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Macronutrient Composition Influence on Breast Cancer Risk in Hispanic and Non-Hispanic White Women: The 4-Corners Breast Cancer Study

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Abstract

The association of dietary macronutrient composition with risk of breast cancer is not well understood. We investigated the macronutrient composition of diet in the 4-Corners Breast Cancer Study. Logistic regression models were used for case-control comparisons adjusted for age, center, education, smoking, total activity, calories, dietary fiber, dietary calcium, height, parity, recent hormone exposure, reference year body mass index (BMI), and the interaction of BMI and recent hormone exposure. Breast cancer risk declined with increasing dietary fat and increased with carbohydrates similarly across ethnicity and menopausal status. Associations of carbohydrate (direct) and fat (inverse), particularly saturated and monounsaturated fat, with breast cancer were present among normal and overweight postmenopausal women and absent among obese postmenopausal women. No substantive differences were noted in the association of macronutrients with risk of breast cancer between non-Hispanic white and Hispanic women. Associations of the macronutrients carbohydrate and fat with breast cancer risk were attenuated among postmenopausal obese women.

INTRODUCTION

Invasive breast cancer kills more than 40,000 women every year (1). However, there is little understanding of the relative contributions of dietary macronutrient composition to breast cancer rates. The rates of breast cancer (2) and obesity (3) differ among ethnic groups; the rate of breast cancer among Hispanic women is approximately one-third less than the rate among non-Hispanic white women (2), while the rate of obesity is higher (3). Our data suggest that the association between dietary patterns and dietary composition with rates of obesity differ when comparing Hispanic and non-Hispanic white control participants from the 4-Corners Breast Cancer Study (4). Additionally, these dietary patterns were differentially associated with risk of breast cancer; Western diet was associated with increased risk, whereas Native Hispanic and Mediterranean diets were associated with decreased risk (5).

There has long been the hypothesis that the fat composition of the diet is associated with breast cancer (6–10), but the literature does not consistently support that hypothesis. Some data do suggest an association between fat and breast cancer risk (11). The Women's Health Initiative reported that the 8-yr lowfat diet intervention was associated with a statistically non-significant reduction in postmenopausal breast cancer incidence (11). It may be important to note that risk was reduced among women with greater adherence to the lowfat diet. A recent co-hort study reported that positive associations of dietary fat and postmenopausal invasive breast cancer were confined to women who did not use hormone replacement at baseline (12). It is possible that the association of breast cancer with fat composition is operable within specific ranges of energy or fat intake or within specific subpopulations (12,13).

Information regarding the protein content of diet more often appears in the literature as a food-based analysis than as protein per se. For example, a prospective study suggested improved survival with consumption of protein from fish, dairy foods, and poultry (14). Meats cooked at high temperatures or to well-done are also reported to be positively associated with breast cancer. A recent meta-analysis suggested that there may be a small reduction in risk associated with soy intake among premenopausal women (15). Nonetheless, the role of protein as an energy-contributing macronutrient in breast cancer etiology is of interest.

We examined the association of energy and energy-contributing macronutrients (percent of calories from fat, protein, and carbohydrate) with risk for breast cancer women participating in the 4-Corners Breast Cancer Study, which uses a case-control design to study breast cancer etiology. We compared cases and controls stratified by ethnicity, menopausal status, and menopausal status within ethnicity and by body size [body mass index (BMI), waist circumference, and waist-to-hip ratio].

METHODS

Participants were from the four corner states of Arizona, Colorado, New Mexico, and Utah. Eligibility criteria included women between 25 and 79 yr of age, resident of the

geographically defined area of each state, and Hispanic, American Indian (not living on reservations), or non-Hispanic white. State tumor registries were used to identify and confirm case eligibility. The Utah, New Mexico, and Arizona (minority populations) state cancer registries are National Cancer Institute funded Surveillance Epidemiology and End Results (SEER) registries; Arizona (general) and Colorado registries are part of the Centers for Disease Control National Program of Cancer Registries. Eligible cases had a histological confirmed diagnosis for either in situ or invasive breast cancer (International Classification of Diseases for Oncology sites C50.0–C50.6 and C50.8–C50.9) between October 1999 and September 2004. Cases were identified as Hispanic or Native American from registry abstract data when available or by using the Generally Useful Ethnic Search System that identifies combinations of letters in last names to identify Hispanic women.

Controls were selected from the target populations and were frequency matched on the distribution of ethnicity and 5-yr age groups in cases. Controls under age 65 were randomly selected from a commercial mailing list in Arizona and Colorado and randomly selected from driver license lists in New Mexico and Utah. In all states, women age 65 and older were randomly selected from Center for Medicare Services lists. All participants signed informed written consent prior to participation; the study was approved by the Institutional Review Board for Human Subjects at each institution.

