Title
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Journal
JAMA Internal Medicine, 173(14)

ISSN
2168-6106

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Publication Date
2013-07-22

DOI
10.1001/jamainternmed.2013.6536

Peer reviewed

Published in final edited form as:
JAMA Intern Med. 2013 July 22; 173(14): 1318–1326. doi:10.1001/jamainternmed.2013.6536.

Fat intake after diagnosis and risk of lethal prostate cancer and all-cause mortality

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Abstract

Importance—Nearly 2.5 million men currently live with prostate cancer in the United States, yet little is known about diet after diagnosis and prostate cancer progression and overall mortality.

Objective—Examine post-diagnostic fat intake in relation to lethal prostate cancer and all-cause mortality.

Design, Setting, Participants—Prospective study of 4577 men with non-metastatic prostate cancer in the Health Professionals Follow-up Study (1986–2010).

Exposures—Post-diagnostic saturated, monounsaturated, polyunsaturated, *trans*, animal, and vegetable fat intakes.

Outcomes—Lethal prostate cancer (distant metastases or prostate cancer-specific death) and all-cause mortality.

Results—We observed 315 events of lethal prostate cancer and 1064 deaths (median follow-up = 8.4 y). Crude rates per 1000 person-years for lethal prostate cancer were (highest v. lowest quintile): 7.6 v. 7.3 for saturated, 6.4 v. 7.2 for monounsaturated, 5.8 v. 8.2 for polyunsaturated, 8.7 v. 6.1 for *trans*, 8.3 v. 5.7 for animal, and 4.7 vs. 8.7 for vegetable fat. For all-cause mortality, the rates were: 28.4 v. 21.4 for saturated, 20.0 v. 23.7 for monounsaturated, 17.1 v. 29.4 for polyunsaturated, 32.4 v. 17.1 for *trans*, 32.0 v. 17.2 for animal, and 15.4 v. 32.7 for vegetable fat. Post-diagnostic vegetable fat was associated with lower risk of lethal prostate cancer [hazard ratio (HR; 10% energy): 0.71; 95%CI: 0.51, 0.98; *p*: 0.04] and all-cause mortality [HR (10% energy):

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This work was presented in a poster on October 25th and 26th 2012 at the Prostate Cancer Foundation Retreat in Carlsbad, CA.

All authors contributed to the analysis and interpretation of the data and the critical revision of the manuscript for important intellectual content. None of the funding sources had any role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

None of the authors have any personal or financial conflicts of interest.

0.74; 95%CI: 0.61, 0.88; *p*: 0.001]. No other fats were associated with lethal prostate cancer. Saturated and *trans* fats after diagnosis were associated with higher all-cause mortality [HR (5% energy): 1.30; 95% CI: 1.05, 1.60; *p*: 0.02 and HR (1% energy): 1.25; 95% CI: 1.05, 1.49; *p*: 0.01, respectively].

Conclusions—Among men with non-metastatic prostate cancer, replacing carbohydrate and animal fat with vegetable fat may reduce risk of all-cause mortality. The potential benefit of vegetable fat for prostate cancer-specific outcomes merits further research.

INTRODUCTION

Nearly 2.5 million men currently live with prostate cancer in the United States, and over 241,000 were diagnosed in 2012.[1] Dietary fat has been extensively studied in relation to incident prostate cancer with mixed results.[2–7] Studies of advanced disease are more consistent than studies examining total prostate cancer, suggesting fat intake may be relevant to disease progression.[8] Yet little is known about post-diagnostic fat intake and prostate cancer progression or overall survival.

Three prospective case-only studies have examined fat intake in relation to prostate cancer death. Saturated fats have been associated with higher risk of prostate cancer death, while marine fatty acids and monounsaturated fat have been associated with lower risk of prostate cancer death.[9–11] However, all of these studies had relatively few events, asked men with prostate cancer to recall their diet prior to diagnosis, and were conducted in unscreened populations.

Thus, we prospectively examined post-diagnostic consumption of saturated, monounsaturated, polyunsaturated, *trans*, animal, and vegetable fats in relation to risk of lethal prostate cancer and all-cause mortality among men with non-metastatic prostate cancer in the Health Professionals Follow-up Study. Based on prior studies, we hypothesized that saturated fat intake after diagnosis would be associated with higher risk of lethal prostate cancer.

METHODS

Study Population

The Health Professionals Follow-up Study was initiated in 1986 among 51,529 male health professionals 40–75 years old. Participants reported medical diagnoses, medication, weight, height, smoking, and physical activity at baseline and every two years thereafter; the average questionnaire response rate exceeds 90%. Prostate specific antigen (PSA) screening practices were added in 1994. Dietary data were collected at baseline and every four years thereafter. The Institutional Review Boards of the Harvard School of Public Health and University of California, San Francisco approved this study.

