DOI:10.1093/jnci/djt027
Advance Access publication March 14, 2013

ARTICLE

High- and Low-Fat Dairy Intake, Recurrence, and Mortality After Breast Cancer Diagnosis

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Manuscript received August 2, 2012; revised January 16, 2013; accepted January 17, 2013.

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Background Dietary fat in dairy is a source of estrogenic hormones and may be related to worse breast cancer survival. We evaluated associations between high- and low-fat dairy intake, recurrence, and mortality after breast cancer diagnosis.

Methods We included 1893 women from the Life After Cancer Epidemiology study diagnosed with early-stage invasive breast cancer from 1997 to 2000, who completed the Fred Hutchinson Cancer Research Center Food Frequency Questionnaire after diagnosis. A total of 349 women had a recurrence and 372 died during a median follow-up of 11.8 years, with 189 deaths from breast cancer. We used delayed entry Cox proportional hazards regression to evaluate associations between categories of the cumulative average of dairy fat at baseline and at follow-up 5 to 6 years later and subsequent outcomes. Tests of statistical significance were two-sided.

Results In multivariable-adjusted analyses, overall dairy intake was unrelated to breast cancer–specific outcomes, although it was positively related to overall mortality. Low-fat dairy intake was unrelated to recurrence or survival. However, high-fat dairy intake was positively associated with outcomes. Compared with the reference (0 to <0.5 servings/day), those consuming larger amounts of high-fat dairy had higher breast cancer mortality (0.5 to <1.0 servings/day: hazard ratio [HR] = 1.20, 95% confidence interval [CI] = 0.82 to 1.77; and ≥1.0 servings/day: HR = 1.49, 95% CI = 1.00 to 2.24, P_{trend} = .05), higher all-cause mortality (P_{trend} < .001), and higher non–breast cancer mortality (P_{trend} = .007); the relationship with breast cancer recurrence was positive but not statistically significant. The higher risk appeared consistent across different types of high-fat dairy products.

Conclusions Intake of high-fat dairy, but not low-fat dairy, was related to a higher risk of mortality after breast cancer diagnosis.

J Natl Cancer Inst;2013;105:616–623

Many studies (1–14) have evaluated whether dairy intake is related to breast cancer; results are equivocal (15). A recent meta-analysis of prospective cohort studies found a modest inverse association of dairy intake and breast cancer risk, but study heterogeneity was high (16). Individual studies have shown positive (12), inverse (4,6,7,10,11), and null (1,2,9,14,17) associations. One study found that associations varied by levels of fat; greater consumption of high-fat dairy intake was positively related whereas consumption of low-fat dairy intake was inversely related to breast cancer risk (8). Researchers have hypothesized a variety of mechanisms through which dairy might influence breast cancer risk, including calcium, vitamin D, insulin-like growth factors (18,19), conjugated linoleic acid (20), and estrogenic hormones (21). Equivocal findings could be related to the counteracting effects of a multiplicity of factors that may act on breast cancer. However, because estrogens are considered the major etiologic pathway to breast cancer, the influence of dairy intake on estrogens should be strongly considered in understanding how dairy affects breast cancer–specific outcomes.

The Melbourne Collaborative Cohort Study, which included women from Australia, New Zealand, the United Kingdom, Italy, and Greece, found that dairy intake was statistically significantly related to higher levels of estradiol and free estradiol (21). Ganmaa and Sato hypothesized that estrogen and progesterone levels are markedly elevated in dairy products consumed in the Western world compared with those produced in traditional herding societies because most of the milk in the West is produced by pregnant cows, with production enabled both by genetic modification of dairy cows as well as modifications to their feed (22,23). However, because estrogenic hormones reside primarily in fat, levels of female hormones may be substantially lower in skim vs whole milk (24). Insight as to the influence of dairy on breast cancer outcomes may be gained by separately evaluating associations of high- vs low-fat dairy intake and hormonal cancers. Equivocal findings in previous studies could be related to differing patterns of high- and low-fat dairy consumption in different populations and the failure to distinguish high- vs low-fat consumption.

