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Mediterranean Diet After Prostate Cancer Diagnosis and Urinary and Sexual Functioning: the Health Professionals Follow-up Study

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Abstract

Background—Men with prostate cancer often experience urinary and sexual dysfunction after treatment. Previous studies have demonstrated a relationship between dietary factors and these symptoms among men with diabetes or metabolic syndrome. However, there are limited data on whether diet after prostate cancer diagnosis, including a Mediterranean dietary pattern, affects urinary and sexual function among prostate cancer survivors.

Methods—Men diagnosed with non-metastatic prostate cancer in the Health Professionals Follow-up Study (n=2960) from 1986-2012 were prospectively followed for a median of 8.3 years after treatment. Participants completed validated dietary questionnaires every four years and a health-related quality of life assessment in 2010 or 2012. We used generalized linear models to examine associations between post-diagnosis Mediterranean Diet Score (including individual score components and dietary fat subtypes) and quality of life domains (sexual functioning, urinary irritation/obstruction, urinary incontinence) assessed using the Expanded Prostate Cancer Index Composite Short Form (score 0-100; higher scores indicate better function).

Results—No statistically significant relationships were observed between the Mediterranean Diet Score after prostate cancer diagnosis and urinary or sexual function. However, the associations did vary depending on pre-diagnosis urinary and sexual dysfunction for urinary irritation/obstruction and sexual function scores, respectively (p-interactions<0.0001). Men with higher post-diagnosis vegetable intake reported higher urinary incontinence scores (72 versus 76 comparing lowest to

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highest quintile; *p*-trend=0.003). Similarly, higher vegetable intake and lower polyunsaturated fat intake were associated with higher urinary irritation/obstruction scores (vegetable: 80 versus 84 comparing lowest to highest quintile, *p*-trend=0.01; polyunsaturated fat: 84 versus 78 comparing lowest to highest quintile, *p*-trend=0.005), however these associations were observed only among men with urinary symptoms prior to their prostate cancer diagnosis.

Conclusions—Among men with prostate cancer, diet intake after diagnosis was not significantly associated with urinary or sexual function, although some relationships appeared to differ among men with and without symptoms prior to their prostate cancer diagnosis. Higher vegetable intake and lower polyunsaturated fat intake after prostate cancer diagnosis may be associated with better urinary function. However, this analysis was exploratory, and further research is needed to better delineate these relationships and guide dietary recommendations for men with prostate cancer.

Keywords

Mediterranean diet; prostate cancer survivors; erectile dysfunction; lower urinary tract symptoms; quality of life

Introduction

Dietary factors may affect health-related quality-of-life (HRQOL), specifically erectile dysfunction (ED) and lower urinary tract symptoms (LUTS), among healthy adult men. These symptoms are more common among men treated for prostate cancer,[1-9] yet little is known regarding how dietary factors affect urinary and sexual function among men with prostate cancer.

Lifestyle modifications that improve vascular function via increased nitric oxide (NO) production, decreased insulin resistance, or decreased oxidative stress and inflammation may prevent or reverse ED in healthy adult men.[10] Various dietary components (omega-3 fatty acids, antioxidants) are associated with increased NO synthesis.[11] Specific foods (fruits,[12,13] nuts[13], vegetables[14], dairy[14]), nutrients (monounsaturated: saturated fat ratio,[13] flavonoids[15]), and dietary patterns (Mediterranean[16,17] and energy restricted, including high-protein[18,19] and high-carbohydrate[19]) are associated with erectile function in healthy individuals[13-15,20] as well as men with metabolic syndrome.[12,16-19] Notably, men with newly diagnosed diabetes mellitus randomized to a Mediterranean diet had a slower decline in sexual function compared to men randomized to a low-fat diet.[21] Moderate alcohol consumption may also be inversely associated with ED.[22] However, these observed associations may not persist among men with prostate cancer in whom the mechanism of ED could be post-surgical (e.g. nerve injury) or cancer-related (e.g. radiation, biopsies, cancer anxiety).

Diet may also be associated with LUTS; however, data are limited,[23] especially in the setting of invasive treatments for prostate cancer (e.g. prostatectomy, pelvic radiation), and definitions of LUTS are variable (e.g. clinical diagnosis, urinary incontinence, symptom index scores). Among men without prostate cancer, the majority of urinary symptoms are due to bladder outlet obstruction secondary to benign prostatic hyperplasia (BPH). However, coexisting hyperactive bladder due to abnormal autonomic nervous system activity, detrusor

muscle sensitivity, or oxidative damage may also contribute to symptoms.[24-27] Dietary factors may affect multiple components of these pathways. Previous studies among men without prostate cancer reported positive associations between intake of red meat or animal protein[14,28-30], polyunsaturated fat[29,30], and saturated fat[29-31] and incident BPH/LUTS, independent of body mass index (BMI) and/or waist circumference. Conversely, an inverse association has been observed between vegetable intake and incident BPH/LUTS.[14,20]