INTERVIEW AND ANTHROPOMETRIC DATA

Interviews were conducted in English or Spanish (participants chose the language) by trained and certified interviewers. The questionnaires included a diet history questionnaire and a health and lifestyle questionnaire with detailed information on physical activity history, medical and reproductive history, family history, smoking history, and medication use. The referent period for the questions was 1–2 yr prior to cancer diagnosis or selection as a control participant.

Each participant was asked at the conclusion of the interview to identify her race and ethnic background. Women were allowed to report multiple races. Those whose response was Hispanic, Latina, or American Indian and those whose response was white, Caucasian, or non-Hispanic white were included in the present analysis. Those women who self-identified as both Hispanic and white or American Indian and white were classified as Hispanic.

Women who were less than or equal to age 57 and still having regular periods, pregnant or breastfeeding, having periods and/or possibly going through menopause, and women who were having periods on hormone replacement therapy (HRT) were combined as premenopausal. Women who reported that their periods stopped naturally, because of an operation, medication, or because their ovaries were removed, or whose age was >57 yr were assigned a status of postmenopausal.

A computerized, interviewer-administered dietary history questionnaire (DHQ) (16) patterned after the Coronary Artery Disease in Young Adults Study DHQ (17,18) and adapted to include the current food supply and ethnic foods commonly consumed in the Southwestern United States was used to determine food consumption. Fifty-eight anchor questions were asked to elicit responses for consumption of hundreds of individual foods

such as whole milk, skim milk, and lowfat milk. At the end of the DHQ, participants were asked to report foods that they consumed, but that they had not already reported. Nutrient intake was calculated from the reported foods consumed using the Nutrition Data System for Research (NDS-R) Database Regents of the University of Minnesota.

ANTHROPOMETRIC MEASURES

Trained and certified staff measured height, weight, and waist and hip circumferences during an in-person interview, usually in the subject's home. Weight and height were measured twice, with the participant wearing light clothing and without shoes. Weight was measured on a flat, uncarpeted surface, using the TraveLite Portable Digital Scale and was recorded to the nearest 0.5 lb. Height was measured using the Road Rod Stadiometer. The horizontal headboard was lowered to the most superior point on the head and recorded to the nearest 0.25 in. Waist and hip circumferences were measured in sequence and repeated using an inelastic tape measure. The average of the two measurements was used for data analysis. BMI was calculated as weight in kg/height in meters squared and categorized for analysis as <25 (normal weight), 25 to <30 (overweight), and ≥30 (obese).

STATISTICAL METHODS

Statistical analysis was performed using SAS version 9.1 (SAS Institute, Cary, NC). Frequencies and percentages of various aspects of the study population were calculated with respect to race/ethnicity and menopausal status. Logistic regression models were used for case-control comparisons run by race/ethnicity and menopausal status and were adjusted for age, center, education, smoking, total activity, calories, dietary fiber, dietary calcium, height, parity, recent hormone exposure, reference year BMI, and the interaction of BMI and recent hormone exposure. As there were no differences in associations between ethnicities, further analyses were conducted by level of obesity (BMI category as <25, 25 to <30, and ≥30, waist circumference as <35 and ≥35 in, or waist-to-hip-ratio as <0.813 and ≥0.813) and menopausal status.

The interactions of macronutrient composition risk for breast cancer with ethnicity were assessed using multiple logistic regression models on both additive and multiplicative scales rather than assuming the nature of the relationship a priori. Macronutrient composition was utilized as ordered categorical variables in the multiplicative interaction models. Additive interaction, i.e., whether the odds ratio for a given menopause status and level of dietary exposure is significantly greater than the sum of the two individual odds ratios, was assessed using the relative excess risk from interaction (RERI) (19). For multiplicative interactions, we added a variable to our model that was the cross product of the two interaction terms and compared the likelihood ratio for that model with the model without the interaction term using a χ^2 test with 4 degrees of freedom to assess the statistical significance. A likelihood ratio test (1 degree of freedom) was conducted to determine trends in odds ratios (ORs), holding ethnicity and menopausal status constant with dietary factors or macronutrient composition as continuous variables. We designated the significance level for assessment of associations at $P = 0.05$ and for multiple level interactions at $P < 0.05$.

RESULTS

Table 1 shows the distribution of socioeconomic status, BMI, physical activity, and diet intake by ethnicity, menopausal status, and case status. Controls had higher BMI than cases. Cases had higher energy intake and percent of calories from carbohydrate, and lower percent of calories from fat and protein than controls (all ethnicities and menopausal status combined).