Consistent with this hypothesis, a recent study of dairy intake and prostate cancer survival found that greater consumption of whole milk was associated with worse survival but skim milk was associated with improved survival (25). No previous studies have evaluated associations of postdiagnosis high- vs low-fat dairy intake and breast cancer survival. We hypothesized that consumption of high-fat, but not low-fat, dairy foods would be related to a higher risk of recurrence and breast cancer mortality. We examined these associations in 1893 women with invasive breast cancer from the Life After Cancer Epidemiology (LACE) Study.

Methods

Study Population

The LACE Study cohort includes 2264 women diagnosed with early-stage invasive breast cancer from 1997 to 2000 who were recruited primarily from the Kaiser Permanente Northern California (KPNC) Cancer Registry (83%) and the Utah Cancer Registry (12%) from 2000 to 2002. Further details have been provided elsewhere (26). In brief, eligibility criteria included 1) aged 18 to 70 years at enrollment; 2) diagnosis of early-stage primary breast cancer (stage I ≥ 1 cm, II, or IIIA); 3) enrollment between 11 and 39 months postdiagnosis; 4) completion of breast cancer treatment (except adjuvant hormonal therapy); 5) no evidence of recurrence; and 6) no history of other cancers within 5 years prior to enrollment.

Of the total sample, 1893 women provided complete information on baseline diet. Of these, 1513 women provided dietary data at follow-up 6 years later. Of the total sample, 349 women had a recurrence and 372 died of any cause, with 189 (50.8%) dying from breast cancer. Women provided passive consent when they responded to surveys; the study was approved by the institutional review boards of KPNC and the University of Utah.

Data Collection

Breast Cancer Ascertainment. Information on clinical factors was obtained through electronic data sources available from KPNC or from medical chart review for the non-KPNC participants. Data included tumor size, number of positive lymph nodes, hormone receptor status, and treatment (ie, chemotherapy, radiation therapy, and hormonal therapy). Tumor stage was calculated according to criteria of the American Joint Committee on Cancer (4th edition).

Recurrences were ascertained by a mailed semiannual or annual (after April 2005) health status questionnaire asking participants to report events occurring in the preceding 6 or 12 months, respectively. Recurrences included a locoregional cancer recurrence, distant recurrence/metastasis, or development of a contralateral breast primary. Nonrespondents were called by telephone to complete questionnaires. Medical records were reviewed to verify reported outcomes.

Mortality. Participant deaths were determined through KPNC electronic data sources, a family member responding to a mailed questionnaire, or a phone call to the family. Copies of death certificates were obtained to verify primary and underlying causes of death (International Classification of Diseases, Ninth revision). All-cause mortality included death from any cause including breast cancer. Breast cancer–specific death included death attributable to breast cancer as a primary or underlying cause on the death certificate. Death from causes other than breast cancer included all other deaths. A physician reviewer was consulted when the cause of death was unclear.

Assessment of Dairy Intake. Dietary intake during the previous 12 months was assessed using the Fred Hutchinson Cancer Research Center Food Frequency Questionnaire (FHCRC-FFQ) at both the baseline and 6-year follow-up surveys. The FHCRC-FFQ questionnaire is a validated, self-administered, semiquantitative food frequency questionnaire with approximately 120 items (27) and is an adaptation of the 95-item Health Habits and Lifestyle Questionnaire developed by Block and colleagues at the National Cancer Institute (28).

