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Title

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Permalink

Journal

ISSN

Authors

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et al.

Publication Date

DOI

Peer reviewed

Milk and other dairy foods in relation to prostate cancer recurrence: data from the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE™)

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Abstract

Background—High-fat dairy, particularly whole milk, in healthy men may increase risk of aggressive prostate cancer. However, data are limited regarding dairy after prostate cancer diagnosis.

Method—We conducted a prospective study among 1,334 men with non-metastatic prostate cancer in the Cancer of the Prostate Strategic Urologic Research Endeavor. Men answered a food frequency questionnaire in 2004–2005 (median 2 y after diagnosis) and were followed until 2016 for recurrence, defined as: prostate cancer death, bone metastases, biochemical recurrence, or secondary treatment. Multivariate Cox proportional hazards regression was used to calculate hazards ratios (HR) and 95% confidence intervals (CI) for associations between whole and low-fat milk; total, high-fat, and low-fat dairy; and other dairy items and risk of recurrence.

Results—During a median follow-up of 8 y, we observed 137 events. Men who consumed >4 servings/week vs. 0–3 servings/month of whole milk had an 73% increased risk of recurrence (HR: 1.73; 95% CI: 1.00, 2.98; *p*-value: 0.04). Body mass index (BMI) modified the association (*p*-interaction=0.01). Among men with a BMI $\geq$ 27kg/m^2, >4 servings/week vs. 0–3 servings/month of whole milk was associated with a 3-fold higher risk of recurrence (HR: 2.96; 95% CI: 1.58, 5.54; *p*-value=<0.001). No association was seen in men with BMI<27kg/m^2. Low-fat milk and other dairy foods were not associated with recurrence.

Conclusion—In conclusion, whole milk consumption after prostate cancer diagnosis was associated with increased risk of recurrence, particularly among very overweight or obese men. Men with prostate cancer who choose to drink milk should select non-fat or low-fat options.

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The authors declare no potential conflicts of interest

Keywords

whole milk; cancer survivorship; nutrition

INTRODUCTION

Prostate cancer is the most common non-skin malignancy and the third leading cause of cancer death among men in the United States.[1] In 2017, the American Cancer Society estimates that 161,360 men will be diagnosed with, and 26,730 will die, from prostate cancer.[1] An estimated 92% of these men are diagnosed with low-grade, localized prostate cancer,[2] and many seek dietary and lifestyle changes to prevent prostate cancer recurrence or progression.[3,4]

Dairy products have been examined in relation to prostate cancer for several decades, and data generally suggest that dairy products are associated with an increased risk of being diagnosed with prostate cancer among healthy men,[5–14] though results have been inconsistent.[15–17] Less is known about dairy products' influence on prostate cancer after diagnosis.[18,19] We were the first to report that among the 3,918 men in the Health Professionals Follow-up Study (HPFS), those who consumed whole milk more than 4 times per week after prostate cancer diagnosis had a 2-fold increased risk of prostate cancer-specific mortality and a 51% increased risk of prostate cancer recurrence compared to men consuming whole milk <3 times per month.[18] Our group also reported that among the 926 men in the Physicians' Health Study, those who consumed ≥3 servings per day of dairy products after prostate cancer diagnosis had a 2.4-fold increased risk of prostate cancer-specific mortality compared to men having <1 serving per day.[19] Furthermore, a recent Swedish study by Downer *et al.* observed that in 230 men diagnosed with localized prostate cancer, men drinking ≥3 servings per day of high-fat milk had a 6.1-fold increased of prostate-cancer mortality compared to men consuming <1 serving per day.[20]

In this paper, we aimed prospectively examine post-diagnostic intake of dairy foods in relation to risk of prostate cancer recurrence among 1,334 men with non-metastatic prostate cancer who were enrolled in the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE™). CaPSURE is a population-based registry of men with prostate cancer in the United States. Based on the results from prior studies, we hypothesized that those men who consumed more whole milk after diagnosis would have an increased risk of prostate cancer recurrence.

MATERIALS and METHODS

Patient Population

This study was conducted among men enrolled in CaPSURE, an active registry initiated in 1995 that includes over 15,000 men with varying stages of biopsy-proven prostate adenocarcinoma diagnosed at 43 different community practices, academic centers, and VA hospital sites in the United States. In 2004–2006, active participants in CaPSURE were invited via postal mail to participate in the Diet and Lifestyle sub-study; 2,134 men

completed the survey (87% of those invited). The median time from diagnosis to completing the survey was 2 years.