The association of diet with risk of breast cancer was similar among non-Hispanic white and Hispanic women. Risk of breast cancer decreased with a greater percentage of energy from total fat and decreased with increasing percent of calories from saturated and monounsaturated fats regardless of ethnicity (Table 2). There is the suggestion of a decrease in risk associated with increased consumption of polyunsaturated fat among Hispanic women, though little evidence that the association is different than among non-Hispanic whites. Conversely, risk of breast cancer increased with a greater proportion of carbohydrates among both non-Hispanic whites and Hispanic women.

We further examined whether the associations of macronutrients with risk of breast cancer among pre- and perimenopausal and postmenopausal women varied by BMI status (Table 3), waist-to-hip ratio, or waist circumference. Increasing calories from total fat and from monounsaturated fats was associated with decreased risk of breast cancer only among postmenopausal women who were normal weight or overweight, but not obese. No differences were evident by waist circumference or waist-to-hip ratio (data not shown). A greater percentage of energy from carbohydrates was associated with an increase risk of breast cancer among those postmenopausal women who were normal or overweight but no increase in risk among obese women. Among pre- and perimenopausal women with a small waist circumference, a high intake of vegetable protein as a proportion of energy intake was associated with a decreased risk of breast cancer, whereas no perceptible difference in risk associated with vegetable protein intake was found among women with a larger waist circumference (data not shown). A similar but statistically nonsignificant trend was noted when data were stratified by waist-to-hip circumference (data not shown).

DISCUSSION

We recently reported an increased risk of breast cancer with a Western diet pattern and a decreased risk with Mediterranean and Native Hispanic diets (5). Although we anticipated that the quality of fat might explain these differences, it was both carbohydrate and fat. A higher percent of calories from carbohydrates was associated with increased risk of breast cancer. A surprisingly consistent inverse association was observed with calories from total dietary fat and with saturated and monounsaturated fats. A decrease in breast cancer risk with increasing polyunsaturated fats was present only among postmenopausal Hispanic women. Generally, associations were not modified by ethnicity, menopausal status, or body size. However, among Hispanic women, the positive association of breast cancer with calories from carbohydrate and inverse association with calories from monounsaturated fat were overridden by obesity.

Perhaps the aspect that is most clear is that the association of total dietary fat intake and risk of breast cancer is difficult to characterize accurately and likely to continue to generate debate. Indeed, the inverse association of percent of calories from fat with breast cancer risk in the present report is unexpected biologically. Previously published evidence varies from no association of total fat with breast cancer risk (20,21) to a direct association of total fat (12,22,23). It is possible that the results vary with the quality of fat in the diet, as well as other characteristics of diet, lifestyle and hormone status of the study populations.

Positive associations of monounsaturated (12,23), saturated (12,23), and polyunsaturated fats (12,24) with risk of breast cancer have been reported. We observed an inverse association with percent of calories from saturated and monounsaturated fat in the present study, a finding consistent with the inverse association of the Mediterranean dietary pattern with breast cancer risk in this population (5). However, the finding conflicts with the positive association of monounsaturated fats and breast cancer risk from a European cohort study (23). In addition, the inverse association of saturated fat observed in this study appears to conflict with the positive association of the Western dietary pattern we previously reported (5). A positive association was also reported among those who never took HRT with high saturated fat intake, but no association among those who did take HRT in the EPIC study (23). Thiebaut et al. (25) suggest that the food source of α -linolenic acid may determine the direction of the association with breast cancer risk based on differing associations from studies in which meat (26) or fruits and vegetables (27) were the major contributor of α -linolenic acid. Thus a number of explanations for the apparent inconsistent associations of dietary fats with risk of breast cancer observed in the present study compared with prior reports are plausible.

An increasing contribution of carbohydrate to energy was associated with an increased risk of breast cancer. This result is in accordance with case-control studies of Mexican (28) and Italian women (27). A high intake of desserts and sugars has also been reported to increase risk of breast cancer (29). An Italian cohort found increased risk of breast cancer with intake of carbohydrates with a high glycemic index, but not carbohydrates in general (30). Additionally, no significant association of carbohydrates was observed in two other studies (31,32). The carbohydrate intake was lower in general in one of these studies, perhaps explaining the different finding (32). The data used for this report were collected between 1999 and 2004 when carbohydrate restriction for weight management was popular in the United States. Secular differences in food availability and or total diet composition from participants in this study and others may be important to interpretation of results. Nonetheless, an insulin-related mechanism could be responsible for this increased risk of breast cancer associated with carbohydrates and sugars. However, it is apparent that other factors such as range of intake or type of carbohydrate may be important components of this association.