Dietary assessment

The food frequency questionnaire (FFQ) asked men to report their usual intake over the previous year of approximately 130 foods and beverages. In addition, men were asked to report fried food consumption, type of cooking fat, and whether visible fat on meat was consumed. To calculate nutrient intakes, we multiplied the frequency of consumption by the amount of the nutrient in the specified portion of each food and summed across all foods. Nutrient data were obtained from the United States Department of Agriculture.

The correlation between the FFQ and diet records was 0.75 for saturated fat, 0.37 for polyunsaturated fat, and 0.68 for monounsaturated fat.[12] The correlation between the FFQ

and composition of subcutaneous fat was 0.18 for saturated fat, 0.50 for polyunsaturated fat, 0.14 for monounsaturated fat, and 0.29 for *trans* fat;[13] low correlations are expected for saturated and monounsaturated fat due to endogenous synthesis.

Outcome assessment and follow-up

Men were asked every two years if they had been diagnosed with prostate cancer. After a report of prostate cancer, we obtained medical records to verify the diagnosis and abstract information on date of diagnosis, stage, PSA values, Gleason sum, treatments, and metastases. We also sent prostate cancer-specific biennial questionnaires to participants and their doctors to obtain information on PSA values, treatments, and metastases.

Our primary outcomes were lethal prostate cancer, defined as distant metastases or death due to prostate cancer, and all-cause mortality. The occurrence of metastases, including location and date of detection, was determined via review of medical records, the doctor and patient questionnaires, and death certificates. Study physicians confirmed cause of death through medical records and death certificates. A death was attributed to prostate cancer if prostate cancer metastases were present and no more plausible cause of death was mentioned. We ascertained greater than 98% of deaths during follow-up.[14]

Inclusion/exclusion criteria

To be included in this analysis, men had to be free of cancer (except non-melanoma skin cancer) at baseline and diagnosed with non-metastatic prostate cancer in 1986–2010. We excluded men who reported <800 or >4200 kcal/d or were missing >70 items on the baseline FFQ and men missing clinical stage or treatment data, leaving 4,577 men for analysis.

Statistical analysis

We used Cox proportional hazards regression to examine post-diagnostic saturated, monounsaturated, polyunsaturated, *trans*, animal, and vegetable fat intakes in relation to risk of lethal prostate cancer and all-cause mortality. For analyses of lethal prostate cancer, person-time was contributed from diagnosis to distant metastases or death due to prostate cancer, death from other causes, or end of follow-up (January 31, 2010), whichever came first. For all-cause mortality, men were followed from diagnosis until death or end of follow-up. We used calendar time in two-year intervals as our time scale and stratified by years since diagnosis.

We calculated cumulative average post-diagnostic intake from the FFQ preceding diagnosis until end of follow-up.[15] The FFQ preceding diagnosis was used to classify person-time from diagnosis until the next available FFQ under the assumption that disease was present at that time and because men diagnosed with prostate cancer did not change their diet more or less on average compared to men not diagnosed during the same period. For example, for a man diagnosed in 1992, we applied the 1990 FFQ to person-time contributed between 1992 and 1994, the average of the 1990 and 1994 FFQs to person-time contributed between 1994 and 1998, etc. On average, participants completed 2.6 FFQs in the post-diagnostic period.

We used the multivariate nutrient-density model,[16] and modeled replacing carbohydrate with the fat of interest. We also modeled replacing animal fat with vegetable fat and saturated with monounsaturated or polyunsaturated fats. To do so, we included all macronutrients in the model except the macronutrient we were "replacing".[16] We examined the fats continuously and categorically, and modeled the median of each quintile as a continuous term to test for linear trend. We used conventional units of energy change in the continuous models: 5% for the major fats, 1% for *trans* fat, and 10% for animal and

vegetable fats. These values approximate the difference in medians between the highest and lowest quintiles.