Specifically, women were asked how often they consumed dairy foods during the previous year. The portion size of a medium serving was provided, and women were asked whether they consumed a small, medium, or large serving. Dairy products included milk (milk on cereal; milk not on cereal; milk, cream or creamer in coffee or tea), cheese (low-fat cottage cheese; nonfat cheese; part skim or reduced-fat cheese; other cheese), dairy desserts (ice cream; pudding; custard or flan; low-fat or nonfat frozen desserts), and yogurt (nonfat; other). To assess fat level in milk, women were asked, "Did you drink milk or beverages made with milk, such as hot chocolate, during this time period? When you drank milk or milk beverages, was it usually: whole milk, 2% milk, 1% milk or butter milk, nonfat or skim milk, evaporated or condensed milk, soy milk, or don't know?" Women were asked similar questions separately for milk, cream, or creamer used on cereal and milk, cream, or creamer in tea or coffee. Servings per day of dairy were computed as the sum of the number of servings of each of these foods consumed each day multiplied by a factor related to the serving size reported (0.5 = small, 1.0 = medium, 1.5 = large) for each item. Servings per day of low-fat dairy were computed as the sum of servings per day of low-fat (1%, 2%) and nonfat (skim) items, including milk, cheese, desserts, and yogurt. Servings per day of high-fat dairy were computed as the sum of high-fat items, including cream, whole milk, condensed or evaporated milk, other cheese, other yogurt, pudding, ice cream, custard, and flan. Total servings per day of dairy were computed as the sum of servings of all dairy.

To maximize power, to capitalize on the availability of dietary data assessed at more than one time point, and to avoid issues of interpretation if recurrence causes women to alter subsequent diet, we analyzed dietary intake in the following way. For those with recurrence events between baseline and the 6-year follow-up, we assigned dietary intake based on women's self-reported diet at baseline. For women who were free of recurrence at follow-up and who provided dietary data at follow-up, we computed diet as the cumulative average of self-reported intake at baseline and follow-up. If women were free of recurrence by follow-up but were missing dietary data at follow-up, we assigned them baseline dietary intake. We also conducted analyses assigning person-time to the updated cumulative average of previously assessed diet.

We used the following categories: 0 to less than 1.0, 1.0 to less than 2.0, and 2.0 or more servings per day, to analyze total dairy consumption and outcomes and ensure a reasonable distribution across categories. To ensure reasonable distributions and consistency in analyses of low-fat and high-fat dairy, we generated the following categories: 0 to less than 0.5, 0.5 to less than 1.0, and 1.0 or more servings per day. These categories were reasonably consistent with previous analyses of levels of dairy (7,9) in US postmenopausal women.

Other Covariates. Information on other covariates was self-reported at baseline. Data on race, education, smoking, menopausal status, reproductive factors, and body mass index were obtained from the mailed baseline questionnaire.

Statistical Analyses

Using analysis of covariance, we regressed potential confounding variables against categories of high-fat dairy food consumption, adjusted for continuous age.

We employed delayed entry Cox proportional hazards models (SAS PROC PHREG; SAS Institute, Cary, NC) for failure-time data to assess associations of categories of dairy as well as high- and low-fat dairy intake with time to event (29,30). Person-years of follow-up were counted from the date of study entry until the date of recurrence, death, or end of follow-up, whichever came first. Time between diagnosis and dietary assessment was updated in analyses for those with dietary data at baseline and follow-up. We conducted tests for linear trend or continuous variables, as indicated, computing Wald statistics and tests of proportionality with variable by time interactions. Tests of statistical significance were two-sided. Statistically significant results denote P values less than or equal to.05.

Minimally adjusted results were compared with those adjusted for multiple covariates. Initial analyses were adjusted for age and time between dietary assessment and prior breast cancer diagnosis. Analyses were adjusted additionally for factors considered a priori to be important potential confounding variables of the relationship between dairy intake and breast cancer outcomes, including disease severity (stage, tumor size, grade, nodal status, estrogen receptor status, and human epidermal growth factor receptor 2 [HER-2] status), treatment (radiation, chemotherapy, tamoxifen), education, ethnicity, and behavioral and related factors (energy intake, red meat, fiber, and fruit intake, body mass index, physical activity, alcohol intake, smoking status). Reproductive variables were not related to dairy consumption, and their inclusion as covariates did not influence associations, so they were dropped from final models. Covariates for which we had data at follow-up, including time between diagnosis and follow-up, tamoxifen, menopausal status, body mass index, smoking, and alcohol, were updated in analyses using the most recent covariate information.

We also evaluated a model adjusted additionally for nutrients found in dairy, including vitamin D, calcium, potassium, and saturated fat intake, to ascertain whether these explained associations of dairy intake and outcomes.