Others have reported that dietary associations with breast cancer vary by long-term energy balance or body size (13,33,34). The contributions of total and monounsaturated fat to calories were associated with reduced risk of breast cancer except among postmenopausal women who were obese. Similarly, the increased risk associated with high carbohydrate intake was attenuated among postmenopausal obese women. These results are in accord with

those from an Italian cohort of pre- and postmenopausal women that reported decreased risk of breast cancer with increased raw vegetable and olive oil consumption (34), and with glycemic index (30), particularly among normal weight women (BMI <25). Although we observed decreased risk with protein among postmenopausal women with large waist size, the Nurses' Health Study found that the association of dietary fat was inverse among postmenopausal women with a waist circumference greater than 35 in (13). Although the literature is not entirely consistent, the common aspect of these findings is that among postmenopausal women, positive or protective aspects of dietary nutrients or foods are attenuated by larger body size or generalized, as opposed to central obesity.

Case-control studies are susceptible to recall bias. Recently, only small differences in diet (e.g., 1/4 serving of fruit and 1/3 serving of vegetables per day) were found in dietary intake of women when they were newly diagnosed and 2 yr after diagnosis, suggesting little bias in that population (35). Although participation rates in this study were not optimal, we have determined that surname selection of Hispanics was not associated with selection bias of cases and controls from this study (36). The reference period for diet and other exposures was 1 to 2 yr prior to diagnosis with cancer or selection for the study (controls). A recent Japanese study suggests a lag-time for the relationship of dietary fat intake with mortality from breast cancer of 20–32 yr and 19–31 yr for animal protein (37). The lag-time for incidence in our study would be shorter, but differences in background diet and type of fat consumed in Asia and the United States could influence the lag-time. Secular changes in food availability can contribute to the differences in macronutrient composition of diets conducted at different times and across a variety of geographical areas. Nonetheless, in this study, rigorous quality control standards were utilized to ensure the highest quality data collection possible.

Although statistical significance was often not achieved in all ethnic strata, in most cases the strength and direction of associations was similar, suggesting that the differences between the ethnic strata are more related to power or chance than true differences in association. Associations of macronutrient composition with breast cancer risk do appear to vary by body size (BMI) or waist circumference within menopausal status. Some of the reported differences in macronutrient associations with risk for breast cancer between studies may be related to differences in study populations and/or unrecognized confounding. Nonetheless, it suggests that associations of diet with risk for breast cancer are complex.

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TABLE 1
Participant characteristics and dietary composition of non-Hispanic white and Hispanic women

Characteristic	Non-Hispanic White				Hispanic			
	Control		Case		Control		Case	
	n	(%)	n	(%)	n	(%)	n	(%)
Age (yr)								
25–39	116	7.3	99	6.5	97	10.5	93	11.8
40–49	420	26.3	433	28.4	252	27.3	263	33.2
50–59	410	25.6	453	29.7	242	26.2	227	28.7
60–69	371	23.2	356	23.3	214	23.2	146	18.5
70–79	282	17.6	186	12.2	117	12.7	62	7.8
Education								
Elementary	5	0.3	2	0.1	101	11.0	85	10.8
<HS grad/GED	67	4.2	62	4.1	167	18.2	154	19.6
HS grad/GED	343	21.5	308	20.2	242	26.3	218	27.7
Some college	599	37.5	561	36.8	256	27.8	217	27.6
BA/BS or more	584	36.5	593	38.9	154	16.7	113	14.4
Smoker								
Never	939	59.0	839	55.0	600	65.4	523	66.3
Former	451	28.3	482	31.6	202	22.0	171	21.7
Current	202	12.7	204	13.4	116	12.6	95	12.0
Family history of breast cancer								
No	1298	85.1	1133	76.7	727	86.2	616	83.0
Yes	228	14.9	345	23.3	116	13.8	126	17.0
Estrogen receptor (ER) status								
Positive	—	—	830	80.4	—	—	395	74.2
Negative	—	—	202	19.6	—	—	137	25.8
Recent hormone exposure								
No	390	24.5	277	18.3	247	27.1	182	23.2
Yes	1201	75.5	1239	81.7	665	72.9	604	76.8

