interest for this analysis are listed in Table 1. Men were asked how often on average they consumed a specific portion of 127 foods and beverages during the past year, with nine frequency options ranging from <1/mo. to ≥6/d. We also asked participants whether they were eating more, less, or the same amount of each item compared to before their diagnosis. Our FFQ was based on a FFQ that has been used to study diet and chronic disease relations in a variety of populations.[17, 18] In a validation study, the median correlation between two 1-wk diet records and the original FFQ for vegetable and fruit items was 0.58 (range:0.19 for garlic to 0.95 for bananas).[19]

Clinical Follow-up

We abstracted data on treatment, biopsy Gleason sum, stage, prostate specific antigen (PSA), and metastases from medical records or urologists' reports. The National Death Index and Bureau of Vital Statistics were checked for mortality data, and death certificates were used to verify the date and cause of death.

Prostate cancer progression was defined as: prostate cancer death, bone metastases from prostate cancer, biochemical recurrence, or initiation of secondary treatment. A death was attributed to prostate cancer if prostate cancer was listed as the primary, secondary, or tertiary cause of death and no other malignancy was listed as a higher order cause. An outcome of bone metastases was defined as urologist report of: (1) prostate cancer progression to bone, (2) positive bone scan, (3) radiation for metastasis at a bone site, or (4) M1b stage. Biochemical recurrence was defined as two consecutive PSA values ≥0.2ng/ml

≥8 wks after radical prostatectomy or a PSA ≥2ng/ml above post-radiation nadir.[20] Secondary treatment was defined as any treatment initiated ≥6 mos. after primary treatment.[21, 22] The date of prostate cancer progression was the first of the following: prostate cancer death, diagnosis of bone metastases, second PSA ≥0.2ng/ml for radical prostatectomy patients, first PSA ≥2ng/ml above nadir for radiation patients, or initiation of secondary treatment.

Inclusion Criteria

We excluded men with extra-prostatic disease at diagnosis (T-stage≥T3b), men missing treatment information, and men who reported an energy intake outside 800–4200 kcal/d (n=241). To maintain the prospective nature of our analysis and reduce the potential for recall bias, we excluded men whose prostate cancer progressed prior to the FFQ (n=333), resulting in 1,560 men for analysis.

Statistical Methods

We examined associations between post-diagnostic vegetable and fruit intake and prostate cancer progression using Cox proportional hazards regression. Person-time was calculated from date of the FFQ until prostate cancer progression, non-prostate cancer death, last contact, or August 21, 2009, whichever occurred first. We modeled quartiles of vegetables and fruits with indicator variables and tested for linear trends using the median of each quartile as a continuous term.

Model 1 was adjusted for age at diagnosis (continuous), energy intake (continuous), and days from diagnosis to FFQ (continuous). Model 2 included the variables in Model 1 plus prognostic risk at diagnosis (low, intermediate, high), primary treatment (radical prostatectomy, radiation, other/active surveillance, androgen deprivation therapy), body mass index (BMI; <25, 25–29.9, ≥30 kg/m^2), and walking metabolic equivalent task (MET)-h/wk (quartile rank).[23] We classified participants' prognostic risk using modified D'Amico definitions as follows: [High: PSA>20ng/ml or Gleason sum=8–10 or T-Stage≥T3a; else Intermediate: PSA=10.1–20ng/ml or Gleason sum=7 or secondary 4–5 pattern or T-Stage=T2b/T2c (2002) or T2b (1997); else Low: PSA≤10ng/ml and Gleason sum=2–6 and T-Stage=≤T2a].[24, 25] Model 3 was additionally adjusted for quartile ranks of eggs, poultry with skin, fruits, and vegetables other than the exposure of interest. Adjustment for education, income, race, prostate cancer family history, smoking, and intakes of sweets, grains, or dairy did not change the results; therefore these variables were omitted from the final models.

We examined whether biopsy Gleason sum (<7 v. ≥7), age at diagnosis (<60 v. ≥60 y), smoking (ever v. never), BMI (<25 v. ≥ 25 kg/m^2), or walking (< 7.5 v. ≥7.5 MET-h/wk) modified any of the relations using likelihood ratio tests. The cut-points for age at diagnosis and walking were chosen based on their distribution in the study population.