In summary, despite evidence of associations among adult men without cancer, no studies have evaluated the relationship between individual dietary factors and HRQOL among men with prostate cancer. We examined whether post-diagnosis diet was associated with prostate cancer-related HRQOL measures. Extrapolating from studies of diet and ED among men without prostate cancer, we hypothesized that the Mediterranean dietary pattern, and dietary components that are associated with increased NO synthesis (e.g. polyunsaturated fats), would be associated with improved sexual functioning among men initially diagnosed with localized prostate cancer. Similarly, we hypothesized that the Mediterranean dietary pattern, and dietary components with antioxidant properties (e.g. vegetables), would be inversely associated with LUTS among men with prostate cancer.

Material and Methods

Participants

The Health Professionals Follow-up Study is a prospective study of 51,529 U.S. male health professionals who enrolled in 1986 by completing a mailed questionnaire. Participants provided information regarding medical diagnoses, medications, and lifestyle factors and complete biennial follow-up questionnaires to update this information (response rate 96%). After participants reported a prostate cancer diagnosis, we obtained medical records and pathology reports to confirm the diagnosis and record clinical T-stage, Gleason score, treatments, prostate-specific antigen (PSA) values at diagnosis, and presence of metastasis. Biennial follow-up questionnaires were completed by participants to update data on secondary treatment, PSA levels, and clinical progression. In 2010 and 2012, this questionnaire included the Expanded Prostate Cancer Index Composite Short Form (EPIC-26[32]) to assess HRQOL outcomes.

The sample population included 3034 men diagnosed with non-metastatic prostate cancer prior to 2010 who completed the 1986 questionnaire, at least one post-diagnosis dietary assessment, and had complete data on at least one HRQOL subscale in 2010 or 2012. Men who received treatment within 1 year before the HRQOL assessment were excluded (n=74), leaving 2960 men eligible for analysis. This study was approved by the Institutional Review Board of the Harvard School of Public Health.

Measures

Assessment of Mediterranean Diet Score and dietary components—The FFQ assessed usual consumption of approximately 130 food items and supplements over the previous year. A commonly used portion size was specified, and participants indicated frequency of consumption, from never or less than one serving per month to six or more

servings per day. In a validation study, the mean Pearson correlation coefficient for all foods comparing the FFQ and diet records was 0.63, and 73% of the food items had correlation coefficients ≥0.50.[33]

Based on intake of specific food items, we categorized the men by their Mediterranean Diet Score.[34] Participants received 1 point each for consuming less than the median dairy and meat intake calculated separately for each dietary questionnaire cycle; 1 point for alcohol intake between 10 and 50 g/d; and 1 point each for being above the median intake of vegetables, legumes, fruits and nuts, grains, fish, and the ratio of polyunsaturated to saturated lipids (total score range: 0–9). Monounsaturated fat, used in the traditional Mediterranean Diet Score,[34] was not used for the lipid ratio because the main dietary contributor of monounsaturated fat in our cohort from 1986 to 2002 was beef, although olive oil and nuts have replaced beef as the most common source of monounsaturated fat in more recent dietary questionnaire cycles. The Mediterranean Diet Score was evaluated continuously and categorically (0–3, 4–5, and 6–9 points indicating low, moderate, and high Mediterranean diet intake, respectively). We also examined each of the Diet Score components and individual fat subtypes continuously and categorically using quintiles.

Assessment of Health-Related Quality of Life (EPIC-26)—In 2010 and 2012, participants in the Health Professionals Follow-up Study who had been diagnosed with prostate cancer were asked to complete the EPIC-26[32] to assess the frequency and severity of symptoms influencing HRQOL within 5 domains: urinary incontinence; urinary irritation/obstruction; and bowel, sexual, and vitality/hormonal function. Multi-item scale scores were transformed linearly to a 0 to 100 scale with higher scores representing better HRQOL (e.g. *better* sexual function and *less* urinary incontinence or urinary irritation/obstruction). For this analysis, the first available post-diagnosis HRQOL assessment was used.