Characteristic	Non-Hispanic White						Hispanic					
	Control			Case			Control			Case		
	n	(%)	SD	n	(%)	SD	n	(%)	SD	n	(%)	SD
	mean			mean			mean			mean		
Referent year BMI	27.0	6.2	26.8	6.1	0.36	29.1	6.2	28.1	5.8	<.01	<.01	
Hours of vigorous PA/wk	4.9	5.6	4.9	5.6	0.72	4.2	6.0	4.3	6.1	0.60	0.89	
Calories	2120	1014	2213	1035	0.01	2657	1457	2732	1391	0.27	0.03	
Fat (% calories)	34.9	7.7	34.5	7.4	0.15	35.7	7.3	35.1	6.8	0.08	0.02	
Saturated fat (% calories)	11.9	3.4	11.7	3.3	0.25	12.2	3.1	12.1	2.9	0.37	0.12	
Monounsaturated fat (% calories)	12.8	3.2	12.6	2.9	0.02	13.2	3.1	13.0	2.8	0.11	<.01	
Polyunsaturated fat (% calories)	7.4	2.3	7.5	2.3	0.65	7.4	2.5	7.2	2.2	0.08	0.55	
Protein (% calories)	16.0	3.1	15.8	3.0	0.08	15.5	3.1	15.2	2.7	0.09	0.03	
Animal protein (% calories)	10.7	3.3	10.5	3.1	0.16	9.7	3.2	9.7	2.9	0.72	0.27	
Vegetable protein (% calories)	5.2	1.4	5.2	1.4	0.49	5.7	1.6	5.5	1.3	0.01	0.02	
Carbohydrates (% calories)	50.1	9.0	50.6	8.6	0.15	50.4	8.6	51.3	8.3	0.03	0.02	
Dietary fiber (g/1000 calories)	11.81	3.9	11.68	3.9	0.34	12.48	3.8	12.18	3.7	0.10	0.06	
Dietary calcium (mg/1000 calories)	503.3	179.4	497.5	174.0	0.36	455	166.2	455.9	156.0	0.91	0.63	

^a *P* value comparing case/control within each strata of ethnicity.

^b *P* value comparing non-Hispanic White and Hispanic women within case/control status.

TABLE 2

Association of macronutrients with risk of breast cancer stratified by ethnicity

Macronutrients	White, non-Hispanic				Hispanic			
	Control		Case		Control		Case	
	<i>n</i>	<i>n</i>	OR	95% CI	<i>n</i>	<i>n</i>	OR	95% CI
Percent fats								
30.1%	423	420	1.00		205	168	1.00	
30.2–35.5%	400	398	0.90	(0.73, 1.11)	221	241	1.09	(0.81, 1.47)
35.6–40.1%	386	365	0.82	(0.66, 1.02)	252	199	0.76	(0.56, 1.05)
40.2%	382	341	0.72	(0.57, 0.91)	241	180	0.64	(0.46, 0.90)
<i>P</i> trend			<.01				<.01	
<i>P</i> interactions:			Multiplicative = 0.62; Additive = 0.19					
Percent saturated fats								
9.8%	437	437	1.00		189	169	1.00	
9.9–11.9%	402	399	0.90	(0.73, 1.10)	230	197	0.80	(0.59, 1.08)
12.0–14.0%	359	339	0.80	(0.64, 1.00)	267	230	0.71	(0.52, 0.97)
14.1%	393	349	0.73	(0.58, 0.92)	233	192	0.67	(0.48, 0.93)
<i>P</i> trend			<.01				0.02	
<i>P</i> interactions:			Multiplicative = 0.66; Additive = 0.67					
Percent monounsaturated fats								
11.0%	434	446	1.00		197	163	1.00	
11.1–13.0%	407	410	0.86	(0.70, 1.06)	219	234	1.12	(0.83, 1.51)
13.1–15.0%	371	380	0.84	(0.68, 1.04)	263	227	0.83	(0.61, 1.13)
15.1%	379	288	0.59	(0.47, 0.74)	240	164	0.62	(0.44, 0.88)
<i>P</i> trend			<.01				<.01	
<i>P</i> interactions:			Multiplicative = 0.98; Additive = 0.16					
Percent polyunsaturated fats								
5.8%	377	369	1.00		247	208	1.00	
5.9–7.2%	416	375	0.89	(0.72, 1.09)	231	228	1.04	(0.79, 1.38)
7.3–8.8%	395	410	0.99	(0.80, 1.22)	233	188	0.79	(0.59, 1.06)