Our basic model was adjusted for age at diagnosis (years) and energy (kcal/d). For analyses of lethal prostate cancer, our multivariate model was additionally adjusted for treatment (radical prostatectomy, radiation, hormone therapy, other), Gleason sum (<7, 7, >7), clinical stage (T1, T2, T3), diagnostic PSA (4-level ordinal score using category medians), number of PSA screening tests prior to diagnosis (continuous), body mass index (BMI; <25, 25–29.9, 30+ kg/m^2), vigorous activity (3-level ordinal score using category medians), smoking (current 40+ pack-years, current <40 pack-years, quit <10 years ago, quit 10+ years ago, never), calcium (5-level ordinal score using category medians), alcohol (% energy), protein (% energy), the other fats (% energy) (i.e. saturated fat was adjusted for monounsaturated, polyunsaturated, *trans* fats; vegetable fat was adjusted for animal and *trans* fats), and pre-diagnostic intake of the exposure of interest based on the baseline FFQ (5-level ordinal score using category medians). For all-cause mortality, our multivariate model included all of the above plus parental history of myocardial infarction before age 60 (yes/no), high blood pressure at diagnosis (yes/no), diabetes mellitus at diagnosis (yes/no), elevated cholesterol at diagnosis (yes/no), and presence of co-morbidities (yes/no; yes if myocardial infarction, angina, coronary artery bypass or angioplasty, stroke, emphysema/chronic bronchitis/chronic obstructive pulmonary disease, or Parkinson's disease). For lethal prostate cancer, we also considered adjustment for coffee, phosphorous, zinc, vitamin D, vitamin E, choline, lycopene, type II diabetes, walking pace, height, cholesterol-lowering medication, aspirin, secondary treatments, and adjuvant therapies, but the estimates remained essentially the same and we present results from models omitting these variables.

We performed several secondary and sensitivity analyses. First, we examined whether age at diagnosis (<69 v. 69+ y), BMI (<25 v. 25+ kg/m^2), vigorous activity (<3 v. 3+ h/wk), smoking (never v. former/current), time since diagnosis (continuous), Gleason sum (<7 v. 7+), or primary treatment (radical prostatectomy v. other) modified the relations by including a cross-product between the continuous exposure and potential effect modifier in our multivariate model and using a Wald test to test for evidence of effect modification. Second, we examined linoleic acid, alpha-linolenic acid, long-chain omega-3 fatty acids (eicosapentaenoic acid, docosahexaenoic acid, docosapentaenoic acid), and the ratio of omega-6 to omega-3 fatty acids after diagnosis and risk of lethal prostate cancer and all-cause mortality.[17, 18] Third, we examined the results with a 2–6 year lag and compared the change in fat intake from the first to last post-diagnostic FFQ for the whole study population and among events only. Fourth, we examined pre-diagnostic fat intake (baseline and cumulative average) and risk of lethal prostate cancer in our case-only study population. Lastly, we examined risk of prostate cancer-specific death to confirm that the results were similar to those for lethal prostate cancer (an outcome that combines distant metastases and prostate cancer-specific death).

Statistical tests were performed using SAS v. 9.2 and p-values <0.05 were considered statistically significant.

RESULTS

Among 4,577 men with non-metastatic prostate cancer, we observed 315 events of lethal prostate cancer and 1064 deaths over a median follow-up of 8.4 years (25th percentile: 4.6 y; 75th percentile: 12.5 y). The primary causes of death were cardiovascular disease (31.2%), prostate cancer (21.3%), and other cancers (20.6%).

At diagnosis, men who consumed more animal fat had a higher BMI (26.8 vs. 24.9 kg/m^2), engaged in less vigorous activity (9.2 vs. 16.9 MET-h/wk), and were more likely to be current smokers (7 vs. 1%). Men who consumed more vegetable fat were more likely to be diagnosed with moderately differentiated disease (Gleason sum = 7) (37 vs. 32%) and treated via radical prostatectomy (50 v. 45%) (Table 1).

Lethal prostate cancer

Crude rates of lethal prostate cancer (per 1000 person-years) comparing the highest and lowest quintile for each of the fats were: 7.6 v. 7.3 for saturated, 6.4 v. 7.2 for monounsaturated, 5.8 v. 8.2 for polyunsaturated, 8.7 v. 6.1 for *trans*, 8.3 v. 5.7 for animal, and 4.7 vs. 8.7 for vegetable fat.

Men who consumed more vegetable fat after diagnosis had a lower risk of lethal prostate cancer. Replacing 10% of calories from carbohydrate with vegetable fat was associated with a 29% lower risk of lethal prostate cancer (hazard ratio (HR): 0.71; 95% confidence interval (CI): 0.51, 0.98; *p*-value: 0.04) (Table 2). The magnitude of the association was similar, but not statistically significant, when replacing animal fat with vegetable fat (HR: 0.76; 95% CI: 0.52, 1.10; *p*-value: 0.14). When examined categorically, men in the highest quintile of post-diagnostic vegetable fat had a non-significant 36% lower risk of lethal prostate cancer (HR: 0.64; 95% CI: 0.40, 1.01; *p*-trend: 0.06). Post-diagnostic intakes of the other fats, including specific polyunsaturated fatty acids and the ratio of omega-6 to omega-3 fatty acids after diagnosis (see eTable in the Supplement), were not associated with lethal prostate cancer.