We performed a sensitivity analysis excluding events defined by secondary treatment that lacked evidence of a preceding PSA rise. In addition, we were concerned men with higher prognostic risk may increase their tomato intake more than men with lower prognostic risk; therefore we examined whether self-reported change in tomato items was associated with prognostic risk at diagnosis using chi-square tests.

All statistical tests were two-sided and considered significant at $p<0.05$. All analyses were conducted using SAS v. 9.1.3.

RESULTS

We observed 134 events of progression (53 biochemical recurrences, 71 secondary treatments, six bone metastases, four prostate cancer deaths) among 1,560 men during 3,171 person-yrs. The median year of diagnosis was 2002 [interquartile range (IQR): 2000–2003]. The median follow-up after the FFQ was 23 mos. (IQR: 10–32 mos.). Approximately 14% (n=213) of the men who completed the FFQ did not participate in CaPSURE follow-up after the FFQ; these men did not differ from the remaining men in terms of their biopsy Gleason sum, clinical T-stage, primary treatment, or intake of total vegetables, cruciferous vegetables, tomato sauce, or legumes. However, they were younger (mean=63y) compared to the remaining men (mean=65y) (p-value=0.001).

Men who consumed more vegetables were more educated, had higher household incomes, and expended more energy walking than men who consumed the least vegetables (Table 2). We observed a non-significant inverse trend for total vegetables and risk of progression (Table 3), which appeared to be driven by cruciferous vegetables (e.g. broccoli; cabbage, coleslaw; cauliflower; Brussels sprouts; kale, mustard, chard greens). Men in the fourth quartile of post-diagnostic intake of cruciferous vegetables had a 59% reduced risk of prostate cancer progression compared to men in the lowest quartile (hazard ratio (HR): 0.41, 95% confidence interval (CI): 0.22, 0.76; p-trend: 0.003). The remaining vegetable groups were not associated with risk of prostate cancer progression. Most of the individual cruciferous items were inversely related to risk of prostate cancer progression, but none were statistically significant on its own, likely due to the low consumption of these foods (Table 4).

Total fruit and fruit groups, with the exception of berries, were also not associated with risk of prostate cancer progression (Table 5). For berries, there was an inverse association in the age- and calorie-adjusted model (HR comparing extreme quartiles: 0.60; 95%CI: 0.37, 0.97), which was somewhat attenuated and not statistically significant after multivariate adjustment (HR comparing extreme quartiles: 0.68; 95%CI: 0.40, 1.15).

There was no evidence of effect modification by biopsy Gleason sum, BMI, age at diagnosis, or smoking. However, there was an interaction between walking and total vegetable intake (p-interaction = 0.02). Among the 732 men who walked ≥7.5 MET-h/wk after diagnosis (approximately 150 min/wk), total vegetable intake after diagnosis was inversely associated with risk of prostate cancer progression (HR comparing extreme quartiles: 0.35; 95%CI: 0.15, 0.79). There was no association among the 729 men who walked <7.5 MET-h/wk (HR comparing extreme quartiles: 0.91; 95%CI: 0.36, 2.31).

Our results remained unchanged when excluding events defined by secondary treatment without evidence of a preceding PSA rise. Additionally, few men reported any change in tomato intake compared to before diagnosis (≤15%) and there was no association between self-reported change in any tomato item and prognostic risk at diagnosis (data not shown).

DISCUSSION

In this novel analysis of post-diagnostic vegetable and fruit intake and clinical outcomes among men with prostate cancer, we observed a strong inverse association between cruciferous vegetable intake after diagnosis and prostate cancer progression. No other vegetable or fruit group after diagnosis was statistically significantly associated with risk of prostate cancer progression.