Macronutrients	White, non-Hispanic				Hispanic			
	Control		Case		Control		Case	
	<i>n</i>	<i>n</i>	OR	95% CI	<i>n</i>	<i>n</i>	OR	95% CI
8.9%	403	370	0.87	(0.70, 1.09)	208	164	0.77	(0.56, 1.05)
<i>P</i> trend			0.40				0.03	
<i>P</i> interactions:	Multiplicative = 0.32; Additive = 0.08							
Percent protein								
13.7%	364	357	1.00		269	235	1.00	
13.8–15.6%	384	397	1.06	(0.86, 1.30)	252	226	0.99	(0.76, 1.29)
15.7–17.5%	393	353	0.94	(0.76, 1.17)	208	174	0.94	(0.71, 1.24)
17.6%	450	417	0.97	(0.78, 1.21)	190	153	0.90	(0.66, 1.22)
<i>P</i> trend			0.56				0.45	
<i>P</i> interactions:	Multiplicative = 0.99; Additive = 0.55							
Percent animal protein								
8.2%	352	339	1.00		293	258	1.00	
8.3–10.0%	354	345	0.98	(0.79, 1.22)	245	208	0.92	(0.71, 1.19)
10.1–12.2%	415	439	1.08	(0.87, 1.33)	227	181	0.85	(0.65, 1.11)
12.3%	470	401	0.88	(0.70, 1.11)	154	141	0.97	(0.70, 1.34)
<i>P</i> trend			0.42				0.57	
<i>P</i> interactions:	Multiplicative = 0.73; Additive = 0.18							
Percent vegetable protein								
4.5%	485	485	1.00		176	153	1.00	
4.6–5.3%	418	418	1.09	(0.89, 1.33)	222	212	1.12	(0.83, 1.53)
5.4–6.1%	336	336	0.86	(0.68, 1.09)	234	210	1.08	(0.78, 1.51)
6.2%	352	352	0.85	(0.64, 1.14)	287	213	0.92	(0.61, 1.37)
<i>P</i> trend			0.14				0.62	
<i>P</i> interactions:	Multiplicative = 0.98; Additive = 0.36							
Percent carbohydrates								
44.7%	412	348	1.00		220	159	1.00	
44.8–50.1%	380	386	1.31	(1.06, 1.62)	238	204	1.26	(0.94, 1.68)
50.2–56.1%	409	403	1.34	(1.08, 1.65)	224	210	1.51	(1.12, 2.04)

Macronutrients	White, non-Hispanic				Hispanic			
	Control		Case		Control		Case	
	<i>n</i>	<i>n</i>	OR	95% CI	<i>n</i>	OR	95% CI	
56.2%	390	387	1.48	(1.06, 1.62)	237	215	1.70	(1.23, 2.34)
<i>P</i> trend			<.01		<.01			
<i>P</i> interactions:			Multiplicative = 0.78; Additive = 0.50					

Notes. Adjusted for age, center, education, smoking, total activity, calories, dietary fiber, dietary calcium, height, parity, recent hormone exposure, BMI, and interaction of recent hormone exposure and BMI.

TABLE 3

Association of macronutrients with risk of breast cancer stratified by BMI status

Pre/Perimenopause														
BMI < 25 kg/m ²					BMI 25–29.9 kg/m ²					BMI 30 kg/m ²				
Macronutrients	Control		Case			Control		Case			Control		Case	
	<i>n</i>	<i>n</i>	OR	95% CI		<i>n</i>	<i>n</i>	OR	95% CI		<i>n</i>	<i>n</i>	OR	95% CI
Percent fats														
30.1%	107	120	1.00			58	39	0.59	0.36, 0.98		28	28	0.82	0.45, 1.50
30.2–35.5%	102	114	0.83	0.56, 1.23		65	71	0.84	0.54, 1.31		54	50	0.77	0.47, 1.26
35.6–40.1%	80	104	0.93	0.61, 1.41		52	67	0.92	0.57, 1.48		55	60	0.73	0.45, 1.20
40.2%	98	104	0.66	0.43, 1.01		62	54	0.54	0.33, 0.88		60	51	0.52	0.31, 0.86
<i>P</i> trend			0.07					0.93					0.20	
<i>P</i> interactions:					Multiplicative = 0.94; Additive = 0.61									
Percent saturated fats														
9.8%	97	113	1.00			43	35	0.73	0.43, 1.25		31	25	0.64	0.35, 1.19
9.9–11.9%	107	102	0.74	0.50, 1.10		67	71	0.82	0.53, 1.29		40	41	0.82	0.48, 1.41
12.0–14.0%	92	121	0.93	0.62, 1.41		58	63	0.76	0.47, 1.22		64	71	0.78	0.48, 1.24
14.1%	91	106	0.77	0.50, 1.18		69	62	0.61	0.37, 0.98		62	52	0.55	0.33, 0.91
<i>P</i> trend			0.28					0.52					0.87	
<i>P</i> interactions:					Multiplicative = 0.84; Additive = 0.71									
Percent monounsaturated fats														
11.0%	112	138	1.00			63	45	0.54	0.34, 0.87		29	33	0.85	0.47, 1.51
11.1–13.0%	103	119	0.72	0.49, 1.05		65	79	0.80	0.51, 1.23		54	54	0.70	0.43, 1.13
13.1–15.0%	85	108	0.73	0.49, 1.10		56	66	0.70	0.44, 1.11		65	65	0.55	0.34, 0.88
15.1%	87	77	0.46	0.30, 0.72		53	41	0.39	0.23, 0.66		49	37	0.38	0.22, 0.66
<i>P</i> trend			<.01					0.49					0.02	
<i>P</i> interactions:					Multiplicative = 0.97; Additive = 0.14									
Percent polyunsaturated fats														
5.8%	108	116	1.00			64	43	0.58	0.36, 0.94		43	35	0.74	0.43, 1.26