To be eligible for this analysis, men had to have been diagnosed with non-metastatic prostate cancer and completed the lifestyle survey prior to cancer recurrence (n=1,412). We excluded men who reported implausible energy intakes (<800 or >4200 kcal/d; n=78), leaving 1,334 men eligible for analysis.

Diet Assessment

Participants completed a validated semi-quantitative food frequency questionnaire (FFQ) that contained detailed questions about servings and frequency of specific dairy foods; fruits; vegetables; eggs and meat; breads, cereals and starches; beverages; sweet baked goods; and oils and fats as well as history, dosage, and frequency of vitamins, minerals, and supplements.[21–24]

To ascertain usual post-diagnostic dairy intake, men were asked to report how often, on average over the past year, they consumed the following dairy foods: skim or low fat milk (8 ounce glass or with cereal), whole milk (8 ounce glass or with cereal), cream (tablespoon), sour cream (tablespoon), non-dairy coffee whitener (teaspoon), sherbert or ice milk (1/2 cup), ice cream (1/2 cup), yogurt (1 cup), cottage or ricotta cheese (1/2 cup), cream cheese (1 ounce), other cheese (1 slice or 1 ounce), margarine added to food or bread, and butter added to food or bread. There were nine frequency categories ranging from never or less than once per month to 6 times per day. Men were also asked whether they consumed more, less, or the same amount of each dairy food compared to before diagnosis. Though many men did not respond (32.4%), the vast majority of those that responded reported no change (88.8%), preventing us from examining the association between change in whole milk intake and risk of prostate cancer recurrence.

Outcome Assessment and Clinical Follow-up

Information collected in the CaPSURE registry through medical record review and urologists' reports includes biopsy results and TNM staging, surgical pathology, PSA values, hospital admissions and procedures.

The primary outcome for this analysis was prostate cancer recurrence, including the following events: biochemical recurrence, initiation of secondary treatment, development of bone metastases, or death due to prostate cancer. Biochemical recurrence was defined as two consecutive PSA values 0.2 ng/mL or greater eight or more weeks after radical prostatectomy or three consecutive increases in PSA above nadir after radiation therapy. Secondary treatment was defined as treatment initiated six or more months after the patient's primary treatment ended. A patient was determined to have bone metastases if his physician reported: 1) distant prostate cancer progression to bone, 2) a positive bone scan, 3) radiation for metastasis at a bone site, or 4) M1b stage in TNM staging. Death data were obtained through the National Death Index and Bureau of Vital Statistics, and confirmed through review of medical records and death certificates. The date of prostate cancer recurrence was the first of the following: midpoint between post-radiation nadir and first PSA increase for

radiation patients, date of second PSA increase for radical prostatectomy patients, date of secondary treatment, bone metastases due to prostate cancer, or prostate cancer death.

Intake of whole milk may also increase risk of death due to cardiovascular disease, due to its saturated fat content,[25,26] though this has been recently challenged.[27,28] Given this possibility, we considered a secondary composite outcome that included deaths due to other causes in addition to events of prostate cancer-specific recurrence.

Statistical Analysis

Follow-up for this analysis was accrued from time of FFQ until prostate cancer recurrence, death due to other causes, or last contact date as of April 2016, whichever came first.

We categorized men according to their post-diagnostic intake of dairy foods based on the distribution in the population and consistency with prior publications. For whole milk consumption, we used the categories reported by Pettersson *et al.*: 0–3 servings/month, >3 servings/month to 4 servings/week, and >4 servings/week.[18] Other dairy foods were categorized based on intake and distribution of this population as follows: total dairy, high-fat dairy, and low-fat dairy (<1 serving/day, 1 to <2 servings/day, 2 to <4 servings/day,   4 servings/day); ice cream, yogurt, other cheese (excluding cottage cheese and cream cheese), and butter (<1 serving/week, 1 to <5–6 servings/week, and   5–6 servings/week); and cream, sherbert, cottage cheese, and cream cheese (<1 serving/week and   1 serving/week).