Results were similar, but not statistically significant, in secondary and sensitivity analyses. For a 10% increase in calories from vegetable fat, the HRs (95% CI) were: 0.71 (0.51, 1.00) when examining a 2–6 year lag, 0.67 (0.44, 1.01) when examining prostate cancer-specific death (226 events), 0.71 (0.47, 1.05) when examining cumulative average pre-diagnostic diet, and 0.84 (0.63, 1.12) when examining baseline pre-diagnostic diet. None of the pre-diagnostic fat intakes were statistically significantly associated with risk of lethal prostate cancer. Lastly, men who developed lethal prostate cancer did not change their fat intake more or less on average over follow-up compared to the study population as a whole, and there was no evidence of effect modification by age at diagnosis, BMI, activity, smoking, time since diagnosis, Gleason sum, or primary treatment.

All-cause mortality

For all-cause mortality, the crude rates (per 1000 person-years) comparing the highest and lowest quintile of each of the fats were: 28.4 v. 21.4 for saturated, 20.0 v. 23.7 for monounsaturated, 17.1 v. 29.4 for polyunsaturated, 32.4 v. 17.1 for *trans*, 32.0 v. 17.2 for animal, and 15.4 v. 32.7 for vegetable fat.

Men who consumed more vegetable fat after diagnosis had a lower risk of all-cause mortality. Replacing 10% of calories from carbohydrate with vegetable fat was associated with a 26% lower risk of death (HR: 0.74; 95% CI: 0.61, 0.88; *p*-value: 0.001) (Table 3). The association was stronger when replacing animal fat with vegetable fat (HR: 0.66; 95% CI: 0.54, 0.81; *p*-value: <0.001). When examined categorically, men in the highest quintile of post-diagnostic vegetable fat had a 35% lower risk of death (HR Q5 v. Q1: 0.65; 95% CI: 0.52, 0.83; *p*-value <0.001).

In addition, a 5% increase in saturated fat was associated with a 30% higher risk of death (HR: 1.30; 95% CI: 1.05, 1.60; *p*-value: 0.02) and a 1% increase in *trans* fat was associated with a 25% higher risk of death (HR: 1.25; 95% CI: 1.05, 1.49: *p*-value: 0.01). When examined categorically, greater polyunsaturated fat intake after diagnosis was associated

with lower all-cause mortality (HR Q5 v. Q1: 0.73; 95% CI: 0.57, 0.94; *p*-trend: 0.004), and replacing 5% of calories from saturated fat with polyunsaturated fat after diagnosis was associated with 34% lower risk of death (HR: 0.66; 95% CI: 0.48, 0.90; *p*-value: 0.01).

Post-diagnostic intake of monounsaturated, linoleic acid, alpha-linolenic acid, long-chain omega-3 fatty acids, and the ratio of omega-6 to omega-3 fatty acids were not significantly associated with risk of death (see eTable in the Supplement). There was no evidence of effect modification by age at diagnosis, BMI, activity, smoking, time since diagnosis, Gleason sum, or primary treatment.

Food sources of vegetable fat

To assess whether the observed associations with vegetable fat were driven by specific foods, we examined post-diagnostic intake of the top food sources of vegetable fat in our study population (e.g. oil-based dressing, margarine, mayonnaise, nuts) and risk of lethal prostate cancer and all-cause mortality adjusting for all of the variables in our multivariate models described above, except intakes of fats, protein, alcohol, and pre-diagnostic diet. A one serving (1 Tbsp) per day increase in oil-based dressing after diagnosis was suggestively associated with a 29% lower risk of lethal prostate cancer (HR: 0.71; 95% CI: 0.50, 1.00) and a 13% lower risk of death (HR: 0.87; 95% CI: 0.72, 1.05). A one serving (1 ounce) per day increase in nuts after diagnosis was suggestively associated with an 18% lower risk of lethal prostate cancer (HR: 0.82; 95% CI: 0.67, 1.01) and an 11% lower risk of death (HR: 0.89; 95% CI: 0.79, 0.99). Post-diagnostic intakes of mayonnaise and margarine were not associated with risk of lethal prostate cancer or all-cause mortality.

DISCUSSION

In this prospective analysis, vegetable fat intake after diagnosis was associated with a lower risk of lethal prostate cancer and all-cause mortality.