This is the first study to examine cruciferous vegetable intake after diagnosis in relation to clinical outcomes among men with prostate cancer. However, two recent prospective studies

reported inverse associations between cruciferous vegetables or glucosinolate, a metabolite of cruciferous vegetables, and risk of incident prostate cancer. Kirsh et al. reported a 40% reduced risk of incident extra-prostatic prostate cancer comparing men with high and low cruciferous vegetable intake (HR: 0.60, 95%CI: 0.36, 0.98; p-trend: 0.02).[26] In the EPIC-Heidelberg cohort, high glucosinolate consumption was associated with a 32% decreased risk of incident prostate cancer (HR Q4 versus Q1: 0.68; 95%CI: 0.48, 0.97; p-trend: 0.03).[27]

Glucosinolates are hydrolyzed to form isothiocyanates and indoles, which have anti-carcinogenic effects *in vitro* and *in vivo.*[28–31] The isothiocyanate, sulforaphane, promotes apoptosis and cell cycle arrest in prostate cancer cells.[32–34] Phenethyl isothiocyanate inhibits prostate cancer cell growth and migration, reduces androgen receptor levels, impairs mRNA translation, and promotes transcription of p21.[35–38] Additionally, indole-3-carbinol promotes cell cycle arrest, growth inhibition, and apoptosis, and has been shown to inhibit components of oncogenic cell signaling pathways.[39–41] In humans, consumption of broccoli sprouts inhibited histone deacetylase in blood[42] and a broccoli-rich diet altered global gene expression in the prostate.[43]

Furthermore, Joseph et al. observed a stronger inverse relation between broccoli consumption and prostate cancer risk among men with the glutathione S-transferase mu 1 (GSTM1)-present genotype compared to men with null deletions in this gene.[44] Glutathione S-transferase enzymes are induced by metabolites of cruciferous vegetables and may reduce risk of prostate cancer progression through detoxification of carcinogens and elimination of reactive oxidative species.[45]

We observed evidence of an interaction between total vegetable intake after diagnosis and walking, similar to results from the control arm of the Women's Healthy Eating and Living trial among women with breast cancer.[46] In that study, women who consumed ≥5 servings/d of vegetables and fruits and engaged in physical activity equivalent to walking 30 min/d 6 d/wk had a 44% reduced risk of mortality compared to women who consumed <5 servings/d of vegetables and fruits and engaged in <30 min/d 6 d/wk of activity (HR: 0.56; 95% CI: 0.31, 0.98). Future studies should consider the possible synergy between plant-based diets and physical activity in reducing risk of prostate cancer progression.

The null association for tomato sauce was contrary to our hypothesis and the previously observed inverse association.[7] We considered whether the lack of an inverse association for tomato sauce was due to reverse causation (e.g. men with higher prognostic risk at diagnosis increased their tomato sauce intake more than men with low prognostic risk), but there was no association between change in any tomato item and prognostic risk at diagnosis. Overall, the results of intervention studies on tomato sauce and/or lycopene supplementation after prostate cancer diagnosis in relation to intermediate endpoints have been inconsistent,[11, 47] and further research on the role of tomatoes after prostate cancer diagnosis is needed.

No other study has examined post-diagnostic intake of legumes in relation to clinical outcomes in men with prostate cancer. However, our observation of no association between post-diagnostic legume intake and prostate cancer progression is consistent with many prospective studies on incident prostate cancer in Western populations, although two reported inverse associations.[6, 48–50] In the Multi-Ethnic Cohort Study, greater legume consumption was associated with small to moderate reductions in risk of total and aggressive incident prostate cancer (HR: 0.89, 95% CI: 0.89, 0.99 for total; HR: 0.74, 95% CI: 0.61, 0.91 for aggressive).[48] However, this association was only significant among Latinos, who had much higher legume consumption than any other ethnic group. A recent meta-analysis reported similar variation across ethnic groups, with evidence of a protective

association in Asian populations, but no association in Western populations.[50] Associations between dietary factors and risk of incident prostate cancer versus post-diagnostic intake and prostate cancer progression likely differ, and more research is needed before firm conclusions may be drawn. Yet, based on the available data, if there is an effect of legumes on prostate cancer progression, it appears to be modest and likely varies across populations depending on their level of legume intake.