We did not evaluate associations by race/ethnicity because we did not have adequate power.

Results

Study participants contributed 21 273 person-years of follow-up. Follow-up ranged from 1.8 to 14.7 years, with a median of 11.8 years.

Women who consumed the greatest amount of high-fat dairy had higher levels of physical activity, lower alcohol intake, higher body mass index, and were less likely to be never-smokers. They also had higher fiber and red meat intake and, as expected, higher consumption of nutrients found within dairy. Disease characteristics were unrelated to high-fat dairy intake. Consumption of high-fat dairy was unrelated to reproductive factors (Table 1).

Consumption of High- and Low-Fat Dairy Intake

Consumption of dairy intake was relatively limited (median = 1.4 servings/day) (Table 2). Women reported the largest intake of low-fat milk and butter and relatively limited consumption of low-fat dairy dessert, low-fat cheese, and high-fat yogurt. Overall, low-fat dairy intake (median = 0.7 servings/day) was greater than high-fat dairy intake (median = 0.5 servings/day).

Dairy Intake and Breast Cancer Outcomes

In minimally adjusted analyses, we found no statistically significant associations between overall dairy intake and outcomes, although dairy intake was positively related to overall mortality in multivariate-adjusted analyses (Table 3). Low-fat dairy intake was inversely related to all-cause mortality in minimally adjusted analyses, but it was unrelated to outcomes in multivariable-adjusted analyses ($P > 0.05$, all associations). By contrast, in minimally and multivariable-adjusted results, high-fat dairy intake was positively related to mortality outcomes. In multivariable-adjusted analyses, compared with the reference (0 to <0.5 servings/day), those consuming larger amounts of high-fat dairy had higher breast cancer mortality (0.5–1.0 servings/day: hazard ratio [HR] =1.20, 95% confidence interval [CI] = 0.82 to 1.77; >1.0 servings/day: HR = 1.49, 95% CI = 1.00 to 2.24; $P_{trend} = .05$), higher all-cause mortality ($P_{trend} < 0.001$), and higher non–breast cancer mortality ($P_{trend} = 0.007$). There was a suggestion of an increased risk of recurrence with 1 or more servings per day of high-fat dairy intake, but the association was not statistically significant (Table 4). Associations with diet assessed as the updated cumulative average were virtually identical to those in Tables 3 and 4 (data not shown). Tests of proportionality were not statistically significant.

Adjustment for nutrients within dairy, including calcium, vitamin D, and potassium, had little effect on associations. However, high-fat dairy and saturated fat intake were sufficiently correlated ($r = 0.70$; $P < .001$) that we were unable to evaluate independent associations.

We attempted to evaluate whether particular dairy foods explained the association between high-fat dairy intake and outcomes. We had limited power to examine these associations, but results suggested that overall associations were not attributable to one or two specific foods (data not shown).

Discussion

Consistent with much previous literature, we found no overall association between dairy intake and recurrence or breast cancer–specific survival. However, and as expected, high-fat dairy intake was

Table 1. Selected baseline characteristics by category of high-fat dairy intake in the Life After Cancer Epidemiology (LACE) cohort (N = 1893)*