Multivariate Cox Proportional Hazards regression models were utilized to calculate hazards ratios (HRs) and 95% confidence intervals (CI) to estimate the associations between the dairy foods and prostate cancer recurrence. A simple model was adjusted for age at diagnosis (years), daily calories (log kcal/d), and years from diagnosis to FFQ. Multivariate models were adjusted for the variables in the simple model as well as pre-treatment CAPRA score (high, intermediate, low).[29] smoking status (current, past, never); body mass index (BMI, kg/m^2); walking pace (<3 miles/hour,   3 miles/hour); and primary treatment (radical prostatectomy, radiation therapy, hormonal therapy, other). We also considered adjustment for education and other dietary factors, including eggs, poultry with skin, and cruciferous vegetables,[30,31] but the effect estimates were unchanged so these variables were omitted from the final model.

One potential biological mechanism underlying an association between our primary exposure of interest, whole milk, and risk of prostate cancer recurrence is saturated fat.[32] Accordingly, we did a secondary analysis adjusting our multivariate model for total saturated fat intake. We examined whether the point estimate for whole milk was attenuated in this model, suggesting that saturated fat may be part of the biologic pathway between whole milk and recurrence.

In addition, we examined whether age at diagnosis, time from diagnosis to FFQ, BMI, walking pace, pre-treatment CAPRA score, or primary treatment modified the association between whole milk intake and risk of prostate cancer recurrence. To do so, we dichotomized each of the potential effect modifiers (at the median for continuous variables) and included a cross-product term between whole milk and the effect modifier of interest in

our multivariate model. We then used a Wald test to assess whether there was evidence of effect modification. For treatment, we categorized men as treated by radical prostatectomy (yes/no). We also examined the association between whole milk and risk of prostate cancer recurrence among the 875 men (65%) treated via radical prostatectomy. These interactions should be interpreted with caution, however, as statistically significant findings could be due to chance.

All statistical analyses were done using SAS v.9.4 for Windows (SAS Institute, Inc, Cary, NC, USA). Two-sided p-values <0.05 were considered statistically significant.

RESULTS

We observed 137 events of prostate cancer recurrence among 1,334 men diagnosed with non-metastatic prostate cancer over 9,630 person-years of follow up. These events included 56 secondary treatments, 68 biochemical recurrences, 3 prostate cancer bone metastases, and 10 prostate cancer-specific deaths. The median [25th–75th percentile] time from diagnosis to FFQ completion was 2.2 [1.2–3.7] years and median follow-up after FFQ completion was 8.0 [4.0–10.0] years.

Table 1 depicts the characteristics of 1,334 men with prostate cancer by category of whole milk intake. Less than 10% of men reported >4 servings/week of whole milk (110; 8%). The median age [25th–75th percentile] of men who reported >4 servings/week of whole milk was 66 [60–71], similar to men reporting >3 servings/month to 4 servings/week (66 [61–72]), and slightly older than men who consumed 0–3 servings/month who had a median age of 65 [59–70]. They had a higher calorie intake (2156 [1822–2670]) compared to both the >3 servings/month to 4 servings/week group (1993 [1563–2561]) and the 0–3 servings/month group (1912 [1516–2319]). However, BMI did not differ across categories of whole milk intake. Additionally, men who drank the most whole milk were more likely to be current smokers and have high prognostic risk disease at diagnosis.

Table 2 shows the HR and 95% CI for whole and skim/low fat milk as well as total dairy, high-fat dairy, and low-fat dairy and risk of prostate cancer recurrence. Men consuming >4 servings/week of whole milk had an 73% increased risk of recurrence [HR: 1.73; 95% CI: 1.00, 2.98; p-trend=0.04] compared to men consuming 3 servings/month (Table 2). When we added saturated fat to the multivariate model, our results were attenuated (>4 servings/week vs. 3 servings/month of whole milk [HR: 1.66; 95% CI: 0.96, 2.87], suggesting that the saturated fat content of whole milk contributes to the positive association observed. There was a suggestive association between high-fat dairy intake and risk of prostate cancer recurrence [HR: 1.56; 95% CI: 0.86, 2.85; p-trend=0.08], perhaps driven by whole milk, but the association was not statistically significant. There was no association between skim/low fat milk, low fat dairy, or total dairy consumption and risk of prostate cancer recurrence. No other dairy items including: ice cream, yogurt, other cheese (excluding cottage and cream cheeses), butter, cream, sherbert, cottage cheese, and cream cheese were associated with risk of prostate cancer recurrence (Supplemental Table).