Data Analysis

Generalized linear models were used to examine relationships between the Mediterranean Diet Score, dietary components and dietary fats, and EPIC-26 subscales for urinary or sexual function. Initial models (Model 1) controlled for age at diagnosis (continuous, years), time since treatment (continuous, years), and energy (continuous, kilocalories/day). Time since diagnosis of prostate cancer was used for 48 men who indicated that they received treatment but were missing a treatment date. The median time from diagnosis and treatment to HRQOL assessment was 8.2 and 8.4 years, respectively. For multivariate analyses (Model 2), *a priori* covariates identified in the literature were forced into the multivariate model, including clinical stage (T1, T2, T3), grade (Gleason score <7, 7, >7), primary treatment type (radical prostatectomy, radiation, hormone therapy, active surveillance or watchful waiting, other), PSA at diagnosis (<4, 4 to <10, 10 to ≤20, >20 ng/ml), body mass index (BMI; continuous, kg/m^2), smoking status (never, former quit ≥10 years, former quit <10 years, current <40 pack-year history, current ≥40 pack-year history), and presence of comorbidities (yes/no) from participant report of myocardial infarction, stroke, emphysema/chronic obstructive pulmonary disease, Parkinson's disease, coronary artery bypass or coronary angioplasty, and diabetes between 1986 and 2010. Additional covariates were included in Model 2 if they met both *a priori* criteria of P <0.20 in Model 1 and their

addition to Model 1 changed the Mediterranean Diet Score beta-coefficient more than 10%. Variables included in Model 2 based on the above criteria were family history of prostate cancer (yes/no), walking pace (easy <2 mph, normal 2-2.9 mph, brisk 3-3.9 mph), vigorous physical activity (quintiles of MET-hrs/week), and weightlifting (tertiles of MET-hrs/week). The following variables were tested but did not meet criteria for inclusion in Model 2: non-vigorous physical activity, race/ethnicity, marital status, multivitamin use, vitamin E and selenium supplement use, vitamin D intake, and percentage of energy from carbohydrates or protein.

Next, we conducted a sensitivity analysis excluding men who reported taking medications to treat urinary symptoms or ED at the time of HRQOL assessment (n=64 and 385 excluded, respectively, Model 3). We also conducted a sensitivity analyses adjusting for coffee intake in addition to variables in Model 2 for urinary endpoints only (Model 4). Finally, we ran Model 2 excluding all men who received adjuvant treatment within 1-2 years of completing the HRQOL assessment (n=37), which is an expansion of the exclusion criteria where men who received adjuvant treatment within 1 year of HRQOL assessment were excluded (Model 5). In addition, we were interested in evaluating post-diagnosis diet adjusting for pre-diagnosis diet, however, pre- and post-diagnosis Mediterranean Diet Score and dietary components were highly correlated (Pearson correlation coefficients=0.4-0.6, except dairy r=0.2), therefore we adjusted for pre-diagnosis diet in addition to variables in Model 2 in a sensitivity analysis (Model 6).

To ensure a prospective analysis and limit the potential for reverse causation, we used data from dietary questionnaires preceding the HRQOL assessment. Specifically, for participants with HRQOL assessed in 2010, dietary exposure variables were cumulatively updated post-diagnosis until 2006. For participants with HRQOL assessed in 2012, dietary exposure variables were cumulatively updated post-diagnosis until 2010. All other covariates were simply updated using the most recent questionnaire.

Linear trends were examined using the median of each dietary intake category/quintile as a continuous variable. *A priori* interaction tests included age at diagnosis (<70, ≥70 years), time since treatment (<5, 5 to <10, ≥10 years), treatment type (limited to radical prostatectomy, radiation and hormone therapy), pre-diagnosis erectile dysfunction (yes/no; sexual functioning endpoint only), and pre-diagnosis BPH or severe LUTS (yes/no; urinary endpoints only). We hypothesized that an association between post-diagnostic diet and urinary or sexual dysfunction would be attenuated among older men, men who received recent treatment, and men with side effects of surgery or pre-existing symptoms prior to diagnosis. Interactions between dietary intake and potential effect modifiers were assessed by entering cross products of dietary intake with the potential modifiers of interest in multivariate models and reported if p-interaction <0.0001 due to the large number of interaction tests. Based on the observation of effect modification based on pre-diagnosis ED and BPH/LUTS, we report results for sexual and urinary function scores stratified by these conditions, respectively. All analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

Results

Compared to men in the lowest category of Mediterranean Diet Score, those with the highest scores had longer times from treatment to HRQOL questionnaire, lower BMI, lower caloric intake, were more likely to engage in weightlifting and vigorous physical activity, and were less likely to have ED prior to prostate cancer diagnosis (TABLE 1).

