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Dietary Fat and Breast Cancer in Postmenopausal Women According to Ethnicity and Hormone Receptor Status: The Multiethnic Cohort Study

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Abstract

Dietary fat has been widely studied as a risk factor for breast cancer, with little consistency in results. The Multiethnic Cohort Study (MEC) provides an opportunity to assess this relationship for possible hetero-geneity across different racial/ethnic groups, as well as by stratification on several other variables associated with risk. Therefore, we investigated the associations between dietary fat, overall and by type, and breast cancer risk among 85,089 postmenopausal women who entered the MEC by completing a comprehensive dietary questionnaire in 1993 to 1996. During a mean follow-up of 12 years, 3,885 incident invasive breast cancer cases were identified. The multivariate HR [95% confidence interval (CI)] for the highest versus lowest quintile of intake was 0.94 (95% CI, 0.85–1.05) for total fat and 0.93 (95% CI, 0.83–1.04) for saturated fat. Other specific types of dietary fat, including individual fatty acids, were not related to risk of postmenopausal breast cancer. We found no heterogeneity in these null findings across the five ethnic groups. Furthermore, we found no evidence that the association between dietary fat and postmenopausal breast cancer risk differed by estrogen/progesterone receptor status, tumor stage, body mass index, hormone replacement therapy use, follow-up period, family history of breast cancer, and smoking status at baseline. In conclusion, this comprehensive prospective analysis in the MEC does not support a role of adult intake of dietary fat in the etiology of postmenopausal breast cancer.

Introduction

The impact of diet, and particularly dietary fat, on breast cancer risk has been extensively studied (1). However, the results for dietary fat have been inconsistent and its role in the etiology of breast cancer remains controversial (2, 3). Several combined analyses have been conducted on the basis of published results or pooled data. Summary estimates for the

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relative risk indicated a mild increase in the risk of breast cancer related to higher dietary fat in an early meta-analysis of 16 case–control studies and 7 cohort studies in 1993 (4) as well as an updated meta-analysis by the same group 10 years later that included 31 case–control and 14 cohort studies (5). However, 2 pooled analyses of cohort studies only, in 1996 and 2001 (6, 7), failed to find any association. Furthermore, a recent meta-analysis of studies of animal fat intake and breast cancer risk also found no association (8). Although dietary measurement error has been cited as one of the reasons for lack of a significant association between dietary fat and breast cancer risk (9), 2 recent studies with large populations detected a weak but significant increase in breast cancer risk among women with a higher fat intake (10, 11). However, these studies were conducted in mostly white populations and could not examine possible differences by race/ethnicity.

The Multiethnic Cohort consists of participants from 5 ethnic groups. This diversity tends to lead to more variability in the range of dietary exposures: the average ranged from 27% in Japanese women to 32% in African American women for percentage of energy from total fat and from 7.4% to 9.5% for percentage of energy from saturated fat for these groups. In this study, we investigated the associations between dietary fat, overall and by type, and breast cancer risk among postmenopausal women in the Multiethnic Cohort. In addition, we conducted analyses to determine whether the risk of breast cancer associated with dietary fat differs according to ethnicity, as well as several other variables such as hormone receptor status.

Methods

Study population

The Multiethnic Cohort was established to study diet and cancer and has been described in detail elsewhere (12). In brief, more than 215,000 adults aged 45 to 75 years entered the cohort by completing a 26-page mailed questionnaire in 1993 to 1996. The study targeted African Americans, Native Hawaiians, Japanese, Latinos, and whites who were residents of Hawaii and California, mainly Los Angeles County, identified through drivers' license files, the Health Care Financing Administration files, and the Hawaii Voters' Registration file.

More than 99,800 women were postmenopausal at baseline and eligible for the analysis. Women who did not report their menopausal status and were older than 55 years at cohort entry were assumed to be postmenopausal and accounted for 8.7% of the eligible population. For the current analyses, we excluded women who were not from 1 of the 5 targeted racial/ethnic groups (n = 6,443) and who had prior breast cancer on the basis of questionnaire report or on information from tumor registry linkages (n = 4,683). In addition, women with invalid diets based on total energy intake or its components were excluded (n = 3,673). Therefore, a total of 85,089 women were included in the final analyses.

Breast cancer case identification

Incident cases of breast cancer were identified by linkage of the cohort to the Surveillance, Epidemiology, and End Results (SEER) cancer registries covering Hawaii and California. Because emigration outside the catchment area has been low (<5%), few incident cases are likely to have been missed. In addition, the cohort was linked to the Hawaii and California state death files and to the National Death Index file. Case and death ascertainment was completed through December 31, 2007. During the average follow-up period of 12.4 years, a total of 3,885 incident invasive cases were identified among the 85,089 postmenopausal women who were available for analysis.