Limitations of this study include our lack of pre-diagnostic diet, loss to follow-up, and few events. Our lack of pre-diagnostic diet prevents us from concluding the association we observed between post-diagnostic cruciferous vegetable intake was independent of what the men consumed prior to diagnosis. In addition, 14% of participants did not participate in CaPSURE follow-up after the FFQ, and thus were considered lost to follow-up immediately after completing the FFQ. Fortunately, these men did not differ from the remaining men in terms of their vegetable intake or clinical prognostic factors, and therefore it is unlikely that loss of these men biased our results. Lastly, we acknowledge that this is a small study and caution is warranted in interpreting the strong inverse relation we observed between post-diagnostic cruciferous vegetables and risk of prostate cancer progression. While suggestive, further study of cruciferous vegetables in men with prostate cancer is needed from randomized controlled trials before translating these results to clinical practice.

In conclusion, cruciferous vegetable consumption after diagnosis was strongly associated with reduced risk of prostate cancer progression among men initially diagnosed with non-metastatic prostate cancer. These data strengthen the rationale to investigate the phytochemicals of cruciferous vegetables in men with prostate cancer, and if confirmed, provide dietary guidance for men with prostate cancer.

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Table 1

Vegetable and fruit groups of interest.

Vegetable Groups	
Carrots/yams	Raw carrots, cooked carrots, yams/sweet potatoes
Cruciferous vegetables	Broccoli; cabbage/coleslaw; Brussels sprouts; cauliflower; kale/mustard/chard greens
Green/leafy vegetables	Cooked spinach; raw spinach; iceberg or head lettuce; romaine/leafy lettuce; celery
Legumes	Tofu/soybeans; string beans; peas/lima beans; beans/lentils
Squash	Yellow/winter squash, eggplant/zucchini
Tomatoes (fresh)	Tomatoes, tomato juice
Tomato sauce	Tomato sauce, pizza
Total vegetables	All of the above plus red chili sauce, mixed vegetables, beets, alfalfa sprouts, and garlic
Fruit Groups	
Apples/pears	Fresh apples or pears, apple juice or cider
Berries	Strawberries, blueberries
Citrus fruits	Oranges, orange juice, grapefruit, grapefruit juice
Fruit juice	Orange juice, grapefruit juice, apple juice or cider, other juice
Total fruits	All of the fruit groups plus raisins or grapes, prunes, bananas, cantaloupe, watermelon, peaches/apricots/plums
Total fruit excluding juice	Fresh apples or pears, strawberries, blueberries, oranges, grapefruit, raisins or grapes, prunes, bananas, cantaloupe, watermelon, peaches/apricots/plums

Table 2

Baseline characteristics of 1,560 men with prostate cancer by total vegetable intake after diagnosis.

Quartile of total vegetable intake[1]		**Q1**		**Q2**		**Q3**		**Q4**		
Median servings/d		**1.4**		**2.4**		**3.6**		**5.7**		
Characteristic		**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**p-value[2]**
Age at Diagnosis	<60 y	88	23	102	26	109	28	117	30	0.23
	60–69.9 y	184	47	183	47	175	45	157	40	
	≥70 y	117	30	106	27	106	27	116	30	
Race	Other	5	1	4	1	8	2	9	2	0.37
	African American	7	2	11	3	8	2	15	4	
	Caucasian	376	97	375	96	372	96	366	94	
Education	Grade school	27	8	23	6	18	5	19	5	<0.01
	High school	176	49	143	40	138	38	132	36	
	College	73	20	97	27	87	24	88	24	
	Graduate school	84	23	98	27	118	33	128	35	
Income	<$20,000	32	10	17	5	20	6	24	7	<0.01
	$20–75,000	218	65	210	63	196	58	179	53	
	≥$75,000	86	26	109	32	120	36	132	39	
BMI (kg/m^2)	<25	102	26	103	26	90	23	126	32	0.06
	25–29.9	217	56	207	53	216	56	183	47	
	≥30	67	17	79	20	83	21	81	21	
Smoking	Current	31	8	24	6	15	4	24	6	0.44
	Former	202	52	206	54	213	55	207	54	
	Never	152	39	155	40	157	41	155	40	
Walking (quartile median MET-hr/wk)	Quartile 1 (1)	117	33	85	23	73	20	75	21	<.01
	Quartile 2 (4)	88	25	110	30	95	26	86	24	
	Quartile 3 (10)	92	26	99	27	110	30	102	28	
	Quartile 4 (26)	62	17	74	20	91	25	102	28	
PSA at diagnosis (ng/ml)	≤10 ng/ml	312	83	317	84	327	86	323	86	0.19
	10.1–20 ng/ml	50	13	47	13	46	12	34	9	
	>20 ng/ml	14	4	12	3	7	2	18	5	