Urinary Incontinence

Higher post-diagnosis vegetable intake was associated with modestly higher urinary incontinence scores (*better* urinary function). Men in the highest quintile of vegetable intake had a mean urinary incontinence score of 76 out of 100 compared to 72 among men in the lowest quintile of vegetable intake (p-trend=0.003; TABLE 2). This association remained statistically significant in all sensitivity analyses, including adjustment for pre-diagnosis diet (data not shown). Similarly, men with higher post-diagnosis alcohol intake reported higher urinary incontinence scores (*better* urinary function) (71 versus 74 comparing lowest to highest quintile; p-trend=0.03), however this association disappeared after adjusting for pre-diagnosis alcohol intake (data not shown). Conversely, men in the highest quintile of monounsaturated and polyunsaturated fat intake after prostate cancer diagnosis reported lower urinary incontinence scores (*worse* urinary function) compared to men in the lowest quintile of intake (monounsaturated fat: 75 versus 71 comparing lowest to highest quintile; p-trend=0.02; polyunsaturated fat: 76 versus 72 comparing lowest to highest quintile; p-trend=0.04). However, these associations were attenuated in sensitivity analyses and were absent after adjusting for pre-diagnosis intake (data not shown). Mediterranean Diet Score and other individual score components or dietary fat subtypes were not associated with urinary incontinence scores. In summary, higher vegetable intake after prostate cancer diagnosis was associated with lower rates of self-reported urinary incontinence.

Urinary irritation/obstruction among men with history of BPH/LUTS

Higher vegetable intake was also associated with higher urinary irritation/obstruction scores (*better* urinary function) among the subset of men with BPH/LUTS prior to their prostate cancer diagnosis (80 versus 84 comparing lowest to highest quintile; p-trend=0.01; p-interaction<0.0001; TABLE 3), but not among men without urinary symptoms prior to diagnosis. Conversely, lower post-diagnostic polyunsaturated fat intake was associated with higher urinary irritation/obstruction scores (*better* urinary function) (84 versus 78 comparing lowest to highest quintile; p-trend=0.005). These associations remained statistically significant in all sensitivity analyses. Fruit intake was associated with higher urinary irritation/obstruction scores among men with BPH/LUTS prior to prostate cancer diagnosis, however this association was not robust in sensitivity analyses (data not shown). In summary, higher vegetable intake and lower polyunsaturated fat intake after prostate cancer diagnosis was associated with lower rates of self-reported urinary irritation/obstruction symptoms among men with a previous history of BPH/LUTS.

Urinary irritation/obstruction among men without history of BPH/LUTS

Among the subset of men without BPH/LUTS prior to their prostate cancer diagnosis, higher post-diagnosis fish intake was associated with marginally higher urinary irritation/

obstruction scores (*better* urinary function) (71 versus 74 comparing lowest to highest quintile; *p*-trend=0.05; TABLE 3). This association remained statistically significant in pre-specified sensitivity analyses, including adjustment for pre-diagnosis fish intake, although was attenuated after excluding men who reported taking medications to treat urinary symptoms at the time of HRQOL assessment (*p*-trend=0.07; data not shown). Mediterranean Diet Score and other individual score components or dietary fat subtypes were not associated with urinary irritation/obstruction scores. In summary, diet after prostate cancer diagnosis was not significantly associated with self-reported urinary irritation/obstruction among men without a previous history of BPH/LUTS.

Sexual Function

Post-diagnostic Mediterranean Diet Score, score components and dietary fat subtypes were not associated with sexual function scores. However, we did observe evidence of effect modification of these relationships by the presence of ED prior to prostate cancer diagnosis (*p*-interaction<0.0001). Among men without ED prior to diagnosis of prostate cancer, those in the highest quintile of post-diagnosis monounsaturated fat intake reported higher sexual functioning scores (*better* sexual function) compared to men in the lowest quintile (34 versus 36 comparing lowest to highest quintile; *p*-trend=0.03; TABLE 4). This association was robust in most pre-specified sensitivity analyses, including adjustment for pre-diagnosis intake, although it was attenuated after further adjustment for carbohydrate intake (*p*-trend=0.09; data not shown). Higher post-diagnostic polyunsaturated fat intake was borderline associated with higher sexual functioning scores, however, this association was no longer statistically significant in sensitivity analyses. Among men who reported symptoms of ED prior to their prostate cancer diagnosis, post-diagnostic diet was not associated with sexual functioning. In summary, diet after prostate cancer diagnosis was not significantly associated with self-reported sexual function.

Discussion

In this prospective cohort study of men with non-metastatic prostate cancer, post-diagnostic Mediterranean Diet Score was not associated with urinary or sexual function. However, a modest association was observed between post-diagnostic vegetable intake and higher urinary incontinence scores (*better* urinary function). Higher post-diagnosis vegetable intake and lower polyunsaturated fat intake were also associated with modestly higher urinary irritation/obstruction scores (*better* urinary function), but these associations were limited to men with a history of BPH/LUTS prior to prostate cancer diagnosis.

