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Background More than 20 studies have investigated the relation between meat and dairy food consumption and breast cancer risk with conflicting results. Our objective was to evaluate the risk of breast cancer associated with meat and dairy food consumption and to assess whether non-dietary risk factors modify the relation.

Methods We combined the primary data from eight prospective cohort studies from North America and Western Europe with at least 200 incident breast cancer cases, assessment of usual food and nutrient intakes, and a validation study of the dietary assessment instrument. The pooled database included 351 041 women, 7379 of whom were diagnosed with invasive breast cancer during up to 15 years of follow-up.

Results We found no significant association between intakes of total meat, red meat, white meat, total dairy fluids, or total dairy solids and breast cancer risk. Categorical analyses suggested a J-shaped association for egg consumption where, compared to women who did not eat eggs, breast cancer risk was slightly decreased among women who consumed <2 eggs per week but slightly increased among women who consumed ≥1 egg per day.

Conclusions We found no significant associations between intake of meat or dairy products and risk of breast cancer. An inconsistent relation between egg consumption and risk of breast cancer merits further investigation.

Keywords Breast neoplasms, meat, dairy, epidemiology, dietary studies, pooled analysis

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More than 20 studies have investigated the relation between meat and dairy food consumption and breast cancer risk. Of the studies during the last decade that have evaluated the association between intake of meat and breast cancer risk, four (two case-control,[1,2] two prospective[3,4]) found no statistically significant association while four (one case-control,[5] three prospective[6–8]) reported a direct relation. A meta-analysis of 12 case-control and 5 cohort studies published between 1966 and 1993 reported an increased risk of breast cancer with high versus low meat intake (relative risk [RR] = 1.18, 95% CI : 1.06–1.32). The association with red meat consumption, evaluated in seven of these studies, was stronger (RR = 1.54, 95% CI : 1.31–1.82) than that observed for total meat consumption. A statistically significant association was not observed for poultry intake (RR = 0.94, 95% CI : 0.78–1.13).[9]

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Results on the association of non-fermented milk consumption with breast cancer have also been conflicting, with two studies observing an inverse relation,[10,11] one observing a direct effect,[8] and three observing no statistically significant association.[3,7,12] The meta-analysis referenced above reported an increased risk of breast cancer with high versus low consumption of milk (RR =1.20, 95% CI : 1.04–1.30) and with high versus low consumption of cheese (RR = 1.20, 95% CI : 1.02–1.40).[9]

To provide a comprehensive summary of the relation between meat and dairy consumption and breast cancer risk, we investigated these associations and potential non-dietary effect modifiers in the Pooling Project of Prospective Studies of Diet and Cancer (Pooling Project), using the primary data from eight large prospective studies.

Methods

Study inclusion

The Pooling Project has been described previously.[13] We obtained the primary data from eight prospective studies[3,7,14–19] (Table 1) that met the following inclusion criteria: (1) the study initially included at least 200 incident breast cancer cases, (2) diet assessment at baseline using a comprehensive food frequency questionnaire, and (3) availability of a validation study of the diet assessment instrument or closely related instrument. Follow-up was conducted via questionnaires and the inspection of medical records and/or linkage to tumour and death registries and was estimated to be more than 90% complete in all cohorts. The Nurses' Health Study had repeated measurements of dietary intake and was divided into two cohorts—Nurses' Health Study (a) with follow-up from 1980–1986 and Nurses' Health Study (b) with follow-up from 1986–1996. Following the underlying theory of survival data, blocks of person-time in different time periods are statistically independent, regardless of the extent to which they are derived from the same people.[20] Therefore, pooling estimates from these two time periods is equivalent to using a single time period but takes advantage of the enhanced exposure assessment in 1986 compared to 1980. Because data regarding white meat and dairy product consumption were limited in the New York State Cohort, this study was included only in the red meat, milk product, and total dairy fluids analyses.

Dietary variables

Food intake was measured at baseline in each study by food frequency questionnaire. To account for portion size variation between and within study populations, food intake data were analysed as grams (rather than as servings) consumed per day. For the Iowa Women's Health Study, Nurses' Health Study (a), and Nurses' Health Study (b), the frequency data for each food item were converted to grams per day using a weight[21] for the serving size listed on the food frequency questionnaire. For the Adventist Health Study and New York State Cohort, serving sizes were not specified on the food frequency questionnaire, therefore, the most common serving size specified on the questionnaires from the other studies was used to estimate the portion consumed. For all studies, missing responses for food items were coded as zero intake.