Dietary assessment

Dietary intake was assessed by a self-administered Quantitative Food Frequency Questionnaire (QFFQ) with more than 180 food items covering the previous year at baseline (12). The development of the QFFQ has been described (13) and was based on individual food diaries maintained by a sample of men and women from each ethnic group. It was designed to include the minimum set of foods that contributed ≥85% of the intake for nutrients of interest in each ethnic group, as well as foods traditionally consumed by any group regardless of their nutrient contribution. Correlations between the QFFQ and three 24-hour recalls in a calibration study were satisfactory, with a range of 0.42 to 0.74 across the female ethnic groups for energy-adjusted fat intake; correlations were similar for the various fat components (13). Individual dietary intakes of total, saturated, and mono-/polyunsaturated fat, fatty acids, and cholesterol were calculated using a food composition table that has been developed and maintained by the University of Hawaii Cancer Center for the Multiethnic Cohort Study (12). Intakes of total, saturated, and mono-/polyunsaturated fats were expressed as a percentage of total energy intake and those of fatty acids and cholesterol as densities (g or mg/ 1,000 kcal), as we found in the calibration study that energy-adjusted intakes were better correlated with the reference instrument than were absolute intakes (13).

Statistical analysis

We used Cox proportional hazards models with age as the time metric to estimate HR of breast cancer and 95% confidence intervals (CI; refs. 14, 15).

All Cox models were adjusted for time since cohort entry (≤2, 2–5, and >5 years) and ethnicity (African American, Native Hawaiian, Japanese, Latina, and white) as strata variables and age at cohort entry (continuous) as a covariate to account for cohort effect. To ensure that the cohort and period effect were adequately controlled, we compared the results of our models with those using follow-up time as the time metric, with age and year of cohort entry as strata variables, and the results were unchanged. The multivariate models were additionally adjusted for family history of breast cancer (no, yes, missing), education (up to 12 years, more than 12 years, missing), body mass index (BMI: <25, 25–<30, ≥30 kg/m^2, missing), age at menarche (≤12, 13– 14, ≥15 years, missing), age at first live birth (no children, ≤20, 21–30, ≥31 years, missing), number of children for parous women (1, 2–3, ≥4, missing), age at and type of menopause (natural: age <45, 45–<50, 50–<55, ≥:55 years; oophorectomy: age <45, 45–<50, 2:50 years; hysterectomy: age <45, 45–<50, ≥50 years, missing), hormone replacement therapy (no current estrogen use, past estrogen use with or without progestin, current estrogen use without progestin, current estrogen use with past/current progestin, missing), smoking status (never, former, current, missing), energy intake (log transformed), and alcohol use at least once a month in the past year (yes, no).

Dietary intakes were divided into quintiles on the basis of the distribution of the intake among all women in the cohort. HRs were estimated for the upper 4 quintiles relative to the lowest quintile. The proportionality assumption was tested by Kaplan–Meier survival curves and Schoenfeld residuals and was found to be valid. A Wald test was used to test trend by entering the sex- and ethnicity-specific median values within the appropriate overall quintile as a continuous variable in the model. We reran the analyses using calibration-corrected intake values for fat variables; these are the predicted levels resulting from applying a calibration equation regressing the average intake from the three 24-hour recalls on QFFQ intake, as well as other important variables such as age, education, and BMI (13). We conducted analyses separately by estrogen and progesterone receptor (ER/PR) status (ER^+/PR^+, ER^+/PR^-, and ER^-/PR^- cases; there were too few ER^-/PR^+ cases for meaningful analysis) and by tumor stage (localized and regional/distant cases). Breast cancer cases not counted as events, such as ER^-/PR^- cases in the analysis of ER^+/PR^+ tumors, were censored at the age of diagnosis. A Wald test was used to test for heterogeneity across subtypes of cancer using competing risk methodology (16), where each sub-type was a different event. In the competing risk models, we allowed for ethnic-specific effects by ER/PR status or tumor stage to improve the model fit.

We also ran the models stratified by ethnicity (5 groups), BMI (<25, 25–<30, and ≥30 kg/m^2), use of hormone replacement therapy (ever and never users), follow-up period (<5 and ≥5 years), family history of breast cancer (yes and no), and smoking status at baseline (never, former, and current smokers). The *P* values for heterogeneity across subgroups of participants were based on the Wald test of the cross-product terms of the fat trend variables and the subgroup membership indicators. SAS version 9.2 (SAS Institute, Inc.) was used for all analyses.