Quartile of total vegetable intake[1]		**Q1**		**Q2**		**Q3**		**Q4**		
Median servings/d		**1.4**		**2.4**		**3.6**		**5.7**		
Characteristic		**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**p-value**[2]
Biopsy Gleason sum	2–6	266	69	273	71	276	71	270	70	0.99
	7	97	25	89	23	94	24	91	24	
	8–10	21	5	21	5	19	5	22	6	
Clinical T-stage	T1	194	50	219	56	211	54	220	56	0.61
	T2	191	49	169	43	176	45	166	43	
	T3a	4	1	3	1	3	1	4	1	
Treatment	Prostatectomy	228	59	261	67	247	63	230	59	0.13
	Radiation	106	27	94	24	85	22	102	26	
	Other	36	9	19	5	34	9	33	8	
	Hormones	19	5	17	4	24	6	25	6	

Abbreviations: BMI, body mass index; MET, metabolic equivalent task; PSA, prostate specific antigen.

[1]Total vegetables included: tofu/soybeans, string beans, peas/lima beans, beans/lentils, raw carrots, cooked carrots, yams/sweet potatoes, broccoli, cabbage/coleslaw, cauliflower, Brussels sprouts, kale/mustard/chard greens, cooked spinach, raw spinach, iceberg or head lettuce, romaine or leafy lettuce, celery, yellow/winter squash, eggplant/zucchini, tomato sauce, pizza, fresh tomatoes, tomato juice, red chili sauce, mixed vegetables, beets, alfalfa sprouts, and garlic.

[2]P-values estimated using a Pearson chi-square test.

Table 3

Vegetable intake after diagnosis and risk of prostate cancer progression among 1,560 men with non-metastatic prostate cancer at diagnosis.

	Quartile of intake				*p*-trend
	1	**2**	**3**	**4**	
Total vegetables[1]					
Median intake[2]	1.35	2.39	3.63	5.70	
HR (95% CI)[3]	1.0	1.33 (0.84, 2.11)	1.22 (0.76, 1.97)	0.59 (0.33, 1.06)	0.05
HR (95% CI)[4]	1.0	1.28 (0.78, 2.11)	1.31 (0.79, 2.17)	0.62 (0.33, 1.15)	0.10
HR (95% CI)[5]	1.0	1.25 (0.76, 2.05)	1.34 (0.80, 2.23)	0.61 (0.33, 1.13)	0.09
Carrots/yams					
Median intake[2]	0.06	0.19	0.35	0.86	
HR (95% CI)[3]	1.0	1.39 (0.88, 2.20)	0.82 (0.51, 1.32)	0.77 (0.47, 1.26)	0.13
HR (95% CI)[4]	1.0	1.26 (0.77, 2.06)	1.00 (0.61, 1.64)	0.83 (0.48, 1.41)	0.30
HR (95% CI)[5]	1.0	1.34 (0.82, 2.21)	1.15 (0.68, 1.94)	1.00 (0.56, 1.78)	0.71
Cruciferous					
Median intake[2]	0.06	0.21	0.43	0.92	
HR (95% CI)[3]	1.0	0.90 (0.58, 1.39)	0.78 (0.50, 1.23)	0.45 (0.26, 0.77)	0.003
HR (95% CI)[4]	1.0	0.96 (0.60, 1.53)	0.82 (0.51, 1.33)	0.46 (0.26, 0.81)	0.005
HR (95% CI)[5]	1.0	0.95 (0.59, 1.52)	0.77 (0.46, 1.27)	0.41 (0.22, 0.76)	0.003
Green/leafy					
Median intake[2]	0.19	0.49	0.92	1.57	
HR (95% CI)[3]	1.0	1.28 (0.80, 2.04)	1.04 (0.63, 1.71)	0.96 (0.58, 1.60)	0.61
HR (95% CI)[4]	1.0	1.22 (0.75, 2.00)	1.00 (0.60, 1.68)	0.90 (0.53, 1.55)	0.50
HR (95% CI)[5]	1.0	1.25 (0.76, 2.07)	1.04 (0.60, 1.78)	0.92 (0.51, 1.67)	0.56
Legumes					
Median intake[2]	0.13	0.27	0.49	0.93	
HR (95% CI)[3]	1.0	0.64 (0.38, 1.10)	0.76 (0.49, 1.17)	0.77 (0.47, 1.25)	0.47
HR (95% CI)[4]	1.0	0.72 (0.41, 1.27)	0.91 (0.57, 1.45)	0.86 (0.51, 1.46)	0.81