The association between post-diagnostic whole milk consumption and risk of prostate cancer recurrence was modified only by BMI (p-interaction=0.01) among the variables examined. Table 3 shows the relation between whole milk intake and risk of prostate cancer recurrence stratified by BMI (<27 kg/m^2 and ≥27 kg/m^2). Among 651 men with BMI ≥27 kg/m^2 (80 events of recurrence), men consuming >4 servings/week of whole milk after diagnosis had a 3-fold greater risk of prostate cancer recurrence [HR: 2.96; 95% CI: 1.58, 5.54; p-trend=<0.001] when compared to men consuming ≤3 servings/month. In contrast, among the 677 men with BMI <27 kg/m^2 (56 events of recurrence), consuming >4 servings/week of whole milk was not associated with prostate cancer recurrence [HR: 0.52; 95% CI: 0.15, 1.76; p-trend=0.30]. This interaction should be interpreted with caution, given that the number of events among men with higher whole milk intake was limited and the findings could be due to chance.

DISCUSSION

Consistent with Pettersson *et al.*'s findings, our results suggest that whole milk consumption after prostate cancer diagnosis is associated with an increased risk of prostate cancer recurrence.[18] In addition, we observed an interaction between whole milk consumption and BMI. In our study, the association between whole milk and increased risk of prostate cancer recurrence was only observed among men at the upper range of overweight and obese men (BMI ≥27kg/m^2).

Potential mechanisms for the potential effect of dairy on risk of prostate cancer include: high calcium intake decreasing vitamin D levels[14,33–35] and increasing IGF-1 levels,[36,37] fluctuating phosphorus levels modifying vitamin D3 concentrations,[38] and elevated saturated fat intake[32,39] modulating the immune response and inflammation.[40] Our team previously reported that saturated fat intake was associated with an increased risk of prostate cancer-specific mortality among men with prostate cancer in the Physicians Health Study [HR: 2.78; 95% CI: 1.01, 7.64, p-trend=0.05].[32] Indeed, when we adjusted our multivariate model for saturated fat intake, the positive association between whole milk and risk of prostate cancer recurrence was attenuated. This supports the proposed hypothesis that the saturated fat content of whole milk in part contributes to the adverse association observed.

Only three prior studies have examined post-diagnostic dairy intake and clinical outcomes in men with non-metastatic prostate cancer. Pettersson *et al.* reported that men who had the greatest whole milk intake (>4 servings/week) experienced an approximately 2-fold increased risk of lethal prostate cancer [HR: 2.15; 95% CI: 1.28, 3.60; p-trend<0.01] relative to men with the least intake (0–3 servings/month). Whole milk was also associated with a 51% increased risk of biochemical recurrence in this population [HR: 1.51; 95% CI: 1.03, 2.20; p-trend=0.03].[18] There was no association between total dairy consumption and risk of lethal prostate cancer, biochemical, or clinical recurrence. Yang *et al.* reported that post-diagnostic total dairy intake was associated with a 2.4-fold increased risk [HR: 2.41; 95% CI: 0.96, 6.02; p-trend=0.04] of prostate cancer-specific death for men who consumed dairy products ≥3 times/day compared to those consuming <1 serving of dairy per day. They also observed that high-fat dairy and low-fat dairy demonstrated a 30% and 16% increased risk, respectively, of lethal prostate cancer with each serving increase, though both were not

statistically significant [HR: 1.30; 95% CI: 0.97, 1.73; *p*-trend=0.08 and HR: 1.16; 95% CI: 0.88, 1.53; *p*-trend=0.28]. Furthermore, the difference between the risks was not statistically significant (*p*-difference=0.56).[19] Limited reported consumption of whole milk in the study population prevented the investigators from examining whole milk consumption and prostate cancer-related death. Recent findings from Downer *et al.* in a Swedish cohort found that men with localized prostate cancer who had the greatest high-fat milk intake (3 servings/day) had a 6.1-fold increased risk of prostate cancer-related mortality relative to men consuming <1 serving/day [HR: 6.10; 95% CI: 2.14, 17.37; *p*-trend=0.004].[20] When men with advanced prostate cancer were included, increased high-fat milk intake (4.5 servings/day) did not result in a significantly increased risk of prostate cancer-related mortality relative to men consuming <1 serving per day [HR: 1.20; 95% CI: 0.69, 2.09; *p*-value: 0.09].[20]

