Cancer Causes Control (2013) 24:675–684
DOI 10.1007/s10552-013-0146-8

ORIGINAL PAPER

Consumption of dairy and meat in relation to breast cancer risk in the Black Women's Health Study

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Received: 13 September 2012 / Accepted: 4 January 2013 / Published online: 18 January 2013

Abstract
Purpose Dairy and meat consumption may impact breast cancer risk through modification of hormones (e.g., estrogen), through specific nutrients (e.g., vitamin D), or through products formed in processing/cooking (e.g., heterocyclic amines). Results relating meat and dairy intake to breast cancer risk have been conflicting. Thus, we examined the risk of breast cancer in relation to intake of dairy and meat in a large prospective cohort study.
Methods In the Black Women's Health Study, 1,268 incident breast cancer cases were identified among 52,062 women during 12 years of follow-up. Multivariable (MV) relative risks (RRs) and 95 % confidence intervals (CIs) were calculated using Cox proportional hazards models.
Results Null associations were observed for total milk (MV RR = 1.05, 95 % CI 0.74–1.46 comparing ≥1,000–0 g/week) and total meat (MV RR = 1.04, 95 % CI 0.85–1.28 comparing ≥1,000 < 400 g/week) intake and risk of breast cancer. Associations with intakes of specific types of dairy, specific types of meat, and dietary calcium and vitamin D were also null. The associations were not modified by reproductive (e.g., parity) or lifestyle factors (e.g., smoking). Associations with estrogen receptor (ER) positive (+), ER negative (−), progesterone receptor (PR) +, PR−, ER+/PR+, and ER−/PR− breast cancer were generally null.
Conclusions This analysis of African-American women provides little support for associations of dairy and meat intake with breast cancer risk.

Keywords Diet · Breast cancer · Epidemiology · Cohort · African-American

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Introduction

An estimated 226,870 new cases of invasive breast cancers and 39,500 deaths from breast cancer occurred in women in the United States in 2012 [1]. African-American women, compared to white women, have a higher incidence rate of breast cancer prior to age 45, a higher incidence of estrogen receptor negative (ER−) breast cancers, and are more likely to die from breast cancer at every age [1]. Understanding modifiable and preventive factors, particularly related to premenopausal and ER− breast cancer risk, which both have a worse prognosis, is important to reducing these disparities.

Reproductive risk factors, such as higher parity and later age at menarche, may reduce breast cancer risk by influencing lifetime exposure to estrogen. Dietary factors, such as dairy products and meat, may also impact breast cancer risk through modification of estrogen and other hormones levels (e.g., insulin-like growth factor [2–4]). In addition, other components found within dairy foods (e.g., vitamin D [5–12], calcium [5–9], and dietary fat) and meats (e.g., heme iron) or resulting from meat processing or preparation (e.g., heterocyclic amines, *N*-nitrosamines) [13–15] have been hypothesized to modify breast cancer risk.

To date, a large number of studies have examined the association between dairy intake, meat intake, and breast cancer risk; results have been inconsistent [16–20]. A review sponsored by the World Cancer Research Fund (WCRF) and American Institute of Cancer Research (AICR) of 24 cohort and 56 case–control studies in 2007 concluded that the available evidence is insufficient to establish associations between dairy and meat intake and premenopausal or postmenopausal breast cancer risk [16]. Although many studies have examined total and postmenopausal breast cancer, fewer studies have examined premenopausal breast cancer and specific types of breast cancer (e.g., ER−), particularly among African-American women.

The Black Women's Health Study, a large prospective cohort study of African-American women, provided an opportunity to examine associations between dairy and meat intake and risk of breast cancer, particularly breast cancer among younger women and ER− breast cancer. We examined intake of dairy, calcium, vitamin D, and meat with risk of total breast cancer and specific types of breast cancer (e.g., premenopausal, ER+ breast cancer). We further explored whether the associations between intake of dairy, calcium, vitamin D and meat and breast cancer risk are modified by known or suspected risk factors.

Methods

Population

The Black Women's Health Study (BWHS) is conducted among 59,027 African-American women, aged 21–69 years at baseline in 1995 [21]. Women who were subscribers to *Essence* magazine, members of several professional organizations, and friends and relatives of early respondents enrolled by completing health questionnaires on diet, lifestyle factors, medical and reproductive history, and medication use. Every 2 years thereafter, questionnaires were mailed to update information on potential risk factors and to identify new cases of disease. Study participants reside in more than 17 states. The Institutional Review Board of Boston University Medical Center approved the study protocol.

Exposure assessment

Usual frequency of consumption of dairy foods (total milk, whole milk, low-fat milk, hard cheese, yogurt, and ice cream) and meat (total meat, red meat, processed meat, white meat, and fish) during the past year was estimated from a 68-item modified Block Food Frequency Questionnaire (FFQ) completed at baseline in 1995 [22]. In 2001, a modified version of the 1995 FFQ which asked about 85 food items was administered to collect updated dietary information. For each FFQ item, individuals selected from the following: 'never' to '2+ per day' and 'never' to '6 or more per day' for the frequency of intake of foods and beverages, respectively. Individuals selected the appropriate portion size of 'small,' 'medium,' and 'large' for each food item on the 1995 questionnaire; the 2001 questionnaire added the category of "super." A medium portion size was defined for each item (e.g., 8-oz glass of milk), and small and large servings were weighted as 0.5 and 1.5 times a medium serving size, respectively. In 2001, the 'super' portion was equivalent to two times the size of medium. The 1995 FFQ ascertained intake of 8 dairy and 13 meat items; the 2001 FFQ asked about 9 dairy and 15 meat items. There was moderate to high correlation among intakes of various dairy foods. Using the food frequency data, the Pearson correlation coefficients (energy-adjusted and corrected for intra-person variation) for total milk with skim milk was 0.65 and for total milk with whole milk was 0.48. All dairy and meat items were analyzed in gram units. We converted the frequency data to grams consumed per day based on the frequency and serving size for each food item. All dairy and meat items were analyzed in gram units for consistency and comparability across studies; an average serving size of milk is 250 g, while an average serving of meat is approximately 100 g. Nutrient estimates for calcium and vitamin D from the FFQ were calculated using the food composition method [23] using National Cancer Institute's DietCalc software [24]. Energy-adjusted nutrient intakes have been calculated for each nutrient using the residual method [23]. Use of multivitamins and single supplements, including calcium, was also ascertained.