This is the first study to evaluate the association between post-diagnostic dietary intake and LUTS among men with prostate cancer. In our analysis, we observed a positive association between higher post-diagnostic vegetable intake and modestly higher urinary incontinence and urinary irritation/obstruction scores (*better* urinary function) by an average of 4 points. According to prior studies, a weighted mean difference of at least half the minimally detectable difference (urinary incontinence score: 6-9 points; urinary irritation/obstruction score: 5-7 points) suggests that an appreciable number of patients would have a detectable benefit from this dietary change.[35,36] The prior literature examining the relationship between

vegetable intake and LUTS remains inconclusive because associations first noted in early case control studies have been observed in some but not all subsequent prospective cohort studies. Among elderly Chinese men in the MrOS Hong Kong prospective cohort study, higher vegetable intake, particularly dark and leafy vegetables, was associated with greater improvement and less progression of LUTS.[20] However, among men without a history of cancer in the Health Professionals Follow-up Study, vegetable protein and vegetable fat intake were not associated with BPH surgery, high-moderate to severe LUTS, or an enlarged prostate detected by digital rectal examination, although total vegetable intake was not studied.[29] Furthermore, a biological mechanism of the association between vegetable intake and decreased LUTS has not been elucidated although some have suggested that vegetable intake may protect against oxidative damage to the bladder or prostate or influence circulating hormones which affect prostate epithelium growth in the transitional zone.[37]

Conversely, lower polyunsaturated fat intake after prostate cancer diagnosis was associated with higher urinary irritation/obstruction scores by an average of 4 to 6 points. Polyunsaturated fat intake among men in our study was predominantly from olive oil, nuts, and mayonnaise. A previous study reported that polyunsaturated fat intake, including both omega-3 and omega-6 fatty acids, was positively associated with BPH/LUTS among adult men without a history of cancer in the Health Professionals Follow-up Study.[29] Similarly, polyunsaturated fat was positively associated with LUTS in a cross-sectional analysis of men enrolled in the Boston Area Community Health Survey.[31] One hypothesized mechanism of the association between polyunsaturated fat and BPH/LUTS is via lipid peroxidation, such that a high degree of unsaturation of fatty acids leads to higher 5α-reductase and dihydrotestosterone levels and subsequent epithelial and stromal growth in the prostate.[29] We also observed effect modification of the relationship between diet and urinary irritation/obstruction scores, but not urinary incontinence scores, by the presence of BPH or LUTS prior to prostate cancer diagnosis. This finding could represent the differing effects of dietary intake on LUTS due to pre-existing conditions compared to incident LUTS due to prostate cancer or prostate cancer treatment; however, this has not been reported previously and must be confirmed.

Diet after prostate cancer diagnosis does not appear to be associated with sexual function. The Mediterranean diet pattern is associated with small decreases in ED in small, randomized controlled trials among men with diabetes mellitus and metabolic syndrome.[17,21] However, the observed change in sexual function scores in these clinical trials are well below the minimally detectable difference for the EPIC-26 sexual function score (10-12 points) and therefore do not represent clinically meaning changes in sexual function.[35] As suggested by the lower sexual function scores in this study compared to men with prostate cancer on active surveillance in other study populations,[38,39] the effect of Mediterranean diet on sexual functioning may also be diluted among men with prostate cancer and post-surgical or cancer-related sexual dysfunction, which might be less amenable to treatment with dietary changes. One proposed biological mechanism of the previously observed association between Mediterranean dietary pattern and better sexual function is via improved endothelial function, as demonstrated in small experimental studies.[40-42]

We acknowledge that this study has limitations. First, the prospective data used in this analysis are observational therefore residual or unmeasured confounding is possible. We attempted to minimize residual confounding by conducting a thorough literature review and using stepwise regression to build multivariate models with potential confounders forced into the model. Furthermore, we used repeated measurements of dietary intake after prostate cancer diagnosis to more accurately categorize intake and reduce measurement error. Second, we conducted numerous statistical tests and therefore false positive results due to multiple comparisons are possible and confirmatory studies are needed.

Conclusions

Diet intake after prostate cancer diagnosis is not significantly associated with HRQOL. Higher vegetable intake after prostate cancer diagnosis is associated with modestly fewer urinary incontinence symptoms. Higher post-diagnostic vegetable intake and lower post-diagnostic polyunsaturated fat intake may be associated with fewer urinary irritation/obstruction symptoms, however, these associations were only observed among men with a history of BPH/LUTS before their prostate cancer diagnosis. There are limited data examining the association between diet and urinary or sexual function, particularly among men with prostate cancer, therefore many of these analyses were exploratory. Additional research is needed to determine if diet can improve urinary and sexual function in men with localized prostate cancer.