To our knowledge, no prior study has examined fat intake after diagnosis in relation to risk of lethal prostate cancer and all-cause mortality. However, three prior prospective case-only studies conducted in unscreened populations have examined pre-diagnostic fat in relation to prostate cancer death. Among 525 Swedish men, marine fatty acids were associated with lower risk of prostate cancer death (events: 222; HR Q4 v. Q1: 0.59; 95% CI: 0.40, 0.87) and, among the men diagnosed with localized disease (46 events), myristic acid and short-chain saturated fatty acids were associated with higher risk of prostate cancer death (HR Q4 v Q1: 2.39; 95% CI: 1.06, 5.38 and HR Q4 v. Q1: 2.88; 95% CI: 1.24, 6.67, respectively).[10] Among 384 Canadian men with prostate cancer, pre-diagnostic saturated fat intake was associated with higher risk of prostate cancer death (events: 32; HR tertile 3 v. tertile 1: 3.13; 95% CI: 1.28, 7.67).[9] Greater intake of vegetable fat prior to diagnosis was suggestively associated with lower risk of advanced disease at diagnosis in this cohort (odds ratio: 0.84; 95% CI: 0.70, 1.01).[19] In a distinct cohort of 263 Canadian men, pre-diagnostic intake of monounsaturated fat was associated with a lower risk of prostate cancer death (events: 58; HR: 0.3; 95% CI: 0.1; 0.7).[11]

Fat from vegetable sources includes a heterogeneous mix of monounsaturated and polyunsaturated fats. In our study, neither monounsaturated nor polyunsaturated fat were associated with lethal prostate cancer, although the associations were in the protective direction. Red meat and poultry with skin were major sources of monounsaturated and polyunsaturated fat in our study population however, and these foods are also sources of heme iron and heterocyclic amines, which may increase risk of aggressive prostate cancer.[20] We did not have data on meat cooking practices, and thus the relations between the fats and risk of lethal prostate cancer may have been confounded by unmeasured factors associated

with the consumption of animal products. It is also possible that the beneficial associations observed for vegetable fat are due to other components of food sources of vegetable fats. Although we considered adjustment for all known dietary risk factors for prostate cancer (e.g. calcium, vitamin E, lycopene, vitamin D, choline, phosphorous, zinc, etc.) and observed little evidence of confounding, we cannot rule out confounding by unmeasured factors associated with the consumption of the fats examined.

In particular, oils and nuts were among the top food sources of vegetable fats in our population. Consumption of these foods increases plasma antioxidants and reduces circulating insulin, LDL-cholesterol, inflammatory markers, and markers of oxidative stress,[21–33] all of which may affect prostate cancer progression.[34–37] For example, flaxseed supplementation prior to radical prostatectomy has been associated with lower proliferation rates in prostate tumors.[38] Additional studies are needed to examine whether the associations we observed were due to the fat or other components (e.g. phytochemicals) in these foods, or some combination thereof.

Cardiovascular disease was the leading cause of death in this cohort of men with prostate cancer, accounting for nearly one-third of deaths. The beneficial effects of unsaturated fats and harmful effects of saturated and *trans* fats on cardiovascular health are well known and our findings among men with prostate cancer are consistent with the established relations.[39–41] Overall, our findings support counseling men with prostate cancer to follow a heart-healthy diet in which carbohydrate calories are replaced with unsaturated oils and nuts to reduce their risk of all-cause mortality.

In conclusion, among men with non-metastatic prostate cancer, replacing carbohydrate and animal fat with vegetable fat may reduce risk of all-cause mortality. The potential benefit of vegetable fat for prostate cancer-specific outcomes merits further research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank the participants and staff of the HPFS and the following state cancer registries for their invaluable contributions to this project: AL, AZ, AR, CA, CO, CT, DE, FL, GA, ID, IL, IN, IA, KY, LA, ME, MD, MA, MI, NE, NH, NJ, NY, NC, ND, OH, OK, OR, PA, RI, SC, TN, TX, VA, WA, WY. We also thank the Prostate Cancer Foundation for their contribution to the original efforts to collect data from men with prostate cancer in the HPFS.

Dr. Richman had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs. Chan, Willett, and Giovannucci contributed to the conception and design of the study. Drs. Richman, Kenfield, and Willett contributed to the acquisition of the data. Dr. Richman drafted the manuscript. Drs. Richman, Chavarro, and Willett contributed to the statistical analysis. Drs. Stampfer, Willett, and Giovannucci obtained funding. Drs. Kenfield and Chan provided administrative, technical, or material support. Drs. Stampfer, Chan, and Willett provided supervision.

Financial disclosure: This work was supported by grants from the National Institutes of Health (CA141298, CA112355, CA055075, CA133891, and CA098566), Department of Defense (W81XWH-11-1-0529), and the Prostate Cancer Foundation.