Other covariates

On the 1995 baseline questionnaire, BWHS participants provided demographic data and information that included medical and reproductive history, smoking and alcohol use, physical activity, current weight and weight at age 18, waist and hip circumference, adult height, medication use, and use of medical care. The biennial follow-up questionnaires all obtained updated information on weight, physical activity, smoking, alcohol use, and other factors. The 1995 and 1999 questionnaires included questions about family history of cancer. Body mass index (BMI) was calculated as weight in kilograms divided by squared height in meters. Women who reported a hysterectomy but retained one or both ovaries were classified as premenopausal if their current age was less than the 10th percentile of age at natural menopause in the BWHS (43 years), as postmenopausal if their age was greater than the 90th percentile of age at natural menopause in the cohort

(56 years), and as uncertain menopausal status at ages 43–56 years.

Outcome assessment

Participants were followed from entry into the study in 1995 until date of diagnosis of incident breast cancer (defined by ICD-9 code 174.9 [25] or ICD-10 code C50 [26]), date of death, or end of follow-up (through 2007), whichever came first. Follow-up of the baseline cohort has exceeded 80 %. We obtained medical record or cancer registry data for 85 % of cases, and of these, 99.4 % were confirmed. Given the high confirmation rate, we included all self-reported cases, except those that were disconfirmed. We learned of deaths from family members, the US Postal Service, and searches of the National Death Index for non-respondents. Information on breast tumor characteristics, including estrogen receptor (ER) and progesterone receptor (PR) status, was obtained through abstraction of pathology records and cancer registry data and was available for 59 % of the cases. Breast cancer risk factors (e.g., age, education, and lifestyle, and reproductive factors) among cases for which receptor status data were available were similar to those among cases for which receptor status was not obtained [27]. In addition, the two groups were similar with regard to the variables assessed in the present paper; for example, for women with known and unknown receptor status, respectively, the proportions consuming 500 g or more of milk per week were 35.7 and 38.7 %, and the proportions consuming 800 g or more of meat per week were 41.2 and 43.9 %.

Analytic sample

Women were excluded from the analyses if they had a prior cancer diagnosis at baseline ($n = 1{,}475$). In addition, women who had missing or implausible total energy intake (<500 kcal/day or >3,800 kcal/day; $n = 3{,}536$) or were missing more than 10 items on the baseline FFQ ($n = 1{,}954$) were excluded [23], leaving 52,062 women for the analysis.

Statistical analysis

Dietary exposures were modeled both as continuous and as categorical variables according to absolute cut points based on serving sizes and quantiles. Relative risks (RRs) and 95 % confidence intervals (CIs) were calculated by Cox proportional hazards models separately for each individual dairy and meat intake (e.g., total milk intake, and red meat intake). Person-years of follow-up were calculated from the date of baseline questionnaire until the date of breast cancer diagnosis, death, loss to follow-up, or end of follow-up, whichever came first. The model included stratification by age at baseline (in 1-year intervals) and questionnaire cycle and treated the follow-up time (in years) as the time scale, resulting in a time metric that simultaneously accounts for age, calendar time, and time since entry into the study. Multivariable (MV) RRs were adjusted for energy intake (quintiles), age at menarche (years <12, 12–13, ≥14), body mass index (BMI, kg/m^2, <25, 25–29, ≥30), family history of breast cancer (mother or sister), years of education (≤12, 13–15, ≥16), parity and age at first live birth (nulliparous, parity 1–2 and age at first birth <25 years, parity 1–2 and age at first birth 25–29 years, parity 1–2 and age at first birth ≥30 years, parity ≥3 and age at first birth <25 years, parity ≥3 and age at first birth 25–29 years, parity ≥3 and age at first birth ≥30 years), oral contraceptive use (yes/no), menopausal status (postmenopausal, premenopausal, and uncertain), age at menopause (years <35, 35–39, 40–44, 45–49, 50–54, ≥55), menopausal hormone use (yes/no), hours/week of vigorous physical activity (none, ≤2, >2), smoking status (never, former, and current), and drinks/week of alcohol (none, 1–3, 4–6, ≥7). Parity, oral contraceptive use, menopausal status, menopausal hormone use, vigorous activity, smoking status, and alcohol intake were treated as time-dependent variables in the analysis. The proportion of participants with missing data for the covariates was generally low (2–4 %); an indicator variable was used for missing responses [28].

Two different methods were applied to analyze the association between breast cancer risk and dairy and meat intake: the use of baseline diet data only and a cumulative average approach [23, 29]. In analyses using baseline data only, we assessed the 1995 food and nutrient intake data in relation to breast cancer risk from 1995 to 2007. The cumulative average approach reduces within-person variation and better represents long-term diet: dietary data from the baseline questionnaire were used for follow-up from 1995 to 2001, and an average of the dietary intakes from baseline and 2001 questionnaire was used for follow-up from 2001 to 2007. Results from the multivariable-adjusted models based on cumulative average dietary data were similar to those from models that adjusted only for age and models using baseline FFQ data only. Thus, only multivariable models based on cumulative dietary intake are presented.

To test whether there was a linear trend in the risk of disease with increasing intake, a continuous variable with values corresponding to the median value for each exposure category was included in the model, and the coefficient for that variable was evaluated using the Wald test. Further analyses were conducted to examine whether the association between meat intake and breast cancer risk varied by hormonal and other breast cancer risk factors [e.g., parity (parous, nulliparous), alcohol intake (ever, never), smoking status (ever, never), BMI (<30, ≥30 kg/m^2), and hormone use (ever, never)]; for these analyses, the stratification variable was excluded from the model. We additionally stratified by menopausal status for all analyses; those with uncertain menopausal status were excluded from these analyses ($n_{cases} = 175$).To test for multiplicative interaction, the main effect terms for the dietary and stratification factors, along with the cross-product term, were included in the model. The coefficient for the cross-product term was evaluated for statistical significance by the Wald test. To examine the possible presence of a time lag effect, we excluded the first 2 years of follow-up from the analysis.