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TABLE 1

Sociodemographic and clinical characteristics of 2960 men with prostate cancer in the Health Professionals Follow-up Study, by category of post-diagnostic Mediterranean Diet Score*

	Post-diagnostic Mediterranean Diet Score**		
	0-3 (n=1039)	**4 to 5 (n=1015)**	**6 to 9 (n=906)**
Age at Diagnosis, mean (SD)	68 (7)	68 (7)	68 (7)
Years From Treatment to QOL Questionnaire, median (IQR)	7.8 (5-12)	8.3 (5-12)	8.9 (5-13)
White Race, %	94	93	91
Family History of Prostate Cancer, %	24	20	22
Clinical Stage of Disease, %			
T1	65	67	67
T2	34	32	31
T3/T4	2	1	3
Gleason Score, %			
≤6	63	66	62
7	26	24	27
>7	7	6	7
Missing	4	4	5
PSA at diagnosis, %			
<4	13	15	16
4 to <10	63	64	62
10 to <20	17	14	16
≥20	5	4	5
Missing	2	2	2
Primary Treatment, %			
Radical Prostatectomy	54	54	53
Radiation Therapy	35	35	37
Hormonal Therapy	3	3	2
Active Surveillance/None	7	8	7
Other	1	1	1
Body Mass Index, mean (SD)	26.5 (4)	26.0 (4)	25.1 (3)
Presence of Comorbidities, %* **	38	34	37
Smoking Status, %			
Never	52	53	54
Former, quit ≥10 years	40	42	43
Former, quit <10 years	5	3	2
Current, <40 pack-year history	1	1	0
Current, ≥40 pack-year history	2	1	1
Missing	0	0	0

	Post-diagnostic Mediterranean Diet Score**		
	0-3 (n=1039)	4 to 5 (n=1015)	6 to 9 (n=906)
Walking Pace, %			
Easy (<2 mph)	8	8	7
Normal (2-2.9 mph)	21	18	14
Brisk (≥3 mph)	67	70	71
Missing	4	4	8
Any Weightlifting, % ****	28	34	45
Vigorous Physical Activity, MET h/wk, median (IQR) ****	0 (0-9)	0.8 (0-14)	3.9 (0-18)
Calories per day, mean (SD)	2039 (562)	1998 (558)	1958 (538)
Pre-diagnostic Mediterranean Diet Score, %			
0-3	60	29	10
4-5	31	46	31
6-9	10	26	58
ED prior to prostate cancer diagnosis, %	32	27	26
LUTS prior to prostate cancer diagnosis, %	21	23	20
Taking ED medication in 2010-2012, %	13	10	13
Taking LUTS medication in 2010-2012, %	2	2	3

SD=Standard Deviation; IQR=Interquartile Range; PSA=Prostate Specific Antigen; MET= metabolic equivalent task; LUTS=lower urinary tract symptoms; ED=erectile dysfunction

* All descriptive characteristics are age-standardized values except medians, which are reported for variables with skewed distributions.

** For the Mediterranean Diet Score, each participant received 1 point each for being below the median in dairy and meat intake; 1 point for alcohol intake between 10 and 50 g/d; and 1 point each for being above the median intake of vegetables, legumes, fruits and nuts, grains, fish, and the ratio of polyunsaturated to saturated lipids (total score range: 0–9).

*** Presence of comorbidities considered yes if participant reported any of the following between 1986 and 2008: myocardial infarction, stroke, emphysema/chronic obstructive pulmonary disease, Parkinson's disease, coronary artery bypass or coronary angioplasty, and diabetes.

**** For physical activity, MET-hours per week was calculated by multiplying the MET value by the number of hours per week engaged in that activity. Vigorous activities were those with a MET value of ≥6. Weightlifting considered yes if participant recorded any amount of weightlifting per week.

TABLE 2

Geometric mean urinary incontinence score by post-diagnostic Mediterranean Diet Score and dietary components among 2960 men with prostate cancer*

Mediterranean Diet Score	**0-3**		**4-5**	**6-9**		***p trend***
	72 (2)		74 (3)	73 (3)		*0.69*
	Dietary components, by quintile					
Dietary components	**1**	**2**	**3**	**4**	**5**	***p trend***
Legume	73 (3)	74 (3)	72 (3)	72 (3)	73 (3)	*0.45*
Fruit	72 (3)	74 (3)	71 (3)	73 (3)	73 (3)	*0.40*
Total Dairy	73 (3)	73 (3)	74 (3)	71 (3)	72 (3)	*0.09*
Fish	74 (3)	73 (3)	71 (3)	73 (3)	73 (3)	*0.92*
Vegetable	72 (3)	70 (3)	73 (3)	72 (3)	76 (3)	*0.003*
Cereal	72 (3)	73 (3)	74 (3)	73 (3)	72 (3)	*0.91*
Total Meat	75 (3)	72 (3)	73 (3)	72 (3)	72 (3)	*0.25*
Alcohol	71 (3)	71 (3)	73 (3)	74 (3)	74 (3)	*0.03*
Poly:Saturated Fat	73 (3)	73 (3)	72 (3)	71 (3)	73 (3)	*0.93*
Saturated Fat	75 (3)	72 (3)	73 (3)	72 (3)	72 (3)	*0.07*
Monounsaturated Fat	75 (3)	73 (3)	73 (3)	72 (3)	71 (3)	*0.02*
Polyunsaturated Fat	76 (3)	73 (3)	73 (3)	72 (3)	72 (3)	*0.04*