Our study reflects the results of Pettersson and Downer and takes the next step to identify a particularly susceptible subgroup. We observed a statistically significant interaction between whole milk consumption and BMI. Men with BMI 27kg/m^2 who consumed >4 servings/week of whole milk had an increased risk of prostate cancer recurrence compared to those who had <3 servings/month. This association was not observed among men with a BMI <27kg/m^2. It is not known what physiological mechanisms may underlie an interaction between whole milk and BMI, and it is possible that this statistically significant association was due to chance. Obesity is associated with high circulating levels of VEGF and FGF2, enhancing prostate cancer growth; increased angiogenesis; increased DNA damage; and decreased immune function.[41,42] Prior research has shown that saturated fat intake, such as that contained in whole milk, increases risk of obesity, particularly in genetically susceptible subgroups.[43] It is possible that overweight and obese men have greater increases in systemic inflammation and insulin resistance when consuming a high saturated fat diet compared to normal weight men, thereby promoting prostate cancer progression. Additional studies with biomarker data are needed however to elucidate the biologic mechanisms underlying a potential interaction between whole milk, body size, and prostate cancer recurrence.

Strengths of our study include comprehensive data on sociodemographic, lifestyle, and clinical factors, including data reported directly by urologists, and complete, long follow-up. Furthermore, the homogeneity of our cohort of low-risk men reduces the chance that participants change their dietary habits resulting from their diagnosis. There were limitations to also consider. First, we only had one diet assessment a median of 2 years after prostate cancer diagnosis. Thus unlike Pettersson's study,[18] we were not able to examine change in dietary habits pre/post diagnosis or changes over the post-diagnostic period. Second, the population that we studied was predominately Caucasian, potentially limiting the generalizability of our results. Third, a relatively low number of individuals (N=197) reported drinking whole milk regularly (>3/month).

CONCLUSION

In conclusion, whole milk consumption after prostate cancer diagnosis may be associated with an increased risk of prostate cancer recurrence, particularly for very overweight or obese men. Men diagnosed with non-metastatic prostate cancer who choose to drink milk should select non-fat or low-fat options.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Abbreviations used

BMI   Body mass index

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Novelty and Impact

In this prospective study of 1,334 men initially diagnosed with non-metastatic prostate cancer, we observed that men who consumed ≥4 servings/week of whole milk had an 73% increased risk of recurrence compared to men who consumed <3 servings/month. Further, among very overweight and obese men (body mass index ≥27kg/m^2), >4 servings/week vs. 0–3 servings/month of whole milk was associated with a 3-fold higher risk of recurrence.

TABLE I

Characteristics of 1,334 men with prostate cancer in the Diet and Lifestyle substudy of CaPSURE™ (Cancer of the Prostate Strategic Urologic Research Endeavor) by post-diagnostic intake of whole milk

	Servings of Whole Milk		
	0–3/month	**>3/month to 4/week**	**>4/week**
No. of participants	1137	87	110
Age at diagnosis, y, median (IQR)	65 (59–70)	66 (61–72)	66 (60–71)
BMI, kg/m², median (IQR)	27 (25–30)	27 (25–29)	27 (25–29)
Calorie intake, kcal/day, median (IQR)	1912 (1516–2319)	1993 (1563–2561)	2156 (1822–2670)
Smoking (%)			
Current	5	7	15
Past	55	45	46
Never	39	47	35
Unknown	1	1	4
Race (%)			
White	96	93	94
African American	2	5	3
Other	2	2	4
Education (%)			
Some high school	5	5	9
Some college	37	40	46
College graduate	23	15	17
Graduate or professional school	29	28	20
Unknown	7	13	7
Walking Pace (%)			
<3 miles per hour	61	66	69
3 miles per hour	36	30	26
Unknown	3	5	5
Pre-Treatment CAPRA Score (%)			
1	58	59	57
2	27	32	28
3	5	3	6
Unknown	10	6	8
TNM stage (%)			
T1	54	54	58
T2	45	46	38
T3a	1	0	4
Gleason sum at diagnosis, N (%)			
2–6	759 (67)	61 (70)	68 (62)
3+4	186 (16)	12 (14)	17 (15)
4+3	80 (7)	7 (8)	10 (9)
8–10	59 (5)	3 (3)	10 (9)