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	Quartile of intake				*p*-trend
	1	**2**	**3**	**4**	
HR (95% CI)[5]	1.0	0.76 (0.43, 1.36)	1.00 (0.61, 1.61)	0.97 (0.55, 1.68)	0.86
Squash					
Median intake[2]	0.0	0.06	0.13	0.29	
HR (95% CI)[3]	1.0	1.27 (0.82, 1.96)	1.25 (0.77, 2.01)	0.80 (0.48, 1.32)	0.35
HR (95% CI)[4]	1.0	1.26 (0.80, 1.98)	1.11 (0.67, 1.85)	0.75 (0.44, 1.28)	0.25
HR (95% CI)[5]	1.0	1.26 (0.80, 1.99)	1.17 (0.69, 2.00)	0.79 (0.44, 1.40)	0.39
Tomato sauce					
Median intake[2]	0.06	0.13	0.21	0.49	
HR (95% CI)[3]	1.0	0.89 (0.54, 1.46)	1.04 (0.66, 1.63)	0.95 (0.57, 1.58)	0.93
HR (95% CI)[4]	1.0	0.91 (0.54, 1.52)	0.96 (0.60, 1.56)	1.10 (0.65, 1.87)	0.62
HR (95% CI)[5]	1.0	0.91 (0.54, 1.54)	1.02 (0.63, 1.66)	1.20 (0.70, 2.05)	0.42
Tomatoes (fresh)					
Median intake[2]	0.06	0.14	0.43	0.93	
HR (95% CI)[3]	1.0	1.07 (0.63, 1.81)	1.09 (0.67, 1.78)	1.22 (0.74, 1.99)	0.44
HR (95% CI)[4]	1.0	1.13 (0.65, 1.96)	1.17 (0.69, 1.98)	1.34 (0.79, 2.27)	0.29
HR (95% CI)[5]	1.0	1.27 (0.72, 2.22)	1.39 (0.80, 2.39)	1.66 (0.95, 2.90)	0.09

Abbreviations: HR, hazard ratio; CI, confidence interval; FFQ, food frequency questionnaire, BMI, body mass index; MET, metabolic equivalent task.

[1]**Total vegetables** includes all vegetables from the following sub-groups: **carrots/yams** (raw carrots, cooked carrots, yams/sweet potatoes), **cruciferous** (broccoli, cabbage/coleslaw, cauliflower, Brussels sprouts, kale/mustard/chard greens), **green/leafy** (cooked spinach, raw spinach, iceberg or head lettuce, romaine or leafy lettuce, celery), **legumes** (tofu/soybeans, string beans, peas/lima beans, beans/lentils), **squash** (yellow/winter squash, eggplant/zucchini), **tomato sauce** (tomato sauce, pizza), **tomatoes (fresh)** (fresh tomatoes, tomato juice); ***and*** red chili sauce, mixed vegetables, beets, alfalfa sprouts, garlic.

[2]Median intakes reported in servings/d.

[3]Model adjusted for age (yrs), days from diagnosis to FFQ, and daily energy intake (kcal/d).

[4]Model adjusted for variables in Model 1 plus BMI (<25, 25–29.9, ≥30 kg/m^2), prognostic risk (low, intermediate, high), treatment (radical prostatectomy, radiation, active surveillance/other, hormone), and walking (MET-h/wk; quartile ranks). Men missing one or more covariates were omitted (n = 144, 9%).