*Urinary incontinence scores relate to symptoms of dripping or leaking urine and higher scores indicate fewer urinary problems. All values represent geometric mean scores adjusted for age at diagnosis, time since treatment or diagnosis, calories, clinical stage of disease, Gleason score, treatment type, PSA at diagnosis, family history of prostate cancer, and the following covariates were measured at the time of QOL outcome assessment: presence of comorbidities, body mass index, smoking status, walking pace, vigorous physical activity, and any weightlifting (Model 2). *P* trend was calculated using the median of each quartile modeled continuously.

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TABLE 3

Geometric mean urinary irritation/obstruction score by post-diagnostic Mediterranean Diet Score and dietary components among 2960 men with prostate cancer, stratified by BPH/LUTS prior to prostate cancer diagnosis *

Men *without* BPH/LUTS prior to prostate cancer diagnosis (n=2334)						
Mediterranean Diet Score	**0-3**		**4-5**		**6-9**	***p trend***
	85 (1)		86 (1)		85 (1)	*0.80*
	Dietary components, by quintile					
Dietary components	**1**	**2**	**3**	**4**	**5**	***p trend***
Legume	86 (1)	85 (1)	85 (1)	85 (1)	86 (1)	*0.81*
Fruit	86 (1)	86 (1)	85 (1)	85 (1)	86 (1)	*0.62*
Total Dairy	85 (1)	86 (1)	86 (1)	85 (1)	86 (1)	*0.33*
Fish	85 (1)	86 (1)	86 (1)	85 (1)	87 (1)	*0.05*
Vegetable	86 (1)	85 (1)	85 (1)	85 (1)	87 (1)	*0.15*
Cereal	85 (1)	85 (1)	86 (1)	86 (1)	85 (1)	*0.70*
Total Meat	86 (1)	86 (1)	85 (1)	85 (1)	86 (1)	*0.89*
Alcohol	85 (1)	85 (1)	85 (1)	86 (1)	85 (1)	*0.76*
Poly:Saturated Fat	87 (1)	85 (1)	85 (1)	85 (1)	86 (1)	*0.53*
Saturated Fat	86 (1)	85 (1)	86 (1)	85 (1)	85 (1)	*0.54*
Monounsaturated Fat	86 (1)	85 (1)	85 (1)	86 (1)	85 (1)	*0.37*
Polyunsaturated Fat	86 (1)	86 (1)	86 (1)	85 (1)	85 (1)	*0.17*
Men *with* BPH/LUTS prior to prostate cancer diagnosis (n=626)						
Mediterranean Diet Score	**0-3**		**4-5**		**6-9**	***p trend***
	82 (3)		81 (3)		84 (3)	*0.43*
	Dietary components, by quintile					
Dietary components	**1**	**2**	**3**	**4**	**5**	***p trend***
Legume	79 (4)	83 (4)	83 (4)	82 (4)	83 (4)	*0.30*
Fruit	79 (4)	82 (4)	80 (4)	82 (4)	84 (4)	*0.04*
Total Dairy	81 (4)	82 (4)	79 (4)	85 (4)	82 (4)	*0.76*
Fish	80 (4)	82 (4)	82 (4)	83 (4)	81 (4)	*0.64*
Vegetable	80 (4)	82 (4)	83 (4)	84 (4)	84 (4)	*0.01*

Men *without* BPH/LUTS prior to prostate cancer diagnosis (n=2334)						
Mediterranean Diet Score	**0-3**		**4-5**		**6-9**	***p trend***
Cereal	84 (4)	80 (4)	80 (4)	83 (4)	84 (4)	*0.19*
Total Meat	82 (4)	82 (4)	82 (4)	82 (4)	84 (4)	*0.32*
Alcohol	81 (4)	81 (4)	83 (4)	82 (4)	83 (4)	*0.46*
Poly:Saturated Fat	83 (3)	80 (4)	82 (4)	81 (4)	82 (4)	*0.43*
Saturated Fat	83 (4)	83 (4)	81 (4)	81 (4)	81 (4)	*0.15*
Monounsaturated Fat	85 (4)	80 (4)	81 (4)	80 (4)	80 (4)	*0.36*
Polyunsaturated Fat	84 (4)	82 (4)	82 (4)	79 (4)	78 (4)	*0.005*

*Urinary obstruction/irritation scores relate to symptoms of dysuria, nocturia, or urinary retention and higher scores indicate fewer urinary problems. All values represent geometric mean scores adjusted for age at diagnosis, time since treatment or diagnosis, calories, clinical stage of disease, Gleason score, treatment type, PSA at diagnosis, family history of prostate cancer, and the following covariates were measured at the time of QOL outcome assessment: presence of comorbidities, body mass index, smoking status, walking pace, vigorous physical activity, and any weightlifting (Model 2). Results are stratified by pre-diagnosis benign prostatic hyperplasia or severe lower urinary tract symptoms. *P* trend was calculated using the median of each quartile modeled continuously and reported by strata.