Characteristic	Average high-fat dairy servings per day			
	0 to <0.5	0.5 to <1	≥1	P_{trend}
No.	1002	468	423	
Person-years	11,373	5,273	4,627	
Family history of breast cancer, %	20.7	19.0	20.9	.72
Demographic variables				
Age, mean y	58.7	58.6	58.4	.92
Ethnicity, %				
White	79.3	83.9	86.5	.01†
Black	4.5	3.9	3.1	
Asian	7.5	4.1	2.6	
Hispanic/Latino	5.5	4.9	5.2	
Other	3.2	3.2	2.6	
Education ≥ college, %	35.8	40.4	33.7	.09
Severity of disease				
Stage, %				
I	47.8	48.1	46.1	.97†
II	49.0	48.9	50.6	
IIIa	3.1	3.0	3.3	
Nodal involvement, %	35.3	36.2	36.2	.92
Tumor size, cm	2.1	2.1	2.1	.72
ER-positive tumor, %	80.9	82.7	83.3	.48
HER-2-neu receptor–positive, %	14.9	13.5	15.6	.65
Treatment				
Chemotherapy, %	56.8	56.7	56.3	.98
Radiation, %	64.4	59.2	63.7	.14
Tamoxifen, %	65.0	67.7	64.5	.51
Behavioral and related factors				
Body mass index, kg/m^2	27.2	27.6	28.1	.02
Physical activity, METhr/wk	45.4	51.3	59.5	<.001
Never smokers, %	54.8	53.2	48.2	.07
Mean alcohol, g/d	4.9	7.3	7.9	<.001
Dietary factors				
Average low-fat dairy, svg/d	0.99	1.1	0.99	.66
Average red meat intake, svg/d	0.35	0.44	0.56	<.001
Average fruit intake, svg/d	2.1	1.9	2.2	.19
Average fiber intake, g/d	14.7	15.1	15.9	.01
Average vitamin D intake, mcg	3.8	4.4	4.8	<.001
Average dietary calcium intake, mg/d	654	773	858	<.001
Average saturated fat intake, g/d	12.7	18.5	26.3	<.001
Average dietary potassium intake, mg	2329	2527	2738	<.001
Reproductive factors				
Age at menarche < 12 y, %	12.6	12.8	12.5	.04
Age at first birth > 30 y, %	24.5	24.9	24.0	.07
Parity (number of pregnancies ≥ 5 months)	2.3	2.3	2.4	.34
Postmenopausal at diagnosis, %	76.2	74.5	73.8	.36

* Except for age, all variables were age-adjusted. ER = estrogen receptor; HER-2 = human epidermal growth factor receptor 2; MET = metabolic equivalent; svg = serving.

† *P* value, two-sided Mantel–Haenszel χ^2 test.

related to poorer breast cancer survival in long-term breast cancer survivors. We were unable to evaluate associations between high-fat dairy consumption and levels of estrogens. However, the suggestive association of high-fat dairy with breast cancer recurrence, the statistically significant association with breast cancer mortality, and the lack of association of low-fat dairy with breast cancer outcomes were consistent with the hypothesis that dairy fat intake may increase the risk of adverse postdiagnosis breast cancer outcomes through effects on estrogens. To the authors' knowledge, this is the first study of high- and low-fat dairy intake and breast cancer survival.

Dairy foods have been positively associated with hormonal cancers, including prostate (31–33), postmenopausal endometrial cancer (34), and ovarian (35) cancer, although not in all studies (36,37). Previous studies have generally not analyzed high- and low-fat dairy separately, although one study that did (8) report findings with breast cancer risk was consistent with this study's findings. Additionally, in another study, high-fat dairy was positively and low-fat dairy inversely associated with prostate cancer survival (25). In agreement with our findings, butter was also positively associated with risk of breast cancer in the EPIC study (3). Similar to many

Table 2. Intake of dairy in the Life After Cancer Epidemiology (LACE) study

	Servings per day				
	Mean	**25th percentile**	**Median**	**75th percentile**	**Range**
Energy intake, kcal	1415	1073	1339	1693	502–3808
Fiber intake, g	15.0	10.0	14.1	18.7	3.3–46.6
Fruit intake	2.1	1.03	1.69	2.67	0–25.3
Red meat	0.4	0.18	0.34	0.57	0–3.0
All dairy	1.7	0.81	1.42	2.26	0–12.3
High-fat dairy	0.7	0.19	0.47	0.93	0–5.1
Low-fat dairy	1.0	0.28	0.73	1.35	0–10.1
All milk	0.7	0.17	0.45	1.00	0–9.4
High-fat milk	0.0	0.00	0.00	0.00	0–3.6
Low-fat milk	0.6	0.06	0.30	0.82	0–9.4
All cheese	0.3	0.11	0.24	0.47	0–5.0
High-fat cheese	0.2	0.04	0.11	0.28	0–3.0
Low-fat cheese	0.1	0.01	0.06	0.18	0–2.2
All dairy desserts	0.2	0.04	0.11	0.25	0–1.8
High-fat dairy desserts	0.1	0.02	0.06	0.15	0–1.7
Low-fat dairy desserts	0.1	0.00	0.02	0.07	0–1.5
All yogurt	0.2	0.00	0.07	0.26	0–4.0
High-fat yogurt	0.0	0.00	0.00	0.02	0–2.0
Low-fat yogurt	0.1	0.00	0.04	0.21	0–2.2
Butter	0.5	0.13	0.38	0.75	0–5.0