Meat and dairy groups were defined using standard dietetic and nutritional guidelines. For analyses of meat consumption, the main groups were red meat (bacon, ground beef, roast beef, beef steak, pork, veal, lamb, blood pudding, ham, hot dogs, pâté, beef liver, chicken liver, pork liver, turkey liver, kidney, sausage, processed luncheon meats [e.g. ham, corned beef, salami, bologna]), white meat (fish fillet, canned fish, chicken, turkey, shrimp, lobster, scallops, oysters, clams), eggs (boiled, poached, fried, scrambled, omelettes), and total meat products (including all meat containing food items and eggs). Meat

Table 1 Characteristics of the cohort studies included in the pooled analysis of meat and dairy consumption and breast cancer

Study	Duration of follow-up	Baseline cohort size[a]	Age range (years)[b]	No. of cases[c]	Median intake (5th, 95th percentile) (g/day)[d]			
					Total Meat	Eggs	Total dairy fluids	Total dairy solids
Adventist Health Study	1976–1982	15 172	31–90	160	25 (1, 154)	11 (0, 40)	262 (0, 1101)	28 (2, 111)
Canadian National Breast Screening Study	1982–1987	56 837	40–59	419	181 (93, 341)	16 (3, 50)	247 (10, 633)	34 (6, 111)
Iowa Women's Health Study	1986–1995	34 406	55–70	1130	166 (67, 329)	7 (0, 40)	250 (9, 695)	23 (2, 88)
Netherlands Cohort Study	1986–1992	62 377	54–70	937	106 (46, 176)	14 (0, 28)	251 (32, 568)	33 (1, 109)
New York State Cohort	1980–1986	18 475	50–93	367	[e]		[e]	
New York University Women's Health Study	1985–1994	13 261	34–65	385	110 (41, 258)	14 (0, 60)	209 (15, 678)	24 (0, 94)
Nurses' Health Study (a)	1980–1986	89 046	35–60	1023	215 (96, 402)	22 (4, 50)	203 (5, 679)	27 (4, 109)
Nurses' Health Study (b)	1986–1996	68 817[f]	40–66	1638	163 (73, 291)	7 (0, 40)	231 (14, 715)	24 (3, 88)
Sweden Mammography Cohort	1987–1997	61 467	38–76	1320	91 (40, 166)	5 (0, 26)	219 (12, 555)	24 (3, 70)
Pooled Total		351 041		7379				

[a] Excluding women who met study-specific exclusion criteria, reported total energy intakes greater or less than three standard deviations from the study-specific $\log_e$-transformed mean energy intake of the baseline population, or who had been diagnosed prior to the baseline assessment with any cancer other than non-melanoma skin cancer.

[b] Among the cases and nested controls.

[c] Women diagnosed with invasive breast cancer.

[d] Among the controls.

[e] The New York State Cohort only ascertained intake of red meat (median intake = 67 (11, 168) g/day), and milk (median intake = 207 (0, 207) g/day).

[f] The women in Nurses' Health Study (b) were also members of Nurses' Health Study (a).

sub-groups included bacon products, sausage products (blood pudding, sausage), organ products (pâté, beef liver, chicken liver, pork liver, turkey liver, kidney), processed meats (bacon, blood pudding, ham, hot dogs, sausage, processed luncheon meats), poultry (chicken, turkey), seafood (fish fillet, canned fish, shrimp, lobster, scallops, oysters, clams), fish (including canned), and shellfish (shrimp, lobster, scallops, oysters, clams).

For analyses of dairy products, because there is considerable difference in the nutrient content of 100 g of a solid versus a liquid, fluids and solids were separated whenever possible. Therefore, the main dairy groups were total dairy fluids (whole cream, whipped cream, custard or pudding, ice cream, skim milk, 0.5% milk, 1% milk, 2% milk, whole milk, evaporated milk, buttermilk, sherbet, ice milk, sour cream, lite yoghurt, regular yoghurt, yoghurt dressing), and total dairy solids (butter, high fat cheese, low fat cheese, hard cheese, cottage cheese, ricotta cheese, cream cheese, other cheese). Dairy sub-groups included cheese products (high fat, low fat, hard, other), milk products (skim, 0.5%, 1%, 2%, whole, buttermilk, evaporated milk), yoghurt products (lite, regular, dressing), high fat dairy fluids (whole cream, whipped cream, ice cream, 2% milk, whole milk, sour cream, buttermilk, evaporated milk), high fat dairy solids (butter, hard cheese, high fat cheese, cottage cheese, ricotta cheese, cream cheese, other cheese), low fat dairy fluids (skim milk, 0.5% milk, 1% milk, sherbet, ice milk, lite yoghurt, regular yoghurt, yoghurt dressing, custard or pudding), fermented dairy fluids (buttermilk, sour cream, lite yoghurt, regular yoghurt, yoghurt dressing), fermented dairy solids (high fat cheese, low fat cheese, hard cheese, cottage cheese, ricotta cheese, cream cheese, other cheese), high fat non-fermented dairy fluids (whole cream, whipped cream, ice cream, 2% milk, whole milk, evaporated milk), and low fat non-fermented dairy fluids (skim milk, 0.5% milk, 1% milk, sherbet, ice milk, custard or pudding). A low fat dairy solids sub-group was not created, because only one dairy product—low fat cheese—fitted into this group.