Separate analyses were also conducted by hormone receptor status among cases with known ER status ($n = 761$) or PR status ($n = 746$), using the following categories: (1) ER+, (2) ER−, (3) PR+, (4) PR−, (5) ER+/PR+, and (6) ER−/PR−. Due to small number of cases, we were unable to assess ER+/PR− and ER−/PR+ breast cancers. Statistical analyses were done with SAS 9.2. All statistical tests were based on a two-sided p value. Tests with p values <0.05 were considered statistically significant.

Results

Baseline cohort characteristics by total milk intake and total meat intake are summarized in Table 1. Women who consumed greater amounts of milk were heavier, less educated, and less likely to be nulliparous. Individuals who had higher meat consumption were heavier, more likely to smoke, drink, and be parous, and less likely to exercise more than 2 h/week. The median intake of total milk and total meat was 384.5 and 714.4 g/week, respectively.

As shown in Table 2, no statistically significant associations with breast cancer were observed for total milk intake (MVRR = 1.05, 95 % CI = 0.74–1.46 comparing ≥1,000–0 g/week). In addition, no statistically significant association for breast cancer was observed for whole milk or 2 % milk intakes. There were non-significant, modest inverse associations between skim milk, hard cheese, yogurt, and ice cream intakes and risk of breast cancer. Results did not differ by menopausal status.

Dairy products are major contributors to dietary calcium and dietary vitamin D intake. Dietary calcium intake (MVRR = 1.10, 95 % CI = 0.79–1.53 comparing ≥1,000 to <200 mg/day; p trend = 0.51) and dietary vitamin D intake (MVRR = 1.08, 95 % CI = 0.79–1.47 comparing ≥6 to <1 µg/day; p trend = 0.89) were not associated with breast cancer risk. No statistically significant association with breast cancer was observed for use of calcium supplements compared to non-use (MVRR = 1.09, 95 % CI = 0.96–1.24). Results did not differ by menopausal status.

No statistically significant associations with breast cancer were observed for intakes of total meat (MVRR = 1.04, 95 % CI = 0.85–1.28 comparing ≥1,000 to <400 g/week) (Table 3). In addition, no statistically significant association for breast cancer was observed for intakes of red meat, processed meat, white meat, or fish. Menopausal status did not modify the associations between intakes of red meat, processed meat, white meat, fish, and breast cancer risk (Table 3).

As shown in Table 4, no statistically significant associations were observed between total milk intake and breast cancer risk by hormone receptor status (ER+, PR+, ER−, PR−, ER+/PR+, and ER−/PR− breast cancers). However, whole milk intake was inversely associated with ER− breast cancer (MVRR = 0.33, 95 % CI = 0.13–0.84) and PR− breast cancer (MVRR = 0.49, 95 % CI = 0.24–0.99; p trend = 0.11) for ≥250 g/week compared to 0 g/week. In addition, yogurt intake was inversely associated with ER− breast cancer (MVRR = 0.45, 95 % CI = 0.22–0.89; p trend <0.01) and PR− breast cancer (MVRR = 0.56, 95 % CI = 0.32–0.98; p trend <0.01) for ≥454 g/week relative to 0 g/week. Intake of ice cream was inversely associated with ER+ breast cancer (MVRR = 0.62, 95 % CI = 0.41–0.94; p trend = 0.01) and PR− breast cancer (MVRR = 0.62, 95 % CI = 0.38–1.00; p trend = 0.04) for ≥66 g/week compared to 0 g/week. Associations did not differ by hormone receptor status for other specific types of dairy intake.

There were no statistically significant associations of total meat intake with breast cancer risk by hormone receptor status (Table 4). Associations did not differ by receptor status for red meat, processed meat, and white meat. Fish intake was positively associated with ER+ breast cancer (MVRR = 1.25, 95 % CI = 0.99–1.59; p trend = 0.05) and PR+ breast cancer (MVRR = 1.33, 95 % CI = 1.02–1.74; p trend = 0.03) when comparing ≥200 to <100 g/week.

In addition, the association between dietary calcium and dietary vitamin D intake with breast cancer risk did not differ according to receptor status (data not shown). Similar estimates to the overall findings for the association between dairy, dietary calcium, dietary vitamin D and meat intake and breast cancer risk were observed within strata of hormone use, parity, smoking status, and BMI (data not shown).

Cases that occurred close in time to the completion of the FFQ may have altered their diet due to factors such as prediagnostic disease symptoms. In sensitivity analyses that excluded cases diagnosed during the first and second year of follow-up, estimates were similar to the overall estimates (data not shown).

Discussion

In this large prospective cohort of African-American women, null associations were observed for intakes of milk (total, whole, and 2 %), other specific types of dairy

Table 1 Age-standardized means and proportions of baseline cohort characteristics by total milk and meat intake

	Total milk intake (g/week)		Total meat intake (g/week)	
	0	≥1,000	<400	≥1,000
Total *n*	3,471	13,787	10,370	14,760
n (cases)	293	279	229	338
Age (years)	39.0	38.7	38.7	38.5
BMI (kg/m^2)	26.8	28.6	26.5	29.3
Education (%)				
≤12 years	15.8	18.5	17.3	19.1
13–15 years	31.5	36.3	35.1	37.1
≥16 years	52.6	45.2	47.4	43.6
Smoking (%)				
Never	63.9	65.0	68.9	61.7
Former	20.7	19.4	17.9	19.9
Current	15.3	15.4	13.1	18.2
Alcohol (%)				
Non-drinker	74.1	75.8	88.1	81.6
1–3 drinks/week	11.1	12.4	2.3	2.7
≥4 drinks/week	14.3	11.1	8.7	14.8
Family history	6.7	6.1	6.6	6.6
Breast cancer (%)				
Age at menarche (years)	12.3	12.3	12.3	12.3
Age at first live birth (years)	22.3	22.4	22.3	22.1
Nulliparous (%)	43.2	34.1	39.5	34.7
Menopausal status[a] (%)				
Premenopausal	76.6	76.7	76.6	77.4
Postmenopausal	16.8	17.1	17.2	16.9
Strenuous physical activity (%)				
None	32.4	29.7	29.1	33.4
≤2 h/week	34.1	38.1	36.6	37.9
>2 h/week	30.1	28.5	30.8	25.2

Directly age standardized to the age distribution of the analytic cohort

[a] Unknown status not shown

products, dietary calcium, and dietary vitamin D with breast cancer risk. No statistically significant associations were observed for total meat and types of meat and breast cancer risk. The findings were similar for premenopausal and postmenopausal breast cancer. While associations were also generally null for subtypes of breast cancer, defined by hormone receptor status, a few inverse associations were noted with intake of select dairy products. Results were generally similar within strata of hormone use, parity, smoking status, and BMI.