Results

The baseline characteristics of the study population are presented in Table 1 according to total fat intake. Postmenopausal women with higher total fat intake tended to be younger, to be African Americans and Latina, to have less education, to be more obese, and to be younger at menarche and at first live birth, to have more children, to have surgical menopause, to not use hormone replacement therapy, and to consume more energy per day.

Table 2 shows the association of fat, overall and by type, with breast cancer. None of the fat intake variables was significantly associated with breast cancer risk in our cohort. Adjusting for all covariates did not make substantial changes to the associations. This was also true when we removed BMI and age at menarche as adjustment factors to avoid adjusting for intermediate variables in the pathway from dietary fat intake and breast cancer risk: the HRs across the quintiles for saturated fat were 1.00, 1.06, 1.10, 1.04, and 0.97 (P_{trend} = 0.60). We also observed no significant association with very low or very high relative fat intake: using a reference of 30.1% to 35% of energy, the multivariate HR was 0.93 (95% CI, 0.82–1.05) for a fat intake of ≤20% (360 cases) and 0.88 (95% CI, 0.65–1.20) for >45% (44 cases, data not shown). The same associations were seen in analyses using calibration-corrected intakes: the multivariate HR for the highest versus lowest quintile was 0.98 (95% CI, 0.87–1.10) for total fat intake and 0.92 (95% CI, 0.82–1.03) for saturated fat intake (data not shown).

In an analysis stratified by ethnicity, none of the 5 ethnic groups showed a significant relationship of dietary fat with postmenopausal breast cancer risk, although the test for heterogeneity across the ethnic groups was statistically significant for eicosapentaenoic acid and docosahexaenoic acid (Table 3) because of a slight increase in risk among Hawaiians and a slight decrease in risk among Latinas, neither of which were significant. When we examined the associations according to ER/PR status of the tumor, we also observed no significant associations (Table 4). Finally, we examined whether the associations varied by tumor stage, BMI, hormone replacement therapy use, follow-up period, family history of breast cancer, and smoking status. However, none of these factors modified the associations between dietary fat intake and postmenopausal breast cancer (data not shown).

Discussion

In this large Multiethnic Cohort in Hawaii and California, we found no evidence for an association of dietary fat with breast cancer risk among postmenopausal women. Specific types of dietary fat, including specific fatty acids, were also not related to breast cancer risk. Furthermore, we found little evidence that the association between dietary fat and postmenopausal breast cancer risk differed by ethnicity, EP/PR status, or tumor stage. This null finding was consistent in additional analyses stratified by BMI, hormone replacement therapy use, follow-up period, family history of breast cancer, and smoking status at baseline.

A substantial body of data is now available from cohort studies to assess the association between dietary fat and breast cancer risk. A meta-analysis of 14 cohort studies reported that the summary relative risk, comparing the highest and lowest levels of intake, was 1.11 (95% CI, 0.99–1.25) for total fat and 1.15 (94% CI, 1.02–1.30) for saturated fat (5). However, the Pooling Project of Prospective Studies of Diet and Cancer (7), in which the raw data from the individual studies were carefully harmonized before being combined, found no evidence of a significant association between dietary fat intake and the risk of breast cancer (relative risk = 1.09; 95% CI, 1.00–1.19, per a 5% increment of energy from saturated fat). Also, a recent meta-analysis of 11 cohort studies did not support a positive association between animal fat consumption and breast cancer (17). More recent findings from large cohort studies have also been inconsistent. In the NIH-AARP cohort (11), dietary fat intake was directly associated with risk of post-menopausal breast cancer (HR = 1.15; 95% CI, 1.05–1.26, for a 2-fold increase in total fat intake). The European Prospective Investigation into Cancer and Nutrition (EPIC) Study (10) reported a direct association of borderline statistical significance between saturated fat and breast cancer (HR for the highest vs. the lowest quintile = 1.13; 95% CI, 1.00–1.27). In contrast, the most recent report from the Nurses' Health Study, which had a relatively long follow-up period (20 years) compared with other cohort studies, found no associations between dietary fat and postmenopausal breast cancer (18). Three cohort studies in Asia suggested a protective effect of long-chain n-3 fatty acids (19) or an increased risk of breast cancer related to a combination of lower n-3 and higher n-6 intake (20, 21). In the present study, higher n-6/n-3 ratio was not associated with risk in the Asian (Japanese American) group, nor in any of the other ethnic groups.