Table 3. Hazard ratios (HRs) of events by category of total dairy intake in the Life After Cancer Epidemiology (LACE) cohort (N = 1893)*

	Average dairy intake per day, svg/d			
	0 to <1.0	**1.0 to <2.0**	**≥2.0**	P_{trend}†
Total dairy intake, No.	610	703	580	
Recurrence	121	121	107	
HR, age-adjusted*	1.00	0.88	0.95	.81
(95% CI)	(referent)	(0.69 to 1.14)	(0.73 to 1.24)	
HR, multivariable-adjusted model	1.00	0.94	1.13	.38
(95% CI)	(referent)	(0.72 to 1.23)	(0.83 to 1.54)	
Breast cancer deaths	66	69	54	
HR, age-adjusted	1.00	1.00	0.96	.82
(95% CI)	(referent)	(0.71 to 1.41)	(0.67 to 1.38)	
HR, multivariable-adjusted model	1.00	1.16	1.26	.32
(95% CI)	(referent)	(0.81 to 1.67)	(0.81 to 1.95)	
Deaths from all causes	129	136	107	
HR, age-adjusted	1.00	1.02	0.99	.94
(95% CI)	(referent)	(0.80 to 1.30)	(0.77 to 1.29)	
HR, multivariable-adjusted model	1.00	1.28	1.39	.05
(95% CI)	(referent)	(0.99 to 1.66)	(1.02 to 1.90)	
Deaths from non–breast cancer causes	63	67	53	
HR, age-adjusted	1.00	1.05	1.04	.85
(95% CI)	(referent)	(0.74 to 1.48)	(0.72 to 1.50)	
HR, multivariable-adjusted model	1.00	1.40	1.54	.07
(95% CI)	(referent)	(0.95 to 2.05)	(0.99 to 2.39)	

* Age-adjusted model adjusted for age at diagnosis (continuous) and time between diagnosis and dietary assessment. Multivariable-adjusted models adjusted additionally for age, race (white, nonwhite [referent]), education (<college graduate [referent], college graduate), cancer stage at diagnosis (I [referent], II, III), tumor size (continuous), human epidermal growth receptor 2 neu status (positive, negative[referent]), nodal status (no involvement [referent], any involvement), estrogen receptor status (positive, negative [referent]), chemotherapy (yes, no [referent]), radiation (yes, no [referent]), tamoxifen (never, past, current [referent]), comorbidity (yes, no [referent]), menopausal status (pre [referent], post), smoking status (never [referent], past, current), body mass index (<25 [referent] 25–29, ≥30 kg/m^2), physical activity (quartiles; quartile 1 = referent), energy intake (continuous), alcohol intake (0 to <0.5 [referent], 0.5 to <10.0, ≥10 g/d), red meat intake (tertiles; tertile 1 = referent), fiber intake(tertiles; tertile 1 = referent), and fruit intake (tertiles; tertile 1 = referent). CI = confidence interval; svg = serving.

† *P* value, continuous variable.

previous studies of dairy and breast cancer incidence (1,2,9,14,17), we found little evidence of an overall association between dairy and breast cancer outcomes.