	Servings of Whole Milk		
	0–3/month	>3/month to 4/week	>4/week
Unknown	53 (5)	4 (5)	5 (5)
PSA at diagnosis, ng/ml, N (%)			
0–4	208 (18)	11 (13)	18 (16)
4.1–10	745 (66)	62 (71)	70 (64)
10.1–20	112 (10)	9 (10)	15 (14)
20	37 (3)	4 (5)	2 (2)
Unknown	35 (3)	1 (1)	5 (5)
Primary treatment (%)			
Radical prostatectomy	67	56	56
Radiation therapy	22	30	26
Hormonal therapy	5	8	10
Other	5	6	7

TABLE II

Total dairy, high-fat dairy, low-fat dairy, whole milk, and skim/low fat milk intake in relation to risk of prostate cancer recurrence among 1334 men initially diagnosed with nonmetastatic prostate cancer

	0–3/month	>3/month to 4/week	>4/week			P-trend
Intake Frequency (servings)						
Whole milk						
Events/Person-Years	114/7827	5/557	18/616			
Model 1 HR (95% CI)[1]	1	0.54 (0.22–1.32)	1.52 (0.92–2.53)			0.09
Model 2 HR (95% CI)[2]	1	0.53 (0.19–1.44)	1.73 (1.00–2.98)			0.04
	<1/week	1/week to <1/day	1 to <3/day	3/day		P-trend
Skim/low fat milk						
Events/Person-Years	28/1917	36/2441	55/3490	18/1152		
Model 1 HR (95% CI)[1]	1	1.09 (0.67–1.80)	1.14 (0.72–1.79)	1.02 (0.56–1.85)		0.88
Model 2 HR (95% CI)[2]	1	1.07 (0.63–1.83)	1.20 (0.74–1.96)	0.94 (0.48–1.83)		0.91
	<1/day	1 to <2/day	2 to <4/day	4/day		P-trend
Total dairy						
Events/Person-Years	14/1036	46/3048	40/3038	37/1878		
Model 1 HR (95% CI)[1]	1.00	1.15 (0.63–2.09)	0.94 (0.51–1.76)	1.38 (0.72–2.62)		0.33
Model 2 HR (95% CI)[2]	1.00	1.64 (0.81–3.31)	1.28 (0.61–2.66)	2.04 (0.97–4.29)		0.12
High-fat dairy						
Events/Person-Years	25/1690	41/2778	33/2657	38/1875		
Model 1 HR (95% CI)[1]	1.00	1.01 (0.61–1.67)	0.81 (0.48–1.39)	1.32 (0.77–2.25)		0.17
Model 2 HR (95% CI)[2]	1.00	1.16 (0.66–2.05)	0.80 (0.42–1.50)	1.56 (0.86–2.85)		0.08
Low-fat dairy						
Events/Person-Years	34/2131	41/2795	39/2680	23/1394		
Model 1 HR (95% CI)[1]	1.00	0.96 (0.61–1.52)	0.95 (0.60–1.50)	0.95 (0.56–1.64)		0.86
Model 2 HR (95% CI)[2]	1.00	0.99 (0.60–1.62)	1.12 (0.68–1.87)	0.97 (0.53–1.79)		0.93

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[1] Adjusted for age at diagnosis, daily calories, and years from diagnosis to FFQ

[2] Adjusted for variables above plus pre-treatment CAPRA score, current smoking status, BMI, walking pace, and primary treatment

TABLE III

Whole fat milk intake stratified by BMI in relation to risk of prostate cancer recurrence among men initially diagnosed with nonmetastatic prostate cancer (*p*-interaction=0.01)

	Whole Fat Milk Intake Frequency (servings)			
	0–3/month	**>3/month to 4/week**	**>4/week**	***P*-trend**
BMI <27kg/m^2				
Events/Person-Years	49/4090	3/283	4/342	
HR (95% CI)[1]	1.00	0.76 (0.18–3.19)	0.52 (0.15–1.76)	0.30
BMI 27kg/m^2				
Events/Person-Years	64/3727	2/274	14/241	
HR (95% CI)[1]	1.00	0.44 (0.11–1.85)	2.96 (1.58–5.54)	<0.001

[1]Adjusted for age at diagnosis, daily calories, years from diagnosis to FFQ, pre-treatment CAPRA score, current smoking status, BMI, walking pace, and primary treatment