Only 2 randomized intervention trials tested the effect of a low-fat diet on breast cancer risk in women with no previous history of this cancer. In the Women's Health Initiative (WHI), the investigators found a nonsignificant reduction in breast cancer risk among the women in the low-fat intervention arm (22). Although the intervention group experienced a modest weight loss during the early years of the trial, further analysis showed that weight change did not explain the finding. In the second trial, which tested the effect of a low fat/high carbohydrate diet in women at high risk of breast cancer, there was no weight reduction in the intervention group and the investigators found no effect of the dietary intervention (23). Two other fat reduction randomized intervention trials were based on patients who had been diagnosed with breast cancer. In the Women's Intervention Nutrition Study (WINS), dietary fat reduction showed a weak, nonstatistically significant reduction in relapse-free survival among patients with early-stage post-menopausal breast cancer, which was stronger in women with hormone receptor–negative cancers (24). However, as in the WHI trial, the intervention group also showed a modest weight loss. The second trial in patients with breast cancer, known as WHEL (Women's Healthy Eating and Living), tested the effect of a low fat/high vegetable/high fruit/high fiber diet (25). In this trial, the intervention group did not experience any weight loss, and the results were null. Although it is difficult to separate the effects of fat reduction from those resulting from weight loss and/or other simultaneous dietary modifications, there is the additional problem in the trials of patients with breast cancer that the effects of fat reduction may be different for recurrence than for initiation of the cancer.

Types of dietary fat, rather than total fat, may be related to the development of breast cancer (26). A meta-analysis of 3 prospective studies using biomarkers suggested that n-3 fatty acids may have a protective effect, whereas saturated fatty acids and monounsaturated fatty acids were related to an increased risk of breast cancer (27). In the present study, however, none of subtypes of dietary fat or specifi fatty acids showed a significant association with breast cancer.

Findings from both the WINS (24) and the WHI (22) trials suggested that the dietary effect of fat on breast cancer varied by hormone receptor status. In a cohort of postmenopausal women (27), the investigators also found a suggestion that dietary fat may be associated with ER^+/PR^+ tumors and not other breast cancer subtypes. However, the Nurses' Health Study found no variation in risk estimates by ER/PR status (18). In the Multiethnic Cohort, we found that the association of ethnicity and established risk factors and breast cancer risk differed by ER/PR status, which suggests etiologic heterogeneity of hormone receptor–defined subtypes of breast cancer (28). However, the dietary fat–breast cancer relation did not differ across the ER/PR subtypes in the present analysis.

Associations between dietary intake and the risk of breast cancer may vary by menopausal hormone therapy use, as they do for adiposity and breast cancer risk (29), because hormone therapy use is a strong risk factor (30) and may mask the effect of other risk factors on breast cancer development. If dietary fat affects endogenous estrogen levels and subsequently increases risk of breast cancer, this association may be more pronounced among women not using hormone replacement therapy, as was seen in the EPIC Study (10). However, when we restricted our analysis to women not using hormone replacement therapy, we still found no association between dietary fat and breast cancer (HR for the highest vs. lowest quintile of saturated fat = 0.95; 95% CI, 0.79–1.14, data not shown).

Our study has several strengths, beginning with its large size and prospective design. In addition, dietary exposures to fat have a relatively high variability, mainly due to the multiethnic composition of the population, and have been measured by a validated food frequency questionnaire and a comprehensive food composition table. In addition, however, we were able to examine the association separately by ethnicity. We were also able to control for various established or potential risk factors for breast cancer. Nevertheless, there are study limitations to be considered. Timing of the dietary exposure may be an important determinant of breast cancer risk. Maternal and childhood/adolescence dietary exposures may have an impact on breast cancer risk later in life (31). Unfortunately, we only had dietary information at baseline when the participants were 45 years of age or older. Measurement error in dietary exposures may have reduced our ability to detect associations. However, our previous calibration study showed that adjustment for energy intake using nutrient densities improved the quality of the assessments (13). Also, analyzing the data using calibration-adjusted values did not change the results. However, we recognized that the calibration equations were not based on a perfect gold standard, but, rather, on 24-hour recalls which have been found to have correlated errors with QFFQs (32). Nevertheless, on the basis of our relative risks being so close to the null, it is very unlikely that measurement error would explain our findings. For instance, if the true relative risk for the fi quintile for total fat was 1.10 (similar to that in the meta-analysis of 14 cohort studies), simulation studies show that the attenuation factor would have to be less than 0.05 to obtain our observed results with a relative risk of 0.98 in the fifth quintile. This attenuation factor is much less than those found in the OPEN study for absolute protein (0.14–0.16) and especially for percentage of energy from protein (0.32–0.40; ref. 33), and there is no rationale for believing that the MEC QFFQ would perform more poorly than other QFFQs. To further test the influence of measurement error, we also conducted a sensitivity analysis using a small subset of 30 individuals on whom we had serum cholesterol measurements, plus 24-hour recalls and food frequency data. Using the method of triads (34), we found that the effect was further deatte-nuated, but with little evidence of a relative risk in the range that would be considered important. On the basis of this evidence, it is unlikely that moderate or large effects of dietary fat on breast cancer risk would have been missed in our study.