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JAMA Intern Med. Author manuscript; available in PMC 2014 July 22.

Table 1

Age-standardized characteristics of 4,577 men diagnosed with non-metastatic prostate cancer by post-diagnostic animal and vegetable fat intakes.

Characteristic	Extreme quintiles of animal fat intake		*p*-value	Extreme quintiles of vegetable fat intake		*p*-value
	1	5		1	5	
Age at diagnosis, y	69.6 ± 7.1[1]	69.0 ± 7.2	0.02	69.8 ± 7.1	69.3 ± 7.0	0.09
BMI at diagnosis, kg/m^2	24.9 ± 2.9	26.8 ± 3.8	<0.001	25.7 ± 3.5	25.6 ± 3.4	0.46
Vigorous physical activity at diagnosis, MET[2]-h/wk	16.9 ± 26.4	9.2 ± 19.0	<0.001	12.8 ± 21.8	11.8 ± 19.1	0.16
White, %	91	93	0.09	93	93	0.72
Current smokers at diagnosis, %	1	7	<0.001	5	3	0.04
Family history of prostate cancer, %	22	22	0.33	20	23	0.17
Number of questionnaires on which a PSA screening test was reported prior to diagnosis	3.6 ± 1.9	3.3 ± 2.0	<0.001	3.3 ± 1.9	3.6 ± 2.0	<0.001
Clinical T-Stage, %			0.22			0.13
T1	61	59		58	62	
T2	35	37		39	36	
T3	4	3		3	2	
Gleason sum, %			0.48			0.02
2–6	48	49		49	48	
7	35	33		32	37	
8–10	11	13		14	10	
Missing	6	6		6	5	
PSA at diagnosis, ng/ml, %			0.04			0.03
<4	14	12		10	14	
4–9.9	56	55		58	59	
10–19.9	17	20		17	16	
20+	7	7		8	7	
Missing	6	7		6	5	
Treatment, %			0.17			0.03
Radical prostatectomy	46	45		45	50	
Radiation	40	40		41	36	
Hormones	5	6		5	4	
Other	9	10		9	10	

[1] All such values: mean ± standard deviation.

[2] Metabolic equivalent task.

Table 2

Relative risk of lethal prostate cancer among 4,577 men diagnosed with non-metastatic prostate cancer by post-diagnostic fat intake.

	Quintile of intake						Continuous model	
	1	**2**	**3**	**4**	**5**	***P*-trend[1]**	**HR (95% CI)**	***p*-value**
Saturated fat								
Median % energy	6.3	8.2	9.5	10.7	12.7		Unit of change = 5% energy	
Events	64	57	64	66	64			
Model 1 HR (95% CI)[2]	1.0	0.82 (0.57, 1.17)	0.93 (0.66, 1.32)	0.97 (0.69, 1.38)	1.02 (0.72, 1.45)	0.62	1.06 (0.85, 1.32)	0.62
Model 2 HR (95% CI)[3]	1.0	0.79 (0.52, 1.20)	0.86 (0.54, 1.37)	0.88 (0.53, 1.47)	0.84 (0.47, 1.49)	0.74	1.00 (0.68, 1.49)	0.99
Monounsaturated fat								
Median % energy	8.3	10.4	11.7	13.1	15.2		Unit of change = 5% energy	
Events	61	60	64	76	54			
Model 1 HR (95% CI)[2]	1.0	0.89 (0.62, 1.28)	0.91 (0.64, 1.29)	1.13 (0.80, 1.59)	0.94 (0.65, 1.36)	0.84	0.99 (0.80, 1.22)	0.93
Model 2 HR (95% CI)[3]	1.0	0.98 (0.64, 1.49)	0.98 (0.61, 1.57)	1.09 (0.65, 1.83)	0.96 (0.53, 1.73)	0.97	0.88 (0.60, 1.29)	0.51
Polyunsaturated fat								
Median % energy	4.3	5.1	5.8	6.5	7.8		Unit of change = 5% energy	
Events	70	67	63	65	50			
Model 1 HR (95% CI)[2]	1.0	0.92 (0.66, 1.30)	0.84 (0.59, 1.18)	0.87 (0.62, 1.22)	0.78 (0.54, 1.13)	0.18	0.78 (0.51, 1.18)	0.23
Model 2 HR (95% CI)[3]	1.0	0.91 (0.64, 1.30)	0.80 (0.55, 1.17)	0.82 (0.55, 1.22)	0.73 (0.47, 1.15)	0.17	0.82 (0.47, 1.42)	0.48
Trans fat								
Median % energy	0.7	1.0	1.3	1.5	2.0		Unit of change = 1% energy	
Events	52	54	64	70	75			
Model 1 HR (95% CI)[2]	1.0	0.93 (0.64, 1.37)	1.09 (0.75, 1.57)	1.15 (0.80, 1.66)	1.21 (0.84, 1.74)	0.15	1.15 (0.92, 1.43)	0.22
Model 2 HR (95% CI)[3]	1.0	1.03 (0.68, 1.57)	1.14 (0.73, 1.79)	1.12 (0.70, 1.79)	1.27 (0.76, 2.12)	0.31	1.16 (0.85, 1.60)	0.35
Animal fat								
Median % energy	8.1	11.6	14.0	16.6	21.0		Unit of change = 10% energy	
Events	50	62	63	71	69			
Model 1 HR (95% CI)[2]	1.0	1.17 (0.80, 1.70)	1.15 (0.79, 1.68)	1.29 (0.89, 1.86)	1.40 (0.97, 2.02)	0.06	1.23 (0.99, 1.54)	0.06
Model 2 HR (95% CI)[3]	1.0	1.22 (0.81, 1.83)	1.10 (0.72, 1.69)	1.20 (0.76, 1.89)	1.16 (0.70, 1.94)	0.66	0.99 (0.71, 1.38)	0.96
Vegetable fat								