Associations were also evaluated for individual meat and dairy items for which at least five studies provided data.

Statistical analyses

Exclusion criteria

Women were excluded from all analyses if they met study-specific exclusion criteria, reported total energy intakes greater or less than three standard deviations from the study-specific $\log_e$-transformed mean energy intake of the baseline population, or had been diagnosed before baseline with any cancer other than non-melanoma skin cancer.

Selection of cases and sampling of risk sets

To reduce computational burden with little loss of statistical efficiency,[22] the Adventist Health Study, Iowa Women's Health Study, New York State Cohort, New York University Women's Health Study, Nurses' Health Study (a), Nurses' Health Study (b), and Sweden Mammography Cohort were analysed as nested case-control studies with a 1:10 ratio of cases diagnosed with invasive breast cancer to controls. Controls were randomly selected from the group of women who were born in the same calendar year as the case and were alive, were not known to have migrated from the study area, and had not been diagnosed as having breast cancer (including carcinoma *in situ*) before the year in which the case was diagnosed. A nested case-control design also was used for the Canadian National Breast Screening Study, however, investigators of that study selected two controls for each case. The Netherlands Cohort Study used a case-cohort design.[23]

Models and analyses

For the nested case-control studies, incidence rate ratios (RR) were estimated by conditional logistic regression models using SAS PROC PHREG.[24] For the case-cohort study, EPICURE software was used.[25] When applicable, an indicator variable was created to account for missing non-dietary covariate data within a study. Two-sided confidence intervals (CI) were calculated for all effect estimates.

We analysed all meat and dairy food groups and items as continuous variables and exponentiated the regression coefficient to express the results in increments of 100 g per day (except for butter, whole cream, bacon, sausage, and processed meats that were expressed in increments of 10 g per day to more appropriately reflect plausible daily intake). Meat and dairy main groups and sub-groups were also modelled as quartiles. Study-specific quartiles were assigned based on the distributions of the control populations for the nested case-control datasets and the subcohort in the Netherlands Cohort Study. If more than 25% of the controls did not consume the specific dietary variable being evaluated, then the lowest level included all women who reported zero intake and the upper three levels represented tertiled non-zero intakes for that variable. If neither quartiles nor non-zero intake tertiles could be adequately assigned, the study was excluded from the quartile analysis of that dietary variable. To calculate the *P*-value for the test for trend across quartiles, women were assigned the median value of their quartile of intake and this new variable was entered as a continuous term in the regression model. Because egg intake was based on one or two variables in each study, we analysed egg consumption as a categorical variable with cutpoints based on identical absolute intakes across studies.

Non-dietary covariates

Non-dietary covariate information was reported by women in each study using self-administered questionnaires. Variables that were included as potential confounders or effect modifiers of the association between the dietary exposures of interest and breast cancer risk were coded using the categories footnoted in Table 2.

Because most of the studies collected information at baseline only, we assigned menopausal status at follow-up in each study using an algorithm based on an analysis of 42 531 Nurses' Health Study participants who were premenopausal in 1976 and remained premenopausal or had natural menopause by 1992 (details are described in a previous publication[26]). Breast cancer cases and their age-matched controls whose age at follow-up was 51 years or younger were considered to be premenopausal, between 51 and 55 years were considered as having an uncertain menopausal status, and 55 years or older were considered to be postmenopausal. This procedure was not applied to the Iowa Women's Health Study, New York State Cohort, and Netherlands Cohort Study, because these studies only included postmenopausal women.

For the total meat, red meat, white meat, eggs, total dairy fluids, and total dairy solids groups, we also evaluated whether the food group's relation with breast cancer risk was modified

Table 2 Pooled multivariate-adjusted[a] relative risks (RR) (95% CI) of breast cancer for a 100-g per day increment in meat and dairy consumption by menopausal status at follow-up[b]