In conclusion, this prospective study in the Multiethnic Cohort does not support a role of adult intake of dietary fat in the etiology of postmenopausal breast cancer.

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References

1. Lof M, Weiderpass E. Impact of diet on breast cancer risk. Curr Opin Obstet Gynecol. 2009; 21:80–5. [PubMed: 19125007]

2. Willett WC. Diet and breast cancer. J Intern Med. 2001; 249:395–411. [PubMed: 11350564]
3. Thiebaut AC, Kipnis V, Schatzkin A, Freedman LS. The role of dietary measurement error in investigating the hypothesized link between dietary fat intake and breast cancer–a story with twists and turns. Cancer Invest. 2008; 26:68–73. [PubMed: 18181048]
4. Boyd NF, Martin LJ, Noffel M, Lockwood GA, Trichler DL. A meta-analysis of studies of dietary fat and breast cancer risk. Br J Cancer. 1993; 68:627–36. [PubMed: 8353053]
5. Boyd NF, Stone J, Vogt KN, Connelly BS, Martin LJ, Minkin S. Dietary fat and breast cancer risk revisited: a meta-analysis of the published literature. Br J Cancer. 2003; 89:1672–85. [PubMed: 14583769]
6. Hunter DJ, Spiegelman D, Adami HO, Beeson L, van den Brandt PA, Folsom AR, et al. Cohort studies of fat intake and the risk of breast cancer–a pooled analysis. N Engl J Med. 1996; 334:356–61. [PubMed: 8538706]
7. Smith-Warner SA, Spiegelman D, Adami HO, Beeson WL, van den Brandt PA, Folsom AR, et al. Types of dietary fat and breast cancer: a pooled analysis of cohort studies. Int J Cancer. 2001; 92:767–74. [PubMed: 11340585]
8. Alexander DD, Morimoto LM, Mink PJ, Cushing CA. A review and meta-analysis of red and processed meat consumption and breast cancer. Nutr Res Rev. 2010; 23:349–65. [PubMed: 21110906]
9. Bingham SA, Luben R, Welch A, Wareham N, Khaw KT, Day N. Are imprecise methods obscuring a relation between fat and breast cancer? Lancet. 2003; 362:212–4. [PubMed: 12885485]
10. Sieri S, Krogh V, Ferrari P, Berrino F, Pala V, Thiebaut AC, et al. Dietary fat and breast cancer risk in the European Prospective Investigation into Cancer and Nutrition. Am J Clin Nutr. 2008; 88:1304–12. [PubMed: 18996867]
11. Thiebaut AC, Kipnis V, Chang SC, Subar AF, Thompson FE, Rosenberg PS, et al. Dietary fat and postmenopausal invasive breast cancer in the National Institutes of Health-AARP Diet and Health Study cohort. J Natl Cancer Inst. 2007; 99:451–62. [PubMed: 17374835]
12. Kolonel LN, Henderson BE, Hankin JH, Nomura AM, Wilkens LR, Pike MC, et al. A multiethnic cohort in Hawaii and Los Angeles: baseline characteristics. Am J Epidemiol. 2000; 151:346–57. [PubMed: 10695593]
13. Stram DO, Hankin JH, Wilkens LR, Pike MC, Monroe KR, Park S, et al. Calibration of the dietary questionnaire for a multiethnic cohort in Hawaii and Los Angeles. Am J Epidemiol. 2000; 151:358–70. [PubMed: 10695594]
14. Korn EL, Graubard BI, Midthune D. Time-to-event analysis of longitudinal follow-up of a survey: choice of the time-scale. Am J Epidemiol. 1997; 145:72–80. [PubMed: 8982025]
15. Thiebaut AC, Benichou J. Choice of time-scale in Cox's model analysis of epidemiologic cohort data: a simulation study. Stat Med. 2004; 23:3803–20. [PubMed: 15580597]
16. Therneau, TM.; Grambsh, PM. Modeling survival data: extending the Cox model. Springer; New York: 2000.
17. Alexander DD, Morimoto LM, Mink PJ, Lowe KA. Summary and meta-analysis of prospective studies of animal fat intake and breast cancer. Nutr Res Rev. 2010; 23:169–79. [PubMed: 20181297]
18. Kim EH, Willett WC, Colditz GA, Hankinson SE, Stampfer MJ, Hunter DJ, et al. Dietary fat and risk of postmenopausal breast cancer in a 20- year follow-up. Am J Epidemiol. 2006; 164:990–7. [PubMed: 16968865]
19. Wakai K, Tamakoshi K, Date C, Fukui M, Suzuki S, Lin Y, et al. Dietary intakes of fat and fatty acids and risk of breast cancer: a prospective study in Japan. Cancer Sci. 2005; 96:590–9. [PubMed: 16128744]
20. Gago-Dominguez M, Yuan JM, Sun CL, Lee HP, Yu MC. Opposing effects of dietary n-3 and n-6 fatty acids on mammary carcinogenesis: the Singapore Chinese Health Study. Br J Cancer. 2003; 89:1686–92. [PubMed: 14583770]
21. Murff HJ, Shu XO, Li H, Yang G, Wu X, Cai H, et al. Dietary polyunsaturated fatty acids and breast cancer risk in Chinese women: a prospective cohort study. Int J Cancer. 2011; 128:1434–41. [PubMed: 20878979]