Several studies have found inverse associations of dairy and breast cancer risk (4,6,7,10,11), primarily in premenopausal women, suggesting that associations may differ by menopausal status. We

Table 4. Hazard ratios (HRs) of events by category of high- and low-fat dairy intake in the Life After Cancer Epidemiology (LACE) cohort (N = 1893)*

	Average dairy intake per day, svg/d			
	0 to <0.5	0.5 to <1.0	≥1.0	P_{trend}†
High-fat dairy intake, No.	1002	468	423	
Recurrence	176	88	85	
HR, age-adjusted*	1.00	1.11	1.20	.14
(95% CI)	(referent)	(0.86 to 1.43)	(0.92 to 1.55)	
HR, multivariable-adjusted model	1.00	1.22	1.22	.18
(95% CI)	(referent)	(0.92 to 1.65)	(0.91 to 1.65)	
Breast cancer deaths	94	45	50	
HR, age-adjusted	1.00	1.13	1.39	.06
(95% CI)	(referent)	(0.79 to 1.61)	(0.99 to 1.96)	
HR, multivariable-adjusted model	1.00	1.20	1.49	.05
(95% CI)	(referent)	(0.82 to 1.77)	(1.00 to 2.24)	
Deaths from all causes	183	82	107	
HR, age-adjusted	1.00	1.05	1.55	<.001
(95% CI)	(referent)	(0.81 to 1.36)	(1.22 to 1.97)	
HR, multivariable-adjusted model	1.00	1.16	1.64	<.001
(95% CI)	(referent)	(0.88 to 1.53)	(1.24 to 2.17)	
Deaths from non–breast cancer causes	89	37	57	
HR, age-adjusted	1.00	0.96	1.69	.002
(95% CI)	(referent)	(0.65 to 1.40)	(1.21 to 2.36)	
HR, multivariable-adjusted model	1.00	1.06	1.67	.007
(95% CI)	(referent)	(0.71 to 1.59)	(1.13 to 2.47)	
Low-fat dairy intake, No.	722	470	701	
Recurrence	154	71	124	
HR, age-adjusted*	1.00	0.68	0.81	.13
(95% CI)	(referent)	(0.52 to 0.90)	(0.64 to 1.03)	
HR, multivariable-adjusted model	1.00	.81	1.01	.85
(95% CI)	(referent)	(0.61 to 1.09)	(0.78 to 1.32)	
Breast cancer deaths	87	44	58	
HR, age-adjusted	1.00	0.79	0.72	.06
(95% CI)	(referent)	(0.55 to 1.13)	(0.51 to 1.00)	
HR, multivariable-adjusted model	1.00	1.06	1.03	.89
(95% CI)	(referent)	(0.73 to 1.55)	(0.71 to 1.49)	
Deaths from all causes	164	94	114	
HR, age-adjusted	1.00	0.88	0.74	.01
(95% CI)	(referent)	(0.68 to 1.13)	(0.58 to 0.94)	
HR, multivariable-adjusted model	1.00	1.15	1.05	.76
(95% CI)	(referent)	(0.88 to 1.49)	(0.80 to 1.36)	
Deaths from non–breast cancer causes	77	50	56	
HR, age-adjusted	1.00	0.99	0.77	.11
(95% CI)	(referent)	(0.69 to 1.41)	(0.54 to 1.09)	
HR, multivariable-adjusted model	1.00	1.19	1.05	.83
(95% CI)	(referent)	(0.82 to 1.75)	(0.71 to 1.55)	

* Age-adjusted model adjusted for age (continuous), time between diagnosis and dietary assessment, and simultaneously for high- and low-fat dairy intake. Multivariable-adjusted models adjusted additionally for race (white, nonwhite [referent]), education (<college graduate [referent], college graduate), cancer stage at diagnosis (I [referent], II, III), tumor size (continuous), human epidermal growth receptor 2 neu status (positive, negative [referent]), nodal status (no involvement [referent], any involvement), estrogen receptor status (positive, negative [referent]), chemotherapy (yes, no [referent]), radiation (yes, no [referent]), tamoxifen (never, past, current [referent]), comorbidity (yes, no [referent]), menopausal status (pre [referent], post), smoking status (never [referent], past, current), body mass index (<25 [referent] 25–29, ≥30 kg/m^2), physical activity (quartiles; quartile 1 = referent), energy intake (continuous), alcohol intake (0 to <0.5 [referent], 0.5 to <10.0, ≥10 g/d), red meat intake (tertiles; tertile 1 = referent), fiber intake(tertiles; tertile 1 = referent), and fruit intake (tertiles; tertile 1 = referent). CI = confidence interval; svg = serving.