	All Women[c,d]			Premenopausal Women			Postmenopausal Women[d]			
Exposure	RR	(95% CI)	*P*-value[e]	RR	(95% CI)	*P*-value[e]	RR	(95% CI)	*P*-value[e]	***P*-value[f]**
Total Meat	1.02	(0.97–1.08)	0.20	1.00	(0.87–1.14)	0.25	1.04	(0.99–1.09)	0.72	0.99
Red meat	0.98	(0.93–1.04)	0.63	0.97	(0.79–1.20)	0.18	0.97	(0.91–1.03)	0.55	0.85
White meat	1.02	(0.94–1.11)	0.13	0.99	(0.79–1.25)	0.11	1.05	(0.97–1.15)	0.22	0.36
Total Dairy Fluids	0.99	(0.97–1.00)	0.25	0.96	(0.90–1.02)	0.02	1.00	(0.98–1.01)	0.46	0.53
Total Dairy Solids	1.03	(0.95–1.11)	0.43	0.87	(0.68–1.11)	0.99	1.05	(0.94–1.16)	0.30	0.73

[a] Multivariate incidence rate ratios were adjusted for age at menarche (≤11, 12, 13, 14, ≥15 years), interaction between parity (0, 1–2, ≥3) and age at first birth (≤20, 21–25, 26–29, ≥30 years), oral contraceptive use (ever, never), history of benign breast disease (no, yes), family history of breast cancer (no, yes), smoking status (ever, never), education (< high school graduate, high school graduate, > high school graduate), body mass index (weight [kg]/height [m]^2; continuous), height (<1.60, 1.60–<1.65, 1.65–<1.70,1.70–<1.75, ≥1.75 m), alcohol intake (g/day; continuous), and total energy intake (continuous).

[b] Menopausal status at follow-up was determined using the algorithm described in the text.

[c] Also adjusted for menopausal status at follow-up (premenopausal, postmenopausal, uncertain) and the interaction of body mass index and menopausal status at follow-up.

[d] *Also adjusted for postmenopausal hormone use (ever, never).*

[e] The *P*-value, test of heterogeneity, is testing the null hypothesis that the study-specific relative risks do not differ.

[f] The *P*-value, test of effect modification, is testing the null hypothesis that there is no interaction between the food group of interest and menopausal status at follow-up. Studies that did not enrol both premenopausal and postmenopausal women at baseline (Iowa Women's Health Study, New York State Cohort, and the Netherlands Cohort Study) were not included in the interaction analyses.

by other established breast cancer risk factors. For each potential effect modifier, a cross-product term of the ordinal score for the level of each factor (categorical coding described in the footnotes of Table 2; alcohol consumption was categorized as 0, >0–15, and ≥15 g per day; body mass index was categorized as <21, 21–22, 23–24, 25–28, and ≥29 kg/m^2) and intake of the specific food group or food expressed as a continuous variable was included in the multivariate model. Women with missing values of the potential effect modifier were excluded from these analyses. Effect modification by age was analysed in two strata of postmenopausal women dichotomized at age 62. The pooled *P*-value for interaction was obtained using squared Wald statistics that were calculated by pooling the study-specific interaction coefficients and dividing by the square of the standard error of the pooled interaction term and referring the resulting statistics to a χ^2 distribution with one degree of freedom.

Pooling of relative risks

We used a random effects model developed by DerSimonian and Laird[27] to combine study-specific $\log_e$ RR, weighted by the inverse of their variance, to obtain a single pooled estimate. Tests of between-study heterogeneity were conducted using the asymptotic DerSimonian and Laird Q statistic.[27]

Results

In the eight prospective studies included in these analyses, the median total meat intake among the controls ranged from 25 g per day in the Adventist Health Study (where many cohort members are practising vegetarians due to religious guidelines with 8% reporting zero red or white meat intake and 18% reporting total meat intake of ≤5 g per day) to 215 g per day in Nurses' Health Study (a) (Table 1). For reference, 1 quarter-pound hamburger weighs 114 g, ½ chicken breast weighs 86 g, and 1 can of tuna weighs 170 g.[28] Median egg intake (1 egg weighs 50 g[28]) among the controls varied from 5 g per day in the Sweden Mammography Cohort to 22 g per day in the Nurses' Health Study (a). Variability among studies in dairy product consumption among the controls ranged from 203 to 262 g per day of dairy fluids (8 oz of milk weighs 244 g, 6 oz of yoghurt weighs 170 g) and from 23 to 34 g per day of dairy solids (1 oz of cheese weighs 28 g).[28]

When modelled as continuous variables, no significant associations were observed between total meat, red meat, white meat, total dairy fluids, and total dairy solid intakes and risk of breast cancer (Table 2). Statistically significant direct associations within the Nurses' Health Study (b) were observed for the effects of total meat (RR = 1.13 per 100 g per day increment, 95% CI : 1.03–1.21) and white meat (RR = 1.14 per 100 g per day increment, 95% CI : 1.03–1.26). For the effect of total dairy fluids, a statistically significant inverse association was found within the Canadian National Breast Screening Study (RR = 0.93 per 100 g per day increment, 95% CI : 0.87–0.99). There were no other statistically significant study-specific results. There was little evidence of confounding of the unadjusted results by the breast cancer risk factors included in our multivariate models (age-adjusted model data not shown) nor were the results altered by exclusion of cases that occurred in the first year of follow-up (data not shown). There was no evidence of effect modification by menopausal status.