[5]Model adjusted for variables in Model 2 plus quartile ranks of fruits, eggs, poultry with skin, and vegetables intake other than the exposure of interest. Men missing one or more covariates were omitted (n = 144, 9%).

Table 4

Intake of cruciferous vegetables after diagnosis and risk of prostate cancer progression among 1,560 men with non-metastatic prostate cancer at diagnosis.

	Quantile of intake				
	1	2	3	4	p-trend
Broccoli					
Median intake[1]	0.0	0.06	0.14	0.43	
HR (95% CI)[2]	1.0	1.13 (0.69, 1.84)	1.30 (0.78, 2.17)	0.66 (0.36, 1.21)	0.06
HR (95% CI)[3]	1.0	1.18 (0.70, 2.02)	1.51 (0.87, 2.61)	0.80 (0.42, 1.51)	0.22
HR (95% CI)[4]	1.0	1.24 (0.72, 2.12)	1.64 (0.92, 2.93)	0.93 (0.46, 1.88)	0.42
Cabbage/coleslaw					
Median intake[1]	0.0	0.06	0.14		
HR (95% CI)[2]	1.0	1.01 (0.66, 1.55)	0.66 (0.40, 1.09)		0.06
HR (95% CI)[3]	1.0	0.96 (0.60, 1.52)	0.63 (0.37, 1.08)		0.06
HR (95% CI)[4]	1.0	0.97 (0.61, 1.55)	0.65 (0.37, 1.12)		0.09
Cauliflower					
Median intake[1]	0.0	0.06	0.14		
HR (95% CI)[2]	1.0	1.00 (0.69, 1.47)	0.65 (0.40, 1.04)		0.08
HR (95% CI)[3]	1.0	1.02 (0.68, 1.52)	0.64 (0.39, 1.07)		0.10
HR (95% CI)[4]	1.0	1.03 (0.69, 1.54)	0.68 (0.39, 1.16)		0.18
Brussels sprouts					
Median intake[1]	0.0	0.06			
HR (95% CI)[2]	1.0	0.74 (0.51, 1.10)			0.13
HR (95% CI)[3]	1.0	0.75 (0.50, 1.12)			0.16
HR (95% CI)[4]	1.0	0.80 (0.52, 1.21)			0.29
Kale					
Median intake[1]	0.0	0.06			
HR (95% CI)[2]	1.0	0.82 (0.51, 1.32)			0.41
HR (95% CI)[3]	1.0	0.84 (0.51, 1.38)			0.48

	Quantile of intake				
	1	2	3	4	p-trend
HR (95% CI)[4]	1.0	0.85 (0.51, 1.42)			0.53

Abbreviations: HR, hazard ratio; CI, confidence interval; FFQ, food frequency questionnaire, BMI, body mass index; MET, metabolic equivalent task.

[1]Median intake reported in servings/d.

[2]Model adjusted for age (yrs), days from diagnosis to FFQ, and energy (kcal/d).

[3]Model adjusted for covariates in Model 1 plus BMI (<25, 25–29.9, ≥30 kg/m^2), clinical risk (low, intermediate, high), treatment (radical prostatectomy, radiation, active surveillance/other, androgen deprivation therapy), and walking (MET-h/wk; quartile ranks).

[4]Model adjusted for covariates in Model 2 plus quartile ranks of total fruit, eggs, poultry with skin, and other vegetable intake.

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Table 5

Fruit intake after diagnosis and risk of prostate cancer progression among 1,560 men with non-metastatic prostate cancer at diagnosis.