Our results are generally similar to the summary findings from the 2007 report by the WCRF and AICR; the WCRF/AICR panel determined that evidence for an association of dairy or meat with total, premenopausal, or postmenopausal breast cancer is limited [16]. In addition, null associations between dairy and meat intake and breast cancer risk were reported from two recent large European prospective cohort studies, the Swedish Mammography Cohort [19] and the EPIC cohort study [17]. A recent meta-analysis conducted by Dong et al. [18] on total milk consumption and risk of breast cancer in 18 prospective cohort studies found a non-statistically significant inverse association of total milk consumption with breast cancer risk (RR = 0.90, 95 % CI = 0.80–1.02) comparing highest to lowest categories. There was a stronger inverse association of low-fat dairy intake with breast cancer risk [18]. However, there was significant heterogeneity between studies (p value, test for between studies heterogeneity = 0.003).

Other studies have suggested different etiologies may be associated with different breast cancer subtypes

Table 2 Multivariable-adjusted relative risk (MVRR) and 95 % confidence interval (CI) of breast cancer by menopausal status by categories of intake of dairy foods

Dairy foods (g/week)[a]	Type of breast cancer								
	Total			Premenopausal			Postmenopausal		
	n_{cases}	Person-years	MVRR (95 % CI)	n_{cases}	Person-years	MVRR (95 % CI)	n_{cases}	Person-years	MVRR (95 % CI)
Total milk									
0	293	152,373	1.00 (REF)	97	68,239	1.00 (REF)	133	40,151	1.00 (REF)
1–69.9	159	70,027	1.18 (0.83–1.68)	88	46,632	1.50 (0.88–2.53)	53	16,259	0.92 (0.52–1.60)
70–124.9	77	34,711	1.06 (0.70–1.61)	27	23,033	1.07 (0.57–2.01)	45	8,031	1.35 (0.73–2.47)
125–249.9	129	65,353	1.05 (0.73–1.52)	64	45,242	1.07 (0.61–1.86)	44	13,420	1.12 (0.64–1.96)
250–499.9	142	78,194	0.89 (0.62–1.28)	72	54,282	0.98 (0.57–1.69)	57	16,083	0.88 (0.50–1.55)
500–749.9	70	34,776	0.88 (0.57–1.35)	33	22,733	1.10 (0.58–2.05)	25	8,323	0.68 (0.33–1.37)
750–999.9	119	55,421	1.02 (0.69–1.50)	50	37,948	0.82 (0.44–1.51)	52	12,258	1.27 (0.72–2.23)
≥1,000	279	126,373	1.05 (0.74–1.46)	141	86,473	1.24 (0.74–2.08)	112	28,056	1.00 (0.60–1.67)
p_{trend}			0.54			0.55			0.92
Whole milk									
0	1,026	479,660	1.00 (REF)	433	283,121	1.00 (REF)	445	118,955	1.00 (REF)
1–249.9	134	74,892	1.08 (0.85–1.36)	80	54,716	1.26 (0.94–1.70)	36	12,950	0.89 (0.58–1.36)
≥250	108	62,276	0.96 (0.73–1.26)	59	46,745	1.08 (0.75–1.54)	40	10,676	0.86 (0.54–1.37)
p_{trend}			0.83			0.23			0.37
2 % Milk									
0	886	430,888	1.00 (REF)	378	254,580	1.00 (REF)	380	104,712	1.00 (REF)
1–249.9	177	87,775	1.11 (0.90–1.38)	87	62,579	1.08 (0.80–1.46)	60	16,468	1.04 (0.72–1.49)
≥250	205	98,565	1.08 (0.87–1.33)	107	67,423	1.16 (0.87–1.54)	81	21,401	1.09 (0.78–1.52)
p_{trend}			0.37			0.30			0.59
Skim milk									
0	879	443,389	1.00 (REF)	413	280,517	1.00 (REF)	340	97,092	1.00 (REF)
1–249.9	138	67,740	0.80 (0.60–1.05)	62	41,932	0.75 (0.50–1.11)	63	16,129	0.94 (0.61–1.42)
≥250	251	106,099	0.86 (0.69–1.07)	97	62,133	0.80 (0.58–1.11)	118	29,360	0.90 (0.65–1.25)
p_{trend}			0.09			0.10			0.52
Hard cheese									
0	529	253,179	1.00 (REF)	199	129,699	1.00 (REF)	245	68,459	1.00 (REF)
1–24.9	239	106,063	1.01 (0.81–1.25)	107	68,291	1.15 (0.84–1.58)	96	26,468	0.80 (0.57–1.12)
25–49.9	179	81,871	0.85 (0.66–1.10)	88	55,794	0.93 (0.64–1.32)	69	17,695	0.78 (0.52–1.16)
50–74.9	95	50,161	0.91 (0.67–1.23)	54	35,860	1.02 (0.67–1.54)	32	9,544	0.90 (0.56–1.44)
≥75	226	125,954	0.88 (0.68–1.12)	32	9,544	0.90 (0.63–1.26)	79	20,415	0.79 (0.53–1.17)
p_{trend}			0.19			0.38			0.25
Yogurt									
0	709	349,251	1.00 (REF)	304	205,272	1.00 (REF)	295	81,191	1.00 (REF)
1–56.9	69	30,127	1.12 (0.81–1.53)	36	20,158	1.29 (0.85–1.95)	24	6,886	0.96 (0.56–1.65)
57–113.9	114	58,794	1.03 (0.79–1.32)	46	39,970	0.74 (0.49–1.12)	54	12,816	1.34 (0.92–1.93)
114–226.9	114	56,100	1.04 (0.80–1.35)	58	38,136	1.10 (0.76–1.57)	46	12,384	0.98 (0.64–1.51)
227–453.9	84	41,812	0.91 (0.66–1.25)	42	27,840	1.05 (0.68–1.60)	32	9,678	0.75 (0.44–1.27)
≥454	178	81,144	0.91 (0.71–1.17)	86	53,206	1.00 (0.70–1.41)	70	19,626	0.74 (0.49–1.12)
p_{trend}			0.46			0.99			0.16
Ice cream									
0	554	257,752	1.00 (REF)	218	134,326	1.00 (REF)	246	67,580	1.00 (REF)
1–16.9	82	35,428	0.88 (0.62–1.23)	34	23,352	0.74 (0.44–1.23)	34	8,132	0.98 (0.59–1.64)
17–32.9	186	101,014	0.84 (0.66–1.07)	106	70,976	0.90 (0.65–1.25)	63	20,461	0.89 (0.61–1.31)