When intakes of total meat, red meat, white meat, total dairy fluids, and total dairy solids were modelled as quartiles, no trends were observed in the associations of these groups with breast cancer risk (Table 3). In the opposite direction of the hypothesized deleterious association between red meat consumption and breast cancer risk[9], six of the nine study-specific point estimates comparing quartile 4 versus quartile 1 of red meat consumption were below the null (Figure 1).

The difference in median intake between quartiles 4 and 1 ranged from 83 g per day in the Sweden Mammography Cohort to 209 in Nurses' Health Study (a) for total meat intake, from 61 in the Sweden Mammography Cohort to 156 in the Nurses' Health Study (a) for red meat intake, and from 35 in the Adventist Health Study to 128 in the Nurses' Health Study (a) for white meat intake. The difference in median intake between

Table 3 Pooled multivariate-adjusted[a] relative risks (RR) (95% CI) of breast cancer by quartile of meat and dairy consumption

	Quartile 1	Quartile 2		Quartile 3		Quartile 4			
Exposure	RR	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	*P*-value[b]	*P*-value[c]
Total Meat	1.00 (ref)	1.07	(0.99–1.15)	1.02	(0.91–1.15)	1.08	(0.98–1.19)	0.13	0.29
Red meat	1.00 (ref)	1.00	(0.91–1.09)	0.99	(0.92–1.06)	0.94	(0.87–1.02)	0.13	0.58
White meat	1.00 (ref)	0.99	(0.88–1.10)	1.03	(0.91–1.16)	1.02	(0.91–1.13)	0.21	0.11
Total Dairy Fluids	1.00 (ref)	1.00	(0.93–1.07)	0.92	(0.82–1.02)	0.93	(0.84–1.03)	0.09	0.09
Total Dairy Solids	1.00 (ref)	1.02	(0.95–1.10)	0.94	(0.87–1.02)	1.01	(0.93–1.09)	0.94	0.98

[a] Multivariate incidence rate ratios were adjusted for age at menarche (≤11, 12, 13, 14, ≥15 years), interaction between parity (0, 1–2, ≥3) and age at first birth (≤20, 21–25, 26–29, ≥30 years), oral contraceptive use (ever, never), history of benign breast disease (no, yes), family history of breast cancer (no, yes), menopausal status at follow-up (premenopausal, postmenopausal, uncertain), body mass index (weight [kg]/height [m]^2; continuous), the interaction of body mass index and menopausal status at follow-up, postmenopausal hormone use (ever, never), smoking status (ever, never), education (< high school graduate, high school graduate, > high school graduate), height (<1.60, 1.60–<1.65, 1.65–<1.70, 1.70–<1.75, ≥1.75 m), alcohol intake (g/day; continuous), and total energy intake (continuous).

[b] The *P*-value, test for trend, is testing the null hypothesis that there is no significant trend in risk across quartiles.

[c] The *P*-value, test of heterogeneity, is testing the null hypothesis that the study-specific relative risks do not differ comparing quartile 4 to quartile 1.

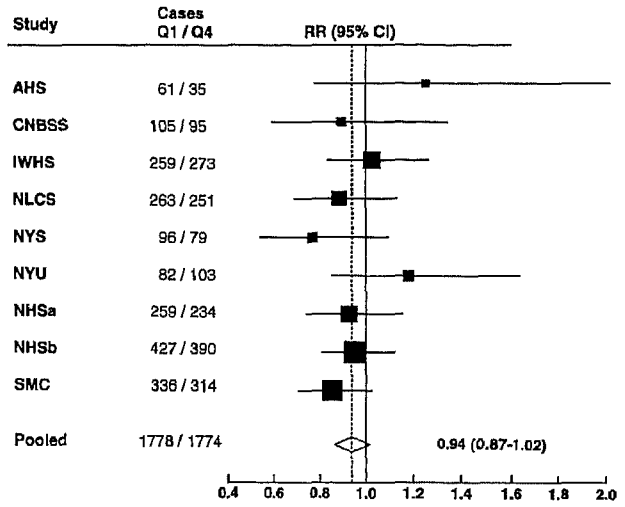

Figure 1 Study-specific and pooled multivariate-adjusted relative risks of breast cancer for red meat consumption—quartile 4 (Q4) versus quartile 1 (Q1)

The black squares and horizontal lines correspond to the study-specific relative risks and 95% confidence intervals, respectively, for the comparison of quartile 4 to quartile 1 of red meat consumption. The area of the black squares reflects the study-specific weight (inverse of the variance). The diamond represents the pooled relative risk and 95% confidence interval. The vertical dash line represents the pooled relative risk.