TABLE 4

Geometric mean sexual functioning score by post-diagnostic Mediterranean Diet Score and dietary components among 2960 men with prostate cancer, stratified by erectile dysfunction prior to prostate cancer diagnosis*

Men *without* ED prior to prostate cancer diagnosis (n=2126)						
Mediterranean Diet Score	**0-3**		**4-5**		**6-9**	***p trend***
	35 (4)		35 (4)		35 (4)	*0.71*
	Dietary components, by quintile					
Dietary components	**1**	**2**	**3**	**4**	**5**	***p trend***
Legume	36 (4)	35 (4)	32 (4)	36 (4)	36 (4)	*0.81*
Fruit	35 (4)	35 (4)	37 (4)	34 (4)	34 (4)	*0.51*
Total Dairy	37 (4)	33 (4)	34 (4)	34 (4)	37 (4)	*0.78*
Fish	35 (4)	35 (4)	34 (4)	34 (4)	37 (4)	*0.15*
Vegetable	35 (4)	32 (4)	35 (4)	35 (4)	37 (4)	*0.17*
Cereal	36 (4)	36 (4)	33 (4)	33 (4)	36 (4)	*0.70*
Total Meat	36 (4)	34 (4)	32 (4)	37 (4)	35 (4)	*0.82*
Alcohol	35 (4)	36 (4)	35 (4)	34 (4)	35 (4)	*0.69*
Poly:Saturated Fat	36 (4)	35 (4)	32 (4)	35 (4)	37 (4)	*0.25*
Saturated Fat	36 (4)	33 (4)	34 (4)	35 (4)	36 (4)	*0.52*
Monounsaturated Fat	34 (4)	32 (4)	36 (4)	36 (4)	36 (4)	*0.03*
Polyunsaturated Fat	35 (4)	35 (4)	33 (4)	34 (4)	38 (4)	*0.05*
Men *with* ED prior to prostate cancer diagnosis (n=834)						
Mediterranean Diet Score	**0-3**		**4-5**		**6-9**	***p trend***
	22 (4)		23 (5)		25 (5)	*0.11*
	Dietary components, by quintile					
Dietary components	**1**	**2**	**3**	**4**	**5**	***p trend***
Legume	21 (5)	24 (5)	23 (5)	25 (5)	23 (5)	*0.26*
Fruit	22 (5)	22 (5)	23 (5)	24 (5)	22 (5)	*0.85*
Total Dairy	22 (5)	20 (5)	25 (5)	21 (5)	22 (5)	*0.68*
Fish	20 (5)	24 (5)	24 (5)	20 (5)	23 (5)	*0.77*
Vegetable	20 (5)	20 (5)	26 (5)	27 (5)	22 (5)	*0.10*

Men *without* ED prior to prostate cancer diagnosis (n=2126)						
Mediterranean Diet Score	**0-3**		**4-5**		**6-9**	***p trend***
Cereal	21 (5)	21 (5)	25 (5)	20 (5)	24 (5)	*0.26*
Total Meat	24 (5)	20 (5)	25 (5)	24 (5)	21 (5)	*0.71*
Alcohol	23 (5)	20 (5)	23 (5)	24 (5)	24 (5)	*0.30*
Poly:Saturated Fat	22 (5)	23 (5)	21 (5)	23 (5)	24 (5)	*0.45*
Saturated Fat	20 (5)	23 (5)	19 (5)	24 (5)	21 (5)	*0.92*
Monounsaturated Fat	20 (5)	24 (5)	20 (5)	23 (5)	24 (5)	*0.36*
Polyunsaturated Fat	23 (5)	22 (5)	21 (5)	22 (5)	25 (5)	*0.30*

*Sexual functioning scores relate to symptoms of erectile dysfunction or anorgasmia, and higher scores indicate fewer sexual problems. All values represent geometric mean scores adjusted for age at diagnosis, time since treatment or diagnosis, calories, clinical stage of disease, Gleason score, treatment type, PSA at diagnosis, family history of prostate cancer, and the following covariates were measured at the time of QOL outcome assessment: presence of comorbidities, body mass index, smoking status, walking pace, vigorous physical activity, and any weightlifting (Model 2). Results are stratified by pre-diagnosis erectile dysfunction. *P* trend was calculated using the median of each quartile modeled continuously and reported by strata.