Table 2 continued

Dairy foods (g/week)[a]	Type of breast cancer								
	Total			Premenopausal			Postmenopausal		
	n_{cases}	Person-years	MVRR (95 % CI)	n_{cases}	Person-years	MVRR (95 % CI)	n_{cases}	Person-years	MVRR (95 % CI)
33–65.9	227	114,197	1.02 (0.81–1.27)	115	81,837	0.99 (0.72–1.35)	83	22,049	1.02 (0.71–1.46)
≥66	219	108,837	0.87 (0.68–1.10)	99	74,091	0.83 (0.59–1.17)	95	24,359	0.91 (0.63–1.30)
p_{trend}			0.43			0.51			0.69

Multivariable relative risks were adjusted for energy intake (quintiles), age at menarche (<12, 12–13, ≥14 years), body mass index (<25, 25–29, ≥30 kg/m^2), family history of breast cancer (mother or sister), education (≤12, 13–15, ≥16 years), parity and age at first live birth (nulliparous, parity 1–2 and age at first birth <25 years, parity 1–2 and age at first birth 25–29 years, parity 1–2 and age at first birth ≥30 years, parity ≥3 and age at first birth <25 years, parity ≥3 and age at first birth 25–29 years, parity ≥3 and age at first birth ≥30 years), oral contraceptive use (yes/no), menopausal status (postmenopausal, premenopausal, and uncertain), age at menopause (<35, 35–39, 40–44, 45–49,50–54, ≥55 years), menopausal hormone use (yes/no), vigorous physical activity (none, ≤2, >2 h/week), smoking status (never, former, current), and alcohol intake (none, 1–3, 4–6, ≥7 drinks/week)

[a] Milk: 18 oz serving is equivalent to 245 g; hard cheese: 1 oz serving is equivalent to 28 g; cottage cheese: 10.5 cups serving is equivalent to 105 g; yogurt: 1 cup serving is equivalent to 227 g; ice cream: 10.5 cups serving is equivalent to 66 g

[16, 30, 31]. When we examined subtypes of breast cancer by hormone receptor status, we observed similar estimates for intake of meat items as those reported for all breast cancers. In the Swedish Mammography cohort, red meat was not associated with ER+/PR+, ER+/PR− and ER−/PR− breast cancers [19]. However, in the Nurses' Health Study II, higher red meat intake was associated with an almost twofold higher risk of ER+/PR+ breast cancers, but not ER−/PR− breast cancers [20].

For dairy intake, there were a few statistically significant trends in the risk estimates according to hormone receptor status—inverse associations of whole milk with ER− and PR− breast cancer, yogurt with ER− and PR− breast cancer, and ice cream with ER+ and PR− breast cancer. Dairy foods have been hypothesized to have pro- and anti-carcinogenic effects. Dairy foods contain nutrients such as calcium, vitamin D, and conjugated linoleic acids [32, 33]. Calcium, vitamin D, and conjugated linoleic acids have been shown to have effects on cell proliferation, differentiation, and/or inhibit tumor development [32–35]. Vitamin D also has been shown to interrupt insulin and insulin-like growth factor 1(IGF-1) activity, which may lower carcinogenic risk as insulin stimulates a rise in free IGF-1, which may promote cell cycle progression and angiogenesis, and is anti-apoptotic [36–42]. Therefore, it is plausible that dairy consumption may reduce breast cancer risk. However, applying a 5 % false-positive rate to our findings, we would estimate that approximately 9 or 10 significant findings may be due to chance; confirmation by other studies of the inverse associations found in our study is needed.

Since diet was measured prior to diagnosis of breast cancer, it is unlikely that the reporting of meat and dairy intake would be systematically biased. Misclassification of meat and dairy intake would likely be non-differential, and such misclassification would have attenuated the relative risk estimates for the relation between intakes of meat and dairy and risk of breast cancer. The use of baseline dietary information only might result in greater misclassification of usual consumption versus diet information from multiple assessments throughout follow-up. In our analyses, measurement of dietary intake was updated during the follow-up so that measurement error was potentially reduced; the results were similar when we examined baseline only or cumulative updated dietary data. We were also not able to assess the potentially carcinogenic compounds that are found in meats, including *N*-nitroso compounds, heterocyclic amines, or polycyclic aromatic hydrocarbons [13–15] as information on items such as cooking methods was not collected. Further, an appreciable proportion of African-Americans, with estimates ranging from 24 to 80 %, have reported having physical discomfort after eating dairy products or have stated they are lactose-intolerant [43, 44]. There was no information in the BWHS on this problem. However, we were able to examine large variation in intakes of the foods under study.

Strengths of the present study include the prospective design, large population, high follow-up rate [27], and high accuracy of self-report of breast cancer [27]. It is possible that individuals who were diagnosed close in time to baseline may have changed their diets due to prediagnostic symptoms. However, in analyses where we excluded the first 2 years of follow-up, the results were similar to the overall results.