AHS = Adventist Health Study, CNBSS = Canadian National Breast Screening Study, IWHS = Iowa Women's Health Study, NLCS = Netherlands Cohort Study, NYS = New York State cohort, NYU = New York University Women's Health Study, NHSa = Nurses' Health Study (a), NHSb = Nurses' Health Study (b), SMC = Sweden Mammography Cohort.

quartiles 4 and 1 ranged from 366 g per day in the Sweden Mammography Cohort to 627 in the Adventist Health Study for total dairy fluids, while the difference ranged from 49 in the Iowa Women's Health Study to 84 in the Adventist Health Study for total dairy solids.

In the continuous analyses (Table 4) for the meat sub-group and specific animal product consumption, the risk of breast cancer was directly related only to egg consumption with risk increasing 22% per 100-g per day (approximately two eggs)

Table 4 Pooled multivariate-adjusted[a] relative risks (95% CI) of breast cancer for a 100-g per day increment in consumption of meat sub-groups and specific animal products[b]

Exposure	Relative risk	(95% CI)	*P*-value[c]
Total Meat			
Red meat			
Ground beef[i,l]	1.09	(0.89–1.34)	0.82
Organ products[e]	1.07	(0.61–1.88)	0.15
Processed meats[d,e]	0.98	(0.96–1.00)	0.99
Bacon products[d,e,i]	0.99	(0.89–1.09)	0.97
Sausage products[d,e,g,j,k]	0.94	(0.83–1.07)	0.31
Hot dogs[e,l]	0.75	(0.39–1.44)	0.57
White Meat			
Poultry[i]	1.05	(0.96–1.13)	0.64
Seafood[i]	1.01	(0.87–1.16)	0.07
Fish[i]	1.01	(0.87–1.17)	0.07
Shellfish[e,f,h,j,l]	0.77	(0.39–1.53)	0.76
Eggs	1.22	(1.03–1.45)	0.36

[a] See footnote [a] for Table 3 for description of how the relative risks were adjusted.

[b] Associations for the specific animal products were only evaluated if intake data were available for a minimum of five cohort studies.

[c] The *P*-value, test of heterogeneity, is testing the null hypothesis that the study-specific relative risks do not differ.

[d] 10-gram per day increment.

[e] The Adventist Health Study was not included in this analysis.

[f] The Canadian National Breast Screening Study was not included in this analysis.

[g] The Iowa Women's Health Study was not included in this analysis.

[h] The Netherlands Cohort Study was not included in this analysis.

[i] The New York State Cohort was not included in this analysis.

[j] The Nurses' Health Study (a) was not included in this analysis.

[k] The Nurses' Health Study (b) was not included in this analysis.

[l] The Sweden Mammography Cohort was not included in this analysis.

increase in daily intake (RR = 1.22, 95% CI : 1.03–1.45). Only the estimates from the Iowa Women's Health Study (RR = 1.44, 95% CI : 1.00–2.08) and Nurses' Health Study (b) (RR = 1.67, 95% CI : 1.20–2.32) were statistically significant. There was no evidence of effect modification by menopausal status for any of these associations (data not shown).

We evaluated the association with egg consumption after controlling for energy-adjusted cholesterol intake. While the pooled relative risk for cholesterol consumption in this updated dataset was 1.03 (95% CI : 1.00–1.07) for a 100-mg per day increment. When egg consumption was included in the model, the relative risk for cholesterol was attenuated (RR = 1.00, 95% CI : 0.95–1.05), but no material change in the relative risk for egg intake was observed (data not shown). In addition, when we controlled for saturated, polyunsaturated, and monounsaturated fat intakes, the effect estimate for egg consumption was unchanged (data not shown).

However, in the categorical analyses, a J-shaped association was observed with risk decreasing for >0–<14 g per day intake (RR = 0.93, 95% CI : 0.82–1.05), 14–<25 g per day intake (RR = 0.94, 95% CI : 0.82–1.09), and 25–<50 g per day intake (RR = 0.98, 95% CI : 0.80–1.21), and increasing for intakes of ≥50 g per day (RR = 1.07, 95% CI : 0.90–1.28) when compared to zero intake.

When meat sub-groups (organ products, processed meats, bacon products, sausage products, poultry, seafood, and fish) were modelled as quartiles, no trends were observed in the associations of these groups with breast cancer risk (data not shown).