	Quartile of intake				
	1	**2**	**3**	**4**	***p*-trend**
Total fruit[1]					
Median intake[2]	0.75	1.75	2.70	4.40	
HR (95% CI)[3]	1.0	1.13 (0.70, 1.80)	0.71 (0.42, 1.19)	0.85 (0.50, 1.44)	0.32
HR (95% CI)[4]	1.0	1.37 (0.82, 2.27)	0.97 (0.56, 1.66)	0.90 (0.50, 1.60)	0.42
HR (95% CI)[5]	1.0	1.41 (0.85, 2.34)	1.04 (0.60, 1.81)	1.01 (0.56, 1.81)	0.73
Apples/pears[1]					
Median intake[2]	0.06	0.14	0.43	0.79	
HR (95% CI)[3]	1.0	0.83 (0.49, 1.42)	0.93 (0.59, 1.47)	1.05 (0.67, 1.65)	0.64
HR (95% CI)[4]	1.0	0.82 (0.47, 1.43)	0.96 (0.59, 1.57)	1.16 (0.73, 1.87)	0.36
HR (95% CI)[5]	1.0	0.86 (0.49, 1.51)	1.01 (0.62, 1.64)	1.27 (0.79, 2.04)	0.23
Berries[1]					
Median intake[2]	0.0	0.06	0.13	0.49	
HR (95% CI)[3]	1.0	0.68 (0.41, 1.12)	0.75 (0.49, 1.17)	0.60 (0.37, 0.97)	0.10
HR (95% CI)[4]	1.0	0.71 (0.42, 1.22)	0.82 (0.52, 1.29)	0.65 (0.39, 1.09)	0.18
HR (95% CI)[5]	1.0	0.70 (0.41, 1.19)	0.84 (0.53, 1.33)	0.68 (0.40, 1.15)	0.27
Citrus[1]					
Median intake[2]	0.06	0.43	0.99	1.46	
HR (95% CI)[3]	1.0	1.25 (0.76, 2.05)	1.10 (0.66, 1.83)	1.14 (0.68, 1.91)	0.85
HR (95% CI)[4]	1.0	1.11 (0.66, 1.86)	1.13 (0.66, 1.93)	1.11 (0.65, 1.90)	0.74
HR (95% CI)[5]	1.0	1.15 (0.68, 1.94)	1.17 (0.68, 2.00)	1.25 (0.72, 2.15)	0.46
Fruit juice[1]					
Median intake[2]	0.0	0.35	0.99	1.43	
HR (95% CI)[3]	1.0	1.39 (0.84, 2.32)	1.07 (0.64, 1.80)	1.41 (0.85, 2.34)	0.45

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	Quartile of intake				
	1	**2**	**3**	**4**	***p*-trend**
HR (95% CI)[4]	1.0	1.58 (0.93, 2.71)	1.17 (0.67, 2.03)	1.39 (0.81, 2.40)	0.58
HR (95% CI)[5]	1.0	1.61 (0.94, 2.75)	1.23 (0.71, 2.14)	1.48 (0.86, 2.56)	0.41
Fruit excluding juice					
Median intake[2]	0.40	1.10	1.84	3.13	
HR (95% CI)[3]	1.0	1.12 (0.70, 1.78)	0.86 (0.53, 1.39)	0.66 (0.39, 1.12)	0.07
HR (95% CI)[4]	1.0	1.19 (0.72, 1.95)	0.97 (0.58, 1.61)	0.69 (0.39, 1.22)	0.13
HR (95% CI)[5]	1.0	1.25 (0.76, 2.05)	1.05 (0.63, 1.76)	0.79 (0.44, 1.41)	0.30

Abbreviations: HR, hazard ratio; CI, confidence interval; FFQ, food frequency questionnaire, BMI, body mass index; MET, metabolic equivalent task.

[1]**Total fruit** included all fruits from the following sub-groups: **apples/pears** (fresh apples or pears, apple juice or cider), **berries** (strawberries, blueberries), **citrus** (oranges, orange juice, grapefruit, grapefruit juice), **fruit juice** (orange juice, grapefruit juice, apple juice or cider, other juice), ***and*** raisins or grapes, prunes, bananas, cantaloupe, watermelon, peaches/apricots/plums.

[2]Median intakes reported in servings/d.

[3]Model adjusted for age (yrs), days from diagnosis to FFQ, and energy (kcal/d).

[4]Model adjusted for covariates in Model 1 plus BMI (<25, 25–29.9, ≥30 kg/m^2), clinical risk category (low, intermediate, high), treatment (radical prostatectomy, radiation, active surveillance/other, androgen deprivation therapy), and walking (MET-h/wk; quartile ranks).

[5]Model adjusted for covariates in Model 2 plus quartile ranks of eggs, poultry with skin, and total vegetables.