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5.9–7.2%	91	104	0.94	0.64, 1.40	61	65	0.95	0.60, 1.50	45	57	1.08	0.66, 1.77
7.3–8.8%	97	114	0.96	0.64, 1.43	50	67	1.09	0.68, 1.75	59	49	0.63	0.39, 1.03
8.9%	91	108	0.91	0.60, 1.36	62	56	0.70	0.43, 1.12	50	48	0.73	0.44, 1.21
<i>P</i> trend			0.74				0.29				0.31	
<i>P</i> interactions:												
Percent protein												
13.7%	91	107	1.00		56	50	0.79	0.49, 1.29	34	48	1.16	0.68, 2.00
13.8–15.6%	107	112	0.96	0.64, 1.42	49	73	1.36	0.85, 2.18	49	53	0.96	0.58, 1.59
15.7–17.5%	91	102	1.07	0.71, 1.62	59	55	0.90	0.56, 1.46	62	40	0.60	0.36, 0.99
17.6%	98	121	1.19	0.79, 1.81	73	53	0.68	0.42, 1.09	52	48	0.89	0.54, 1.47
<i>P</i> trend			0.43				0.20				0.21	
<i>P</i> interactions:												
Percent animal protein												
8.2%	90	102	1.00		40	42	0.96	0.56, 1.63	39	41	0.92	0.53, 1.60
8.3–10.0%	95	98	0.92	0.61, 1.38	60	70	1.08	0.68, 1.73	39	50	1.16	0.68, 1.97
10.1–12.2%	110	125	1.04	0.70, 1.55	62	63	0.92	0.58, 1.47	57	49	0.73	0.44, 1.20
12.3%	92	117	1.13	0.74, 1.72	75	56	0.65	0.40, 1.04	62	49	0.71	0.43, 1.17
<i>P</i> trend			0.70				0.15				0.28	
<i>P</i> interactions:												
Percent vegetable protein												
4.5%	106	147	1.00		78	71	0.65	0.43, 0.99	58	56	0.65	0.41, 1.02
4.6–5.3%	97	132	1.00	0.68, 1.47	58	73	0.92	0.59, 1.45	61	61	0.75	0.47, 1.19
5.4–6.1%	83	70	0.62	0.40, 0.97	55	40	0.57	0.34, 0.95	41	44	0.84	0.49, 1.43
6.2%	101	93	0.72	0.44, 1.17	46	47	0.83	0.47, 1.45	37	28	0.58	0.31, 1.08
<i>P</i> trend			0.10				0.85				0.89	
<i>P</i> interactions:												
Percent carbohydrates												
44.7%	89	112	1.00		76	57	0.59	0.37, 0.92	60	51	0.67	0.41, 1.08
44.8–50.1%	88	117	1.17	0.78, 1.75	58	68	1.05	0.66, 1.66	58	56	0.83	0.51, 1.34
50.2–56.1%	110	104	0.88	0.59, 1.32	53	62	1.20	0.74, 1.94	48	48	1.03	0.61, 1.72
56.2%	100	109	1.23	0.80, 1.88	50	44	0.98	0.58, 1.65	31	34	1.15	0.64, 2.10
<i>P</i> trend			0.54				0.09				0.14	

<i>P</i> interactions:	Multiplicative = 0.13; Additive = 0.16											
	Postmenopause											
	BMI < 25 kg/m ²				BMI 25–29.9 kg/m ²				BMI ≥ 30 kg/m ²			
	Control		Case		Control		Case		Control		Case	
	<i>n</i>	<i>n</i>	OR	95% CI	<i>n</i>	<i>n</i>	OR	95% CI	<i>n</i>	<i>n</i>	OR	95% CI
Percent fats												
30.1%	169	172	1.00		139	134	1.03	0.74, 1.42	126	88	0.72	0.50, 1.03
30.2–35.5%	137	162	1.07	0.77, 1.47	124	127	0.94	0.67, 1.33	135	112	0.78	0.55, 1.11
35.6–40.1%	141	98	0.60	0.42, 0.85	143	125	0.78	0.56, 1.10	163	108	0.61	0.43, 0.87
40.2%	148	114	0.62	0.44, 0.88	134	94	0.58	0.40, 0.84	118	101	0.73	0.50, 1.06
<i>P</i> trend				<.01				<.01				0.79
<i>P</i> interactions:												
Multiplicative = 0.05; Additive = 0.10												
Percent saturated fats												
9.8%	201	188	1.00		141	139	1.15	0.84, 1.57	113	101	1.02	0.72, 1.44
9.9–11.9%	128	144	1.12	0.81, 1.55	136	128	0.98	0.70, 1.36	148	105	0.75	0.53, 1.05
12.0–14.0%	124	93	0.73	0.51, 1.04	142	111	0.76	0.54, 1.07	142	109	0.74	0.52, 1.06
14.1%	142	121	0.76	0.54, 1.08	121	102	0.78	0.55, 1.13	139	94	0.66	0.46, 0.96
<i>P</i> trend				0.05				0.04				0.07
<i>P</i> interactions:												
Multiplicative = 0.82; Additive = 0.73												
Percent monounsaturated fats												
11.0%	169	173	1.00		132	130	1.05	0.76, 1.46	125	82	0.67	0.47, 0.97
11.1–13.0%	138	156	1.03	0.74, 1.42	125	125	0.93	0.66, 1.31	137	109	0.77	0.55, 1.09
13.1–15.0%	136	108	0.70	0.49, 0.98	134	141	0.96	0.68, 1.34	154	116	0.72	0.51, 1.01
15.1%	152	109	0.61	0.43, 0.86	149	84	0.50	0.34, 0.71	126	102	0.72	0.50, 1.04
<i>P</i> trend				<.01				<.01				0.49
Pre/Perimenopause												
BMI < 25 kg/m ²				BMI 25–29.9 kg/m ²				BMI ≥ 30 kg/m ²				