No statistically significant associations were observed between dairy sub-group or specific dairy product intakes and the risk of breast cancer in the continuous analyses (Table 5). There was no evidence of effect modification by menopausal status (data not shown). When the dairy sub-groups (milk products, low fat dairy fluids, low fat non-fermented dairy fluids, high fat dairy fluids, high fat non-fermented dairy fluids, fermented dairy fluids, yoghurt products, high fat dairy solids, fermented dairy solids, cheese products) were modelled as quartiles, no trends were observed in the associations of these groups with breast cancer risk (data not shown).

We investigated whether several non-dietary breast cancer risk factors modified the association between intakes of the main meat and dairy groups and breast cancer risk. Of the 84 interactions tested, two significant pooled interactions were observed: (1) age at first birth and red meat consumption (*P*-value, test of effect modification = 0.03), and (2) age at menarche and total meat consumption (*P*-value, test of effect modification = 0.03). The relative risk for a 100-g per day increment in red meat consumption was 1.08 (95% CI : 0.94–1.24) for women who gave birth at age ≤20 and 0.84 (95% CI : 0.70–1.01) for women who gave birth after age 30. The relation decreased monotonically across the four categories of age at first birth. The relative risk for a 100-g per day increment in total meat consumption was 0.96 (95% CI : 0.89–1.05) for women who began menstruating before age 12 and 1.08 (95% CI : 0.96–1.20) for women who began menstruating at age ≥15. This association was also monotonic across the five categories of age at menarche, although the change in the relative risks across categories was small.

Table 5 Pooled multivariate-adjusted[a] relative risks (95% CI) of breast cancer for a 100-g per day increment in consumption of dairy sub-groups and specific dairy products[b]

Exposure	Relative risk	(95% CI)	*P*-value[c]
Total Dairy Fluids			
Milk products[d,f]	0.99	(0.97–1.00)	0.24
Skim and low fat milk[j]	0.99	(0.97–1.01)	0.27
Whole milk	0.99	(0.96–1.01)	0.53
Low fat dairy fluids	0.99	(0.98–1.01)	0.28
Low fat non-fermented dairy fluids	0.99	(0.97–1.01)	0.23
High fat dairy fluids	0.99	(0.97–1.01)	0.51
High fat non-fermented dairy fluids	0.99	(0.97–1.01)	0.52
Whole cream[e,i,j]	1.01	(0.98–1.04)	0.75
Ice cream[g,j]	1.03	(0.88–1.22)	0.37
Fermented dairy fluids[d]	0.98	(0.94–1.01)	0.88
Yoghurt products[g]	0.98	(0.94–1.01)	0.84
Total Dairy Solids			
High fat dairy solids	1.03	(0.95–1.11)	0.47
Butter[e,g,h]	1.02	(0.95–1.10)	0.04
Cottage cheese[j]	0.97	(0.85–1.09)	0.21
Fermented dairy solids[d]	1.00	(0.91–1.11)	0.26
Cheese products	1.16	(0.98–1.37)	0.50

[a] See footnote for Table 3 for description of how the relative risks were adjusted.

[b] Associations for the specific dairy products were only evaluated if intake data were available for a minimum of five cohort studies.

[c] The *P*-value, test of heterogeneity, is testing the null hypothesis that the study-specific relative risks do not differ.

[d] Components of this sub-group are also included in the low or high fat sub-groups.

[e] 10-gram per day increment.

[f] The New York State Cohort was included ONLY in this dairy product analysis.

[g] The Adventist Health Study was not included in this analysis.

[h] The New York University Women's Health Study was not included in this analysis.

[i] The Nurses' Health Study (a) was not included in this analysis.

[j] The Sweden Mammography Cohort was not included in this analysis.

Discussion

In this analysis of the association between meat and dairy product consumption and the risk of breast cancer using pooled data from eight prospective studies, we found no relation with meat intake, whether evaluated as total meat, red meat, white meat, eight sub-groups, or two specific meats. Our findings suggest a possible modest increase in risk with egg consumption. No relation with dairy products, analysed as total dairy fluids, total dairy solids, ten sub-groups, or seven specific foods, was found.

Our finding of no significant association between meat consumption and breast cancer risk supports the results of several studies[2–4] but contradicts the approximated doubling of risk associated with high versus low red meat intake reported by two prospective studies[6,7]—one of these studies, the New York University Women's Health Study, is included in the present analyses.[7] However, in our analysis, the association for this study was attenuated compared to the previously published result, possibly because we included four additional years of follow-up (1991–1994) in our analysis. When we modelled red meat consumption in quintiles adjusting for energy intake as in the original published report, the association remained attenuated (RR comparing quintile 5 versus quintile 1 = 1.15, 95% CI : 0.81–1.63). However, when we restricted the follow-up to those

diagnosed prior to 1991, we observed a relative risk and 95% CI similar to that of the original publication.