22. Prentice RL, Caan B, Chlebowski RT, Patterson R, Kuller LH, Ockene JK, et al. Low-fat dietary pattern and risk of invasive breast cancer: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. JAMA. 2006; 295:629–42. [PubMed: 16467232]
23. Martin LJ, Li Q, Melnichouk O, Greenberg C, Minkin S, Hislop G, et al. A randomized trial of dietary intervention for breast cancer prevention. Cancer Res. 2011; 71:123–33. [PubMed: 21199800]
24. Chlebowski RT, Blackburn GL, Thomson CA, Nixon DW, Shapiro A, Hoy MK, et al. Dietary fat reduction and breast cancer outcome: interim efficacy results from the Women's Intervention Nutrition Study. J Natl Cancer Inst. 2006; 98:1767–76. [PubMed: 17179478]
25. Pierce JP, Natarajan L, Caan BJ, Parker BA, Greenberg ER, Flatt SW, et al. Influence of a diet very high in vegetables, fruit, and fiber and low in fat on prognosis following treatment for breast cancer: the Women's Healthy Eating and Living (WHEL) randomized trial. JAMA. 2007; 298:289–98. [PubMed: 17635889]
26. Hunter DJ. Role of dietary fat in the causation of breast cancer: counterpoint. Cancer Epidemiol Biomarkers Prev. 1999; 8:9–13. [PubMed: 9950234]
27. Saadatian-Elahi M, Norat T, Goudable J, Riboli E. Biomarkers of dietary fatty acid intake and the risk of breast cancer: a meta-analysis. Int J Cancer. 2004; 111:584–91. [PubMed: 15239137]
28. Setiawan VW, Monroe KR, Wilkens LR, Kolonel LN, Pike MC, Henderson BE. Breast cancer risk factors defined by estrogen and progesterone receptor status: the multiethnic cohort study. Am J Epidemiol. 2009; 169:1251–9. [PubMed: 19318616]
29. Smith-Warner SA, Stampfer MJ. Fat intake and breast cancer revisited. J Natl Cancer Inst. 2007; 99:418–9. [PubMed: 17374825]
30. Lee S, Kolonel L, Wilkens L, Wan P, Henderson B, Pike M. Postmenopausal hormone therapy and breast cancer risk: the Multiethnic Cohort. Int J Cancer. 2006; 118:1285–91. [PubMed: 16170777]
31. De Assis S, Hilakivi-Clarke L. Timing of dietary estrogenic exposures and breast cancer risk. Ann N Y Acad Sci. 2006; 1089:14–35. [PubMed: 17261753]
32. Subar AF, Kipnis V, Troiano RP, Midthune D, Schoeller DA, Bingham S, et al. Using intake biomarkers to evaluate the extent of dietary misreporting in a large sample of adults: the OPEN study. Am J Epidemiol. 2003; 158:1–13. [PubMed: 12835280]
33. Kipnis V, Subar AF, Midthune D, Freedman LS, Ballard-Barbash R, Troiano RP, et al. Structure of dietary measurement error: results of the OPEN biomarker study. Am J Epidemiol. 2003; 158:14–21. [PubMed: 12835281]
34. Kaaks R, Riboli E. Validation and calibration of dietary intake measurements in the EPIC project: methodological considerations. European Prospective Investigation into Cancer and Nutrition. Int J Epidemiol. 1997; 26(Suppl 1):S15–25. [PubMed: 9126530]

Table 1

Baseline characteristics by total fat intake among 85,089 postmenopausal women in the Multiethnic Cohort study, 1993–1996