In conclusion, no statistically significant associations were observed for intakes of meat, types of meat, milk, types of dairy, dietary calcium, and dietary vitamin D with risk of total, premenopausal, and postmenopausal breast

Table 3 Multivariable-adjusted relative risk (MVRR) and 95 % confidence interval (CI) of breast cancer by menopausal status by categories of intake of meat

Meats (g/week)[a]	Type of breast cancer								
	Total			Premenopausal			Postmenopausal		
	n_{cases}	Person-years	MVRR (95 % CI)	n_{cases}	Person-years	MVRR (95 % CI)	n_{cases}	Person-years	MVRR (95 % CI)
Total meat									
<400	229	100,331	1.00 (REF)	103	64,221	1.00 (REF)	103	25,443	1.00 (REF)
400–599.9	262	110,340	1.02 (0.85–1.23)	119	71,461	0.99 (0.75–1.29)	110	26,730	1.01 (0.76–1.32)
600–799.9	241	105,897	1.01 (0.83–1.22)	102	70,534	0.85 (0.63–1.13)	94	24,410	0.95 (0.71–1.28)
800–999.9	198	82,818	1.08 (0.88–1.33)	87	55,375	0.94 (0.69–1.28)	79	18,611	1.05 (0.76–1.44)
≥1,000	338	156,820	1.04 (0.85–1.28)	162	107,936	0.94 (0.69–1.27)	134	33,012	1.04 (0.76–1.42)
p_{trend}			0.60			0.64			0.75
Red meat									
<100	492	197,620	1.00 (REF)	203	124,977	1.00 (REF)	223	51,235	1.00 (REF)
100–199.9	335	141,125	1.00 (0.86–1.15)	151	91,843	1.01 (0.83–1.22)	140	34,124	0.96 (0.77–1.19)
200–299.9	172	84,530	0.90 (0.75–1.09)	75	57,437	0.90 (0.70–1.14)	67	18,367	0.86 (0.65–1.15)
300–399.9	102	49,674	0.95 (0.76–1.19)	49	34,543	0.98 (0.73–1.31)	38	10,036	0.92 (0.64–1.32)
≥400	167	83,257	1.02 (0.83–1.24)	95	60,727	1.01 (0.78–1.30)	52	14,444	0.86 (0.62–1.20)
p_{trend}			0.83			0.89			0.39
Processed meat									
<100	851	364,025	1.00 (REF)	366	237,164	1.00 (REF)	177	44,973	1.00 (REF)
100–199.9	265	116,477	1.01 (0.87–1.17)	130	78,958	1.16 (0.96–1.40)	159	39,485	0.97 (0.77–1.22)
≥200	152	75,704	0.99 (0.82–1.20)	77	53,405	0.92 (0.72–1.18)	184	43,748	0.93 (0.69–1.27)
p_{trend}			0.96			0.97			0.64
White meat									
<100	225	96,243	1.00 (REF)	104	62,246	1.00 (REF)	97	23,951	1.00 (REF)
100–199.9	268	124,886	0.92 (0.77–1.10)	125	81,639	0.90 (0.71–1.13)	105	29,725	0.89 (0.67–1.18)
200–299.9	238	100,044	1.02 (0.84–1.23)	110	66,692	1.02 (0.80–1.29)	99	22,857	1.08 (0.81–1.44)
300–399.9	143	66,033	0.90 (0.72–1.11)	63	43,551	0.90 (0.67–1.20)	61	15,689	0.95 (0.68–1.33)
≥400	394	169,000	1.05 (0.87–1.25)	171	115,399	0.90 (0.72–1.13)	158	10,046	1.12 (0.85–1.47)
p_{trend}			0.45			0.47			0.25
Fish									
<100	453	222,891	1.00 (REF)	217	156,109	1.00 (REF)	177	44,973	1.00 (REF)
100–199.9	407	162,947	1.10 (0.95–1.26)	179	105,715	1.05 (0.87–1.25)	159	39,485	1.00 (0.80–1.25)
≥200	408	170,368	1.03 (0.89–1.19)	177	107,703	0.97 (0.80–1.17)	184	43,748	1.04 (0.83–1.30)
p_{trend}			0.69			0.77			0.71

Multivariable relative risks (MVRRs) were adjusted for energy intake (quintiles), age at menarche (<12, 12–13, ≥14 years), body mass index (<25, 25–29, ≥30 kg/m^2), family history of breast cancer (mother or sister), education (≤12, 13–15, ≥16 years), parity and age at first live birth (nulliparous, parity 1–2 and age at first birth <25 years, parity 1–2 and age at first birth 25–29 years, parity 1–2 and age at first birth ≥30 years, parity ≥3 and age at first birth <25 years, parity ≥3 and age at first birth 25–29 years, parity ≥3 and age at first birth ≥30 years), oral contraceptive use (yes/no), menopausal status (postmenopausal, premenopausal, and uncertain), age at menopause (<35, 35–39, 40–44, 45–49,50–54, ≥55 years), menopausal hormone use (yes/no), vigorous physical activity (none, ≤2, >2 h/week), smoking status (never, former, current), and alcohol intake (none, 1–3, 4–6, ≥7 drinks/week)

[a] Red meat: 1 (3–6 oz) serving is equivalent to 85–143 g; processed meat: 1 (e.g., 1 oz, 1 slice, 1 hotdog) serving is equivalent to 20–45 g; white meat: 1 (4–6 oz) serving is equivalent to 112–140 g; and fish: 1 (3–5 oz) serving is equivalent to 98–112 g

cancer. Further, there was little evidence of association with breast cancer classified according to hormone receptor status. These null results in African-American women, whose dietary patterns differ from those of white women, strengthen confidence that dairy and meat are not important factors in breast cancer incidence.