	Quintile of intake						Continuous model	
	1	**2**	**3**	**4**	**5**	***P*-trend[1]**	**HR (95% CI)**	***p*-value**
Median % energy	10.2	13.0	15.0	17.4	21.6		Unit of change = 10% energy	
Events	71	67	66	70	41			
Model 1 HR (95% CI)[2]	1.0	0.87 (0.62, 1.22)	0.85 (0.60, 1.19)	0.88 (0.63, 1.23)	0.61 (0.41, 0.90)	0.02	0.73 (0.56, 0.96)	0.03
Model 2 HR (95% CI)[3]	1.0	0.91 (0.64, 1.29)	0.92 (0.63, 1.33)	0.86 (0.58, 1.26)	0.64 (0.40, 1.01)	0.06	0.71 (0.51, 0.98)	0.04

Abbreviations: HR, hazard ratio; CI, confidence interval.

[1] *P*-trend calculated by modeling the median of each category as a continuous term.

[2] Cox proportional hazards regression model adjusted for age at diagnosis (continuous), energy (continuous), and time since diagnosis (continuous).

[3] Cox proportional hazards regression model adjusted for variables in Model 1 plus treatment (prostatectomy, radiation, hormones, other), Gleason sum (<7, 7, 8+), clinical stage (T1, T2, T3), PSA at diagnosis (ordinal trend), number of PSA screening tests prior to diagnosis (continuous), body mass index (<25, 25–29.9, 30+ kg/m^2), smoking (current 40+ pack-years, current <40 pack=years, quit <10 y, quit 10+ y, never), vigorous activity (ordinal trend), and intake of calcium (ordinal trend), alcohol (%energy), protein (%energy). Additionally, the fats were adjusted for one another; animal and vegetable fat were adjusted for one another and *trans* fat; and all were adjusted for pre-diagnostic intake of the exposure of interest based on the 1986 FFQ.

JAMA Intern Med. Author manuscript; available in PMC 2014 July 22.

Table 3

Relative risk of all-cause mortality among 4,577 men diagnosed with non-metastatic prostate cancer by post-diagnostic fat intake.