	Quintiles of total fat intake (% energy)				
	<23.4	**23.4–<27.8**	**27.8–<31.5**	**31.5–<35.7**	**≥35.7**
No. of participants	17,169	17,243	17,001	16,854	16,822
Age at cohort entry (mean ± SD), y	63.1 ± 7.6	62.3 ± 7.7	61.7 ± 7.9	61.1 ± 8.0	60.2 ± 8.1
Ethnicity, %					
African American	13.7	15.7	19.1	22.2	32.6
Native Hawaiian	5.8	6.4	7.0	7.0	6.5
Japanese American	38.8	33.5	27.5	21.8	12.1
Latina	17.6	20.9	23.6	25.6	25.1
White	24.1	23.6	22.9	23.5	23.7
Family history of breast cancer, %	11.3	11.4	11.6	11.3	12.0
Education (>high school), %	52.0	51.5	50.4	49.3	46.8
BMI at cohort entry, %					
<25 kg/m^2	58.5	50.6	44.3	40.8	33.9
25–<30 kg/m^2	29.1	32.0	33.8	34.1	33.4
≥30 kg/m^2	12.4	17.4	21.9	25.1	32.7
Smoking status, %					
Never	61.5	59.4	56.6	53.6	45.9
Former	29.4	29.9	30.6	30.5	31.6
Current	9.1	10.7	12.8	15.9	22.6
Age at menarche, %					
≤12 y	45.7	47.8	48.2	49.3	50.9
13–14 y	40.1	39.1	39.1	38.7	36.8
≥15 y	14.2	13.1	12.7	12.0	12.3
Age at first live birth, %					
No children	14.1	12.4	12.2	11.7	12.2
≤20 y	23.4	26.4	29.5	33.2	39.8
21–<31 y	55.9	54.1	52.3	49.3	43.4
≥31 y	6.6	7.0	6.1	5.8	4.7
Number of children for parous women, %					
1	13.1	12.3	12.7	11.9	12.8
2–3	52.7	51.3	48.0	46.6	44.0
≥4	34.3	36.3	39.4	41.6	43.3
Age at and type of menopause, %					
Natural					
<45 y	9.3	9.6	9.9	10.6	11.9
45–<50 y	19.3	19.5	19.8	20.2	19.9
50–<55 y	27.9	27.6	26.4	24.6	21.3
≥55 y	7.9	7.0	7.2	6.5	5.3

	Quintiles of total fat intake (% energy)				
	<23.4	**23.4–<27.8**	**27.8–<31.5**	**31.5–<35.7**	**≥35.7**
Oophorectomy					
<45 y	9.8	10.0	10.4	10.5	12.5
45–<50 y	5.0	5.3	5.1	5.0	4.9
≥50 y	3.1	2.9	2.5	2.4	2.1
Hysterectomy					
<45 y	13.0	13.5	14.3	15.4	17.6
45–<50 y	3.4	3.4	3.1	3.6	3.3
≥50 y	1.3	1.3	1.4	1.3	1.2
Use of hormone replacement therapy, %					
No current or past estrogen use	43.3	43.9	45.9	47.4	50.5
Past estrogen use with or without progesterone	18.8	19.0	19.4	19.1	19.5
Current estrogen-only use	17.0	16.4	15.9	15.8	14.8
Current estrogen use with past/current progesterone	20.9	20.8	18.9	17.8	15.2
Energy intake, kcal/d	1,770 ± 800	1,871 ± 876	1,952 ± 927	2,023 ± 995	2,073 ± 1,079
Alcohol use at least once a month in the past year, %	33.6	36.0	36.9	38.7	37.9

Table 2

Associations between breast cancer and dietary fat among 85,089 postmenopausal women in the Multiethnic Cohort study, 1993–2007