Table 4 Multivariable-adjusted RR (MVRR) and 95 % CI of breast cancer by receptor status for categories of intake of total milk and meat

	Type of breast cancer											
	ER+		ER−		PR+		PR−		ER+/PR+		ER−/PR−	
	n_{cases}	MVRR (95 % CI)	n_{cases}	MVRR (95 % CI)	n_{cases}	MVRR (95 % CI)	n_{cases}	MVRR (95 % CI)	n_{cases}	MVRR (95 % CI)	n_{cases}	MVRR (95 % CI)
Total milk (g/week)												
0	110	1.00 (REF)	73	1.00 (REF)	81	1.00 (REF)	96	1.00 (REF)	78	1.00 (REF)	69	1.00 (REF)
1–69.9	65	0.96 (0.55–1.66)	36	1.30 (0.57–2.96)	55	1.04 (0.56–1.92)	46	1.26 (0.62–2.58)	54	1.25 (0.86,1.79)	36	1.04 (0.67,1.59)
70–124.9	30	0.65 (0.31–1.36)	17	1.32 (0.52–3.36)	21	0.53 (0.21–1.28)	24	1.34 (0.59–3.00)	21	0.97 (0.59,1.58)	17	0.97 (0.55,1.68)
125–249.9	47	0.65 (0.34–1.20)	26	0.84 (0.34–2.07)	39	0.65 (0.32–1.32)	33	0.88 (0.40–1.92)	38	1.00 (0.66,1.49)	25	0.79 (0.48,1.27)
250–499.9	52	0.70 (0.39–1.25)	33	0.84 (0.35–2.01)	41	0.69 (0.36–1.34)	43	0.93 (0.44–1.94)	38	0.84 (0.56,1.26)	29	0.76 (0.48,1.20)
500–749.9	27	0.56 (0.26–1.19)	15	0.96 (0.35–2.58)	21	0.56 (0.23–1.32)	20	0.94 (0.39–2.23)	21	1.00 (0.61,1.64)	15	0.84 (0.47,1.50)
750–999.9	45	0.71 (0.37–1.34)	27	1.08 (0.44–2.63)	37	0.69 (0.33–1.43)	35	1.14 (0.52–2.45)	35	1.08 (0.71,1.63)	25	0.90 (0.55,1.46)
≥1,000	106	0.85 (0.50–1.44)	52	0.88 (0.39–1.99)	84	0.80 (0.44–1.47)	70	1.01 (0.50–2.02)	81	1.16 (0.83,1.63)	48	0.78 (0.52,1.16)
p_{trend}		0.45		0.34		0.32		0.65		0.73		0.14
Total meat (g/week)												
<400	91	1.00 (REF)	47	1.00 (REF)	68	1.00 (REF)	70	1.00 (REF)	68	1.00 (REF)	47	1.00 (REF)
400–599.9	93	0.94 (0.70–1.27)	64	1.20 (0.81–1.75)	85	1.15 (0.83–1.59)	69	0.87 (0.62–1.22)	81	1.09 (0.78,1.52)	60	1.37 (0.74,2.51)
600–799.9	98	1.12 (0.83–1.52)	54	1.06 (0.70–1.59)	77	1.19 (0.84–1.68)	71	0.95 (0.67–1.34)	73	1.13 (0.79,1.59)	48	0.78 (0.38,1.59)
800–999.9	77	1.20 (0.86–1.67)	42	1.05 (0.67–1.64)	56	1.18 (0.80–1.72)	62	1.08 (0.74–1.56)	54	1.13 (0.77,1.66)	40	0.93 (0.44,1.95)
≥1,000	123	1.20 (0.86–1.66)	72	0.99 (0.63–1.54)	93	1.22 (0.84–1.78)	95	0.93 (0.64–1.36)	90	1.18 (0.80,1.73)	69	0.91 (0.44,1.86)
p_{trend}		0.13		0.71		0.35		0.91		0.41		0.65

Multivariable relative risks (MVRRs) were adjusted for energy intake (quintiles), age at menarche (<12, 12–13, ≥14 years), body mass index (<25, 25–29, ≥30 kg/m^2), family history of breast cancer (mother or sister), education (≤12, 13–15, ≥16 years), parity and age at first live birth (nulliparous, parity 1–2 and age at first birth <25 years, parity 1–2 and age at first birth 25–29 years, parity 1–2 and age at first birth ≥30 years, parity ≥3 and age at first birth <25 years, parity ≥3 and age at first birth 25–29 years, parity ≥3 and age at first birth ≥30 years), oral contraceptive use (yes/no), menopausal status (postmenopausal, premenopausal, and uncertain), age at menopause (<35, 35–39, 40–44, 45–49,50–54, ≥55 years), menopausal hormone use (yes/no), vigorous physical activity (none, ≤2, >2 h/week), smoking status (never, former, current), and alcohol intake (none, 1–3, 4–6, ≥7 drinks/week)