† *P* value, continuous variable.

had insufficient power to stratify by menopausal status because women in this cohort were primarily postmenopausal (75%) and there were few adverse outcomes in premenopausal women. Our null associations for low-fat dairy may also be because we were often unable to distinguish nonfat from low-fat items and many "low-fat" items contained considerable fat. Future research should attempt to evaluate whether associations differ for nonfat vs low-fat dairy items and whether associations differ by menopausal status.

Mechanisms proposed to influence breast cancer include calcium and vitamin D, given their potential to decrease cell proliferation and increase cell differentiation (38). In this study, we found these nutrients were unrelated to breast cancer outcomes (data not shown). It was difficult to disentangle the effects of saturated fat intake and high-fat dairy given the large correlation between the two. Despite this correlation, when we examined associations of saturated fat alone, associations for saturated fat were weaker than

for dairy and breast cancer outcomes (data not shown), suggesting that saturated fat intake consumption per se, including saturated fat from nondairy foods (eg, palm kernel, coconut, and cottonseed oils used commonly in processed foods or meat intake), may not be related to outcomes. These findings suggest that saturated fats in dairy foods specifically augment risk.

If high-fat dairy is associated with higher levels of estrogenic hormones, consuming plant-based milks or nonfat dairy products may be a reasonable approach for limiting risk of adverse outcomes, particularly when breast cancer treatment has been completed. A study in mice found that dairy fat augmented effectiveness of chemotherapy against tumor metastasis while protecting against its side effects (39), suggesting possible benefits during early treatment. However, decreasing intake in favor of low-fat intake after treatment may be advisable and is consistent with general nutritional guidelines, which recommend nonfat or low-fat dairy instead of high-fat dairy, to minimize cardiovascular risk (40).

A study strength was the ability to adjust for variables related to breast cancer severity, including stage, tumor size, nodal status, hormone receptor status, and HER-2 status as well as breast cancer treatment. A second strength was the ability to adjust carefully for reproductive history and lifestyle, demographic, and socioeconomic variables. Furthermore, we were able to assess dietary intake at two time points, which may better approximate habitual diet than diet measured at one time point.

One limitation, if women didn't respond, indicated they didn't know, or indicated multiple choices for the type of milk they consumed, whether high- or low-fat, we were not able to assign milk consumption to either the high- or low-fat category, which resulted in an underestimation of intake. In fact, studies of diet employing food frequency questionnaires underestimate intake generally (41,42). We considered employing regression calibration methods to correct for measurement error. However, we lacked dietary validation data in LACE, and the use of data from other studies has been criticized (43). Therefore, unless systematic bias influenced dietary estimates, effect estimates generated here likely underestimate the true effect of high-fat dairy on post–breast cancer outcomes, and we were not able to correct for this. We also had limited power to carefully examine specific dairy foods or associations stratified by variables such as estrogen receptor/progesterone receptor status that might help shed additional light on associations. Future studies should replicate these findings in a larger cohort, with data to enable correction for measurement error.

To summarize, greater intake of high-fat dairy was related to higher risk of breast cancer–specific and non–breast cancer mortality in this cohort of long-term, early-stage breast cancer survivors. High-fat dairy consumption may increase levels of estrogens, which may augment the risk of breast cancer recurrence and mortality.

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Funding

This work was supported by the National Cancer Institute at the National Institutes of Health (grant R01CA129059).

Notes

C.H. Kroenke contributed to conceptualization and design of the study, analysis, writing and interpretation. M. Kwan contributed to data creation and writing. C. Sweeney contributed to editing and data creation. A. Castillo contributed to editing and data creation. B. Caan contributed to data creation and writing. All authors had complete access to the data. All authors of this research paper have approved the final version submitted.

The study sponsors had no role in the design of the study; the collection, analysis, and interpretation of the data; the writing of the manuscript; and the decision to submit the manuscript for publication. The authors also report no conflicts of interest.

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