Macronutrients	Control			Control			Control		
	<i>n</i>	<i>n</i>	OR	95% CI	<i>n</i>	<i>n</i>	OR	95% CI	<i>n</i>
<i>P</i> interactions:	Multiplicative = 0.03; Additive = 0.01								
Percent polyunsaturated fats									
5.8%	137	151	1.00		129	134	1.01	0.72, 1.42	142
									95
5.9–7.2%	152	136	0.78	0.56, 1.09	159	124	0.71	0.51, 1.00	133
7.3–8.8%	155	131	0.69	0.49, 0.97	128	127	0.87	0.61, 1.23	138
8.9%	151	128	0.72	0.51, 1.02	124	95	0.66	0.46, 0.96	129
<i>P</i> trend			0.03				0.07		
<i>P</i> interactions:	Multiplicative = 0.26; Additive = 0.17								
Percent protein									
13.7%	184	168	1.00		131	115	1.04	0.74, 1.45	135
13.8–15.6%	155	143	0.98	0.72, 1.35	141	134	1.06	0.77, 1.46	132
15.7–17.5%	130	118	0.94	0.67, 1.31	121	112	1.02	0.73, 1.44	135
17.6%	126	117	0.93	0.66, 1.32	147	119	0.85	0.61, 1.18	140
<i>P</i> trend			1.00				0.05		
<i>P</i> interactions:	Multiplicative = 0.82; Additive = 0.99								
Percent animal protein									
8.2%	182	171	1.00		134	100		0.73, 1.38	136
8.3–10.0%	159	125	0.81	0.58, 1.11	126	112	0.95	0.68, 1.33	119
10.1–12.2%	138	156	1.14	0.83, 1.57	128	122	1.01	0.72, 1.41	143
12.3%	116	94	0.78	0.54, 1.12	131	112	0.86	0.60, 1.21	144
<i>P</i> trend			0.94				0.17		
<i>P</i> interactions:	Multiplicative = 0.73; Additive = 0.74								
Percent vegetable protein									
4.5%	161	150	1.00		108	107	1.09	0.77, 1.56	148
4.6–5.3%	131	131	1.07	0.76, 1.51	144	127	0.94	0.67, 1.32	145
5.4–6.1%	125	118	0.98	0.68, 1.41	126	125	1.10	0.77, 1.57	137
6.2%	178	147	0.82	0.55, 1.20	162	121	0.82	0.56, 1.21	112
<i>P</i> trend			0.27				0.35		
<i>P</i> interactions:	Multiplicative = 0.23; Additive = 0.43								
Percent carbohydrates									
									0.20

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44.7%	156	112	1.00	130	77	0.86	0.59, 1.25	118	96	1.21	0.83, 1.75	
44.8–50.1%	125	102	1.20	0.83, 1.73	145	130	1.39	0.98, 1.98	140	116	1.31	0.91, 1.88
50.2–56.1%	146	163	1.80	1.28, 2.53	124	131	1.70	1.19, 2.44	148	99	1.14	0.79, 1.65
56.2%	168	169	1.70	1.20, 2.41	141	142	1.89	1.31, 2.72	136	98	1.32	0.90, 1.93
<i>P</i> trend	<.01											
<i>P</i> interactions:	Multiplicative = 0.04; Additive = 0.07											
	0.52											

* Adjusted for age, race, center, education, smoking, total activity, dietary fiber, dietary calcium, height, parity, and recent hormone exposure.

** Additive interaction was assessed using the relative excess risk from interaction (RERI) (19).

*** We added the cross product of the two interaction terms and compared the likelihood ratio for that model with the model without the interaction term using a χ^2 test with 4 degrees of freedom in multiplicative interactions.