Acknowledgments We gratefully acknowledge the continuing dedication of the Black Women's Health Study participants and staff. Data on breast cancer pathology were obtained from several state cancer registries (AZ, CA, CO, CT, DC, DE, FL, GA, IN, IL, KY, LA, MA, MD, MI, NC, NJ, NY, OK, PA, SC, TN, TX, and VA), and results reported do not necessarily represent their views. This study was supported by National Cancer Institute Grant R01 CA058420. The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Cancer Institute or the National Institutes of Health.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. American Cancer Society (2012) Cancer Facts & Figures 2012. American Cancer Society, Atlanta, GA
2. Honegger A, Humbel RE (1986) Insulin-like growth factors I and II in fetal and adult bovine serum. Purification, primary structures, and immunological cross-reactivities. J Biol Chem 261:569–575
3. Zapf J, Froesch ER, Humbel RE (1981) The insulin-like growth factors (IGF) of human serum: chemical and biological characterization and aspects of their possible physiological role. Curr Top Cell Regul 19:257–309
4. Outwater JL, Nicholson A, Barnard N (1997) Dairy products and breast cancer: the IGF-I, estrogen, and bGH hypothesis. Med Hypotheses 48:453–461
5. Cui Y, Rohan TE (2006) Vitamin D, calcium, and breast cancer risk: a review. Cancer Epidemiol Biomarkers Prev 15:1427–1437
6. Heaney RP (2008) Vitamin D and calcium interactions: functional outcomes. Am J Clin Nutr 88:541S–544S
7. Cross HS, Peterlik M (2009) Vitamin D, calcium, and cancer. Anticancer Res 29:3685
8. Peterlik M, Cross HS (2005) Vitamin D and calcium deficits predispose for multiple chronic diseases. Eur J Clin Invest 35:290–304
9. Peterlik M, Grant WB, Cross HS (2009) Calcium, vitamin D and cancer. Anticancer Res 29:3687–3698
10. Giovannucci E (2005) The epidemiology of vitamin D and cancer incidence and mortality: a review (United States). Cancer Causes Control 16:83–95
11. Giovannucci E, Liu Y, Rimm EB et al (2006) Prospective study of predictors of vitamin D status and cancer incidence and mortality in men. J Natl Cancer Inst 98:451–459
12. Guzey M, DeLuca HF (1997) A group of deltanoids (vitamin D analogs) regulate cell growth and proliferation in small cell carcinoma cell lines. Res Commun Mol Pathol Pharmacol 98:3–18
13. Genkinger JM, Koushik A (2007) Meat consumption and cancer risk. PLoS Med 4:e345
14. Lijinsky W (1999) N-Nitroso compounds in the diet. Mutat Res 443:129–138
15. Sinha R, Norat T (2002) Meat cooking and cancer risk. IARC Sci Publ 156:181–186
16. World Cancer Research Fund, Panel AIfCRE (2007) Food, nutrition, physical activity and the prevention of cancer: a global perspective. American Institute for Cancer Research, Washington, DC
17. Pala V, Krogh V, Berrino F et al (2009) Meat, eggs, dairy products, and risk of breast cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. Am J Clin Nutr 90:602–612
18. Dong JY, Zhang L, He K, Qin LQ (2011) Dairy consumption and risk of breast cancer: a meta-analysis of prospective cohort studies. Breast Cancer Res Treat 127:23–31
19. Larsson SC, Bergkvist L, Wolk A (2009) Long-term meat intake and risk of breast cancer by oestrogen and progesterone receptor status in a cohort of Swedish women. Eur J Cancer 45:3042–3046
20. Cho E, Chen WY, Hunter DJ et al (2006) Red meat intake and risk of breast cancer among premenopausal women. Arch Intern Med 166:2253–2259
21. Rosenberg L, Adams-Campbell L, Palmer JR (1995) The Black Women's Health Study: a follow-up study for causes and preventions of illness. J Am Med Women's Assoc 50:56–58
22. Block G, Hartman AM, Dresser CM, Carroll MD, Gannon J, Gardner L (1986) A data-based approach to diet questionnaire design and testing. Am J Epidemiol 124:453–469
23. Willett W (1998) Nutritional epidemiology, 2nd edn. Oxford University Press, New York
24. National Cancer Institute (2005) Diet*Calc analysis program, version 1.4.3. National Cancer Institute, Applied Research Program, Bethesda, MD
25. Puckett CD (1986) The educational annotation of ICD-9-CM; Diseases and procedures tabular lists. Channel Pub, Reno, NV
26. World Health Organization (2009) International statistical classification of diseases and related health problems, 10th revision. World Health Organization, Geneva
27. Palmer JR, Boggs DA, Wise LA, Ambrosone CB, Adams-Campbell LL, Rosenberg L (2011) Parity and lactation in relation to estrogen receptor negative breast cancer in African American women. Cancer Epidemiol Biomarkers Prev 20:1883–1891
28. Smith-Warner SA, Spiegelman D, Ritz J et al (2006) Methods for pooling results of epidemiologic studies: the Pooling Project of Prospective Studies of Diet and Cancer. Am J Epidemiol 163:1053–1064
29. Hu FB, Stampfer MJ, Rimm E et al (1999) Dietary fat and coronary heart disease: a comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. Am J Epidemiol 149:531–540
30. Chen WY, Colditz GA (2007) Risk factors and hormone–receptor status: epidemiology, risk–prediction models and treatment implications for breast cancer. Nat Clin Pract Oncol 4:415–423
31. Chlebowski RT, Anderson GL, Lane DS et al (2007) Predicting risk of breast cancer in postmenopausal women by hormone receptor status. J Natl Cancer Inst 99:1695–1705
32. Lipkin M, Newmark HL (1999) Vitamin D, calcium and prevention of breast cancer: a review. J Am Coll Nutr 18:392S–397S
33. Al Sarakbi W, Salhab M, Mokbel K (2005) Dairy products and breast cancer risk: a review of the literature. Int J Fertil Women's Med 50:244–249
34. Kritchevsky D (2000) Antimutagenic and some other effects of conjugated linoleic acid. Br J Nutr 83:459–465
35. Ip C, Chin SF, Scimeca JA, Pariza MW (1991) Mammary cancer prevention by conjugated dienoic derivative of linoleic acid. Cancer Res 51:6118–6124
36. Jones JI, Clemmons DR (1995) Insulin-like growth factors and their binding proteins: biological actions. Endocr Rev 16:3–34
37. Pietrzkowski Z, Mulholland G, Gomella L, Jameson BA, Wernicke D, Baserga R (1993) Inhibition of growth of prostatic cancer cell lines by peptide analogues of insulin-like growth factor 1. Cancer Res 53:1102–1106
38. Cohen P, Peehl DM, Lamson G, Rosenfeld RG (1991) Insulin-like growth factors (IGFs), IGF receptors, and IGF-binding proteins in primary cultures of prostate epithelial cells. J Clin Endocrinol Metab 73:401–407
39. Ngo TH, Barnard RJ, Leung PS, Cohen P, Aronson WJ (2003) Insulin-like growth factor I (IGF-I) and IGF binding protein-1 modulate prostate cancer cell growth and apoptosis: possible mediators for the effects of diet and exercise on cancer cell survival. Endocrinology 144:2319–2324
40. Kaplan PJ, Mohan S, Cohen P, Foster BA, Greenberg NM (1999) The insulin-like growth factor axis and prostate cancer: lessons from the transgenic adenocarcinoma of mouse prostate (TRAMP) model. Cancer Res 59:2203–2209
41. Ruan W, Powell-Braxton L, Kopchick JJ, Kleinberg DL (1999) Evidence that insulin-like growth factor I and growth hormone are required for prostate gland development. Endocrinology 140:1984–1989
42. DiGiovanni J, Kiguchi K, Frijhoff A et al (2000) Deregulated expression of insulin-like growth factor 1 in prostate epithelium leads to neoplasia in transgenic mice. Proc Natl Acad Sci USA 97:3455–3460
43. Keith JN, Nicholls J, Reed A, Kafer K, Miller GD (2011) The prevalence of self-reported lactose intolerance and the consumption of dairy foods among African American adults are less than expected. J Natl Med Assoc 103:36–45
44. Sahi T (1994) Genetics and epidemiology of adult-type hypolactasia. Scand J Gastroenterol Suppl 202:7–20