	Quintile of intake						Continuous model	
	1	**20**	**3**	**4**	**5**	***P*-trend[1]**	**HR (95% CI)**	***p*-value**
Saturated fat								
Median % energy	6.3	8.2	9.5	10.7	12.7		Unit of change = 5% energy	
Events	191	196	219	216	242			
Model 1 HR (95% CI)[2]	1.0	0.94 (0.77, 1.15)	1.10 (0.90, 1.34)	1.10 (0.91, 1.35)	1.41 (1.16, 1.70)	<0.001	1.34 (1.18, 1.52)	<0.001
Model 2 HR (95% CI)[3]	1.0	0.95 (0.75, 1.20)	1.05 (0.81, 1.37)	1.02 (0.77, 1.37)	1.19 (0.86, 1.63)	0.22	1.30 (1.05, 1.60)	0.02
Monounsaturated fat								
Median % energy	8.3	10.4	11.7	13.1	15.2		Unit of change = 5% energy	
Events	205	237	207	243	172			
Model 1 HR (95% CI)[2]	1.0	1.07 (0.89, 1.29)	0.89 (0.73, 1.08)	1.15 (0.95, 1.38)	1.08 (0.88, 1.33)	0.45	1.08 (0.96, 1.22)	0.20
Model 2 HR (95% CI)[3]	1.0	0.99 (0.79, 1.24)	0.80 (0.62, 1.04)	0.96 (0.72, 1.27)	0.87 (0.63, 1.20)	0.27	0.86 (0.69, 1.07)	0.18
Polyunsaturated fat								
Median % energy	4.3	5.1	5.8	6.5	7.8		Unit of change = 5% energy	
Events	254	242	225	195	148			
Model 1 HR (95% CI)[2]	1.0	0.92 (0.77, 1.09)	0.85 (0.71, 1.02)	0.73 (0.61, 0.89)	0.74 (0.60, 0.91)	<0.001	0.72 (0.57, 0.92)	0.008
Model 2 HR (95% CI)[3]	1.0	0.92 (0.77, 1.11)	0.85 (0.70, 1.04)	0.74 (0.60, 0.93)	0.73 (0.57, 0.94)	0.004	0.77 (0.57, 1.05)	0.10
Trans fat								
Median % energy	0.7	1.0	1.3	1.5	2.0		Unit of change = 1% energy	
Events	149	175	195	261	284			
Model 1 HR (95% CI)[2]	1.0	1.08 (0.87, 1.35)	1.12 (0.90, 1.39)	1.45 (1.18, 1.77)	1.44 (1.17, 1.76)	<0.001	1.30 (1.15, 1.47)	<0.001
Model 2 HR (95% CI)[3]	1.0	1.10 (0.87, 1.40)	1.18 (0.92, 1.52)	1.54 (1.19, 1.99)	1.51 (1.14, 2.01)	0.002	1.25 (1.05, 1.49)	0.01
Animal fat								
Median % energy	8.1	11.6	14.0	16.6	21.0		Unit of change = 10% energy	
Events	154	188	217	235	270			
Model 1 HR (95% CI)[2]	1.0	1.11 (0.89, 1.37)	1.24 (1.01, 1.53)	1.31 (1.07, 1.61)	1.77 (1.45, 2.17)	<0.001	1.53 (1.35, 1.73)	<0.001
Model 2 HR (95% CI)[3]	1.0	1.03 (0.82, 1.29)	1.12 (0.89, 1.43)	1.06 (0.82, 1.36)	1.19 (0.90, 1.57)	0.24	1.19 (0.99, 1.42)	0.06
Vegetable fat								

	Quintile of intake						Continuous model	
	1	**20**	**3**	**4**	**5**	***P*-trend[1]**	**HR (95% CI)**	***p*-value**
Median % energy	10.2	13.0	15.0	17.4	21.6		Unit of change = 10% energy	
Events	273	250	223	184	134			
Model 1 HR (95% CI)[2]	1.0	0.85 (0.72, 1.01)	0.77 (0.64, 0.92)	0.64 (0.53, 0.77)	0.64 (0.52, 0.80)	<0.001	0.69 (0.59, 0.81)	<0.001
Model 2 HR (95% CI)[3]	1.0	0.83 (0.69, 1.00)	0.77 (0.64, 0.94)	0.64 (0.52, 0.78)	0.65 (0.52, 0.83)	<0.001	0.74 (0.61, 0.88)	0.001

Abbreviations: HR, hazard ratio; CI, confidence interval.

[1] *P*-trend calculated by modeling the median of each category as a continuous term.

[2] Cox proportional hazards regression model adjusted for age at diagnosis (continuous), energy (continuous), and time since diagnosis (continuous).

[3] Cox proportional hazards regression model adjusted for variables in Model 1 plus treatment (prostatectomy, radiation, hormones, other), Gleason sum (<7, 7, 8+), clinical stage (T1, T2, T3), PSA at diagnosis (ordinal trend), number of PSA tests prior to diagnosis (continuous), body mass index (<25, 25–29.9, 30+ kg/m^2), smoking (current 40+ pack-years, current <40 pack=years, quit <10 y, quit 10+ y, never), vigorous activity (ordinal trend), high blood pressure at prostate cancer diagnosis (yes/no), elevated cholesterol at prostate cancer diagnosis (yes/no), diabetes mellitus at prostate cancer diagnosis (yes/no), parental history of myocardial infarction before age 60, co-morbidity (yes/no; 'yes' if any of the following: myocardial infarction, coronary artery bypass or angioplasty, stroke, emphysema or chronic obstructive pulmonary disorder, Parkinson's disease), and intake of calcium (ordinal trend), alcohol (%energy), protein (%energy). Additionally, the fats were adjusted for one another; animal and vegetable fat were adjusted for one another and *trans* fat; and all were adjusted for pre-diagnostic intake of the exposure of interest based on the 1986 FFQ.