A limitation of our analysis of the association between meat consumption and breast cancer risk was our inability to assess the effect of cooking method and doneness level, because the data were not collected in most of the studies included in our analyses. Well-cooked meats, especially those cooked to the point of charring, contain heterocyclic amines and other compounds that are known carcinogens.[2,4,5,29] In the Iowa Women's Health Study a positive dose-response relation between doneness of meat and breast cancer risk was found, with women who consistently consumed very well-done hamburger, beef steak, and bacon having a nearly five-fold increase in risk as compared to women who reported consuming these meats rare or medium-done.[29] However, the overall lack of association observed in our pooled analyses suggests no adverse effects of meats as usually cooked.

Another limitation of our analyses is that we could not correct for measurement error, because few of the studies in our analysis conducted food or food-group based analyses in their validation studies.[30–32] In addition, due to among-study differences in questionnaire design, the number of studies included in the sub-group and specific food analyses varied depending on whether the foods comprising a particular sub-group were asked about on a study's questionnaire. Consequently, the power to examine associations for some sub-groups and specific foods is more limited compared with that for analyses of the main meat and dairy groups.

Breast cancer risk was found to increase by 22% with every 100-g per day increment of egg consumption. However, the J-shape of the relation observed in the categorical analysis suggests that the significant linear direct association with egg consumption from the continuous analysis is due to the combination of a non-significant inverse association among women with low egg intake and a non-significant positive association in the high intake range. Our finding may be due to chance, since we examined a large number of specific foods and food groups in these analyses and the association was not monotonic in the categorical analyses.

Eggs are particularly high in cholesterol (425 mg per 100-g portion,[21] US recommended daily allowance (RDA) = 300 mg[33]). However, when egg and cholesterol intakes were modelled simultaneously, the association with eggs changed negligibly, while the association with cholesterol intake became null. We believe that the data are most consistent with the interpretation that the association with cholesterol is due mainly to eggs but that the association with eggs is not necessarily due to cholesterol. These results need to be interpreted cautiously, however, because the Pearson correlations between cholesterol and egg consumption in these studies were high, ranging from 0.67 to 0.84. In addition, when we controlled for saturated, monounsaturated, and polyunsaturated fat intakes, the effect estimate for egg intake was unchanged, suggesting that the fatty acid content of the eggs was not responsible for the positive association that we observed.

We examined a large number of potential interactions (84) between established breast cancer risk factors and these animal product food groups. Two interactions were statistically significant, about what would be expected due to chance, and we are unaware of plausible biological explanations for the specific interactions that we observed.

In our analyses, we formed study-specific quartiles rather than defining categories based on identical absolute intakes, because differences in estimated absolute meat and dairy consumption across the studies in the Pooling Project may be due to differences in questionnaire design, in addition to differences in true intakes among the different populations. This type of analysis would reduce our ability to detect an association if breast cancer risk was higher only above a threshold of intake, and if only a subset of the studies had a substantial number of women consuming above this threshold.[20] However, we observed little evidence that the risk estimates for comparisons of the highest versus lowest quartiles of intake were different among the studies.

In general, we observed little heterogeneity among studies. For analyses of all breast cancer cases combined, the *P*-value test for heterogeneity was only statistically significant for the analysis of butter (*P*-value = 0.04), with the study-specific relative risks varying between 0.89 (95% CI : 0.73–1.08) in the Iowa Women's Health Study to 1.11 (95% CI : 0.97–1.27) in the Canadian National Breast Screening Study. The criteria used to select the studies for inclusion in the Pooling Project were established in part to decrease between-study heterogeneity due to methodological differences. In addition, because we analysed the primary data from each study, we were able to define the food groups using standard criteria, use standardized analytical methods, and control for several breast cancer risk factors using identical categories. However, because these studies were conducted independently, heterogeneity still exists due to differences in geographical location, food frequency questionnaire design, age range, and food intake variability.

In conclusion, we found no significant association between most of the meat and dairy products that we evaluated and breast cancer risk. Our finding of a J-shaped relation with egg consumption warrants further study. Overall, however, this large study does not provide evidence that a diet high in meat and dairy products during mid or later life increases the risk of breast cancer among women in North America and Europe.

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KEY MESSAGES

- The primary data from eight prospective cohort studies were pooled to investigate the association between meat and dairy product consumption and breast cancer risk.
- The analyses included 7379 cases. A nested case-control design with 1:10 matching was applied to the raw data.
- No association was observed between meat and dairy product consumption and breast cancer risk.

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