	Cases	HR (95% CI)[a]	HR (95% CI)[b]
Total fat (% energy)			
<23.4	794	1.00	1.00
23.4–<27.8	855	1.09 (0.99–1.20)	1.08 (0.98–1.19)
27.8–<31.5	792	1.05 (0.95–1.15)	1.03 (0.93–1.14)
31.5–<35.7	771	1.05 (0.95–1.16)	1.03 (0.93–1.14)
≥35.7	673	0.94 (0.85–1.05)	0.94 (0.85–1.05)
P_{trend}		0.27	0.26
Saturated fat (% energy)			
<6.4	831	1.00	1.00
6.4–<7.9	839	1.05 (0.95–1.15)	1.04 (0.94–1.14)
7.9–<9.3	826	1.09 (0.99–1.20)	1.07 (0.97–1.18)
9.3–<10.9	735	1.01 (0.91–1.12)	1.00 (0.91–1.11)
≥10.9	654	0.92 (0.83–1.02)	0.93 (0.83–1.04)
P_{trend}		0.12	0.19
Monounsaturated fat (% energy)			
<8.3	769	1.00	1.00
8.3–<10.0	861	1.13 (1.03–1.25)	1.12 (1.02–1.23)
10.0–<11.5	788	1.07 (0.97–1.19)	1.06 (0.96–1.17)
11.5–<13.1	757	1.06 (0.96–1.17)	1.05 (0.94–1.16)
≥13.1	710	1.02 (0.92–1.13)	1.01 (0.91–1.13)
P_{trend}		0.91	0.83
Polyunsaturated fat (% energy)			
<5.8	759	1.00	1.00
5.8–<6.9	783	1.03 (0.93–1.13)	1.02 (0.92–1.13)
6.9–<7.8	819	1.09 (0.98–1.20)	1.07 (0.97–1.18)
7.8–<9.0	805	1.08 (0.98–1.20)	1.07 (0.97–1.18)
≥9.0	719	0.98 (0.88–1.08)	0.97 (0.88–1.08)
P_{trend}		0.99	0.91
Polyunsaturated/saturated fat ratio			
<0.69	682	1.00	1.00
0.69–<0.81	726	1.06 (0.95–1.18)	1.05 (0.94–1.16)
0.81–<0.93	827	1.19 (1.07–1.32)	1.16 (1.05–1.29)
0.93–<1.10	800	1.08 (0.98–1.20)	1.06 (0.95–1.17)
≥1.10	850	1.08 (0.97–1.20)	1.06 (0.95–1.18)
P_{trend}		0.30	0.50
Total n-3 fatty acids, g/1,000 kcal			
<0.68	769	1.00	1.00

	Cases	HR (95% CI)[a]	HR (95% CI)[b]
0.68–<0.80	813	1.06 (0.96–1.17)	1.04 (0.95–1.15)
0.80–<0.91	748	0.99 (0.89–1.09)	0.98 (0.88–1.08)
0.91–<1.04	792	1.05 (0.95–1.16)	1.04 (0.94–1.15)
≥1.04	763	1.02 (0.92–1.13)	1.02 (0.92–1.13)
P_{trend}		0.81	0.77
α-Linolenic acid, 18:3, g/1,000 kcal			
<0.65	773	1.00	1.00
0.65–<0.76	811	1.04 (0.94–1.15)	1.04 (0.94–1.14)
0.76–<0.86	765	1.00 (0.91–1.11)	0.99 (0.90–1.10)
0.86–<0.99	810	1.08 (0.97–1.19)	1.07 (0.97–1.19)
≥0.99	726	0.97 (0.88–1.08)	0.97 (0.88–1.08)
P_{trend}		0.76	0.78
Eicosapentaenoic acid, 20:5, g/1,000 kcal			
<0.01	742	1.00	1.00
0.01–<0.01	755	1.01 (0.92–1.12)	1.00 (0.90–1.11)
0.01–<0.02	779	1.02 (0.92–1.13)	1.00 (0.91–1.11)
0.02–<0.03	822	1.07 (0.96–1.18)	1.04 (0.94–1.15)
≥0.03	787	1.02 (0.92–1.14)	1.01 (0.90–1.12)
P_{trend}		0.61	0.81
Docosahexaenoic acid, 22:6, g/1,000 kcal			
<0.02	736	1.00	1.00
0.02–<0.03	782	1.06 (0.95–1.17)	1.04 (0.94–1.15)
0.03–<0.04	780	1.04 (0.94–1.16)	1.03 (0.93–1.14)
0.04–<0.06	801	1.05 (0.95–1.16)	1.03 (0.93–1.14)
≥0.06	786	1.04 (0.93–1.15)	1.02 (0.92–1.13)
P_{trend}		0.71	0.93
Total n-6 fatty acids, g/1,000 kcal			
<5.7	746	1.00	1.00
5.7–<6.9	795	1.05 (0.95–1.17)	1.04 (0.94–1.15)
6.9–<7.9	819	1.10 (1.00–1.22)	1.09 (0.98–1.20)
7.9–<9.1	793	1.07 (0.97–1.19)	1.05 (0.95–1.17)
≥9.1	732	1.00 (0.90–1.11)	0.99 (0.89–1.10)
P_{trend}		0.96	0.88
Linoleic acid, 18:2, g/1,000 kcal			
<5.7	741	1.00	1.00
5.7–<6.8	793	1.06 (0.96–1.17)	1.05 (0.95–1.16)
6.8–<7.8	823	1.11 (1.01–1.23)	1.09 (0.99–1.21)
7.8–<9.0	783	1.07 (0.96–1.18)	1.05 (0.95–1.16)
≥9.0	745	1.03 (0.93–1.14)	1.02 (0.92–1.13)
P_{trend}		0.69	0.87
Arachidonic acid, 20:4, g/1,000 kcal			

	Cases	HR (95% CI)[a]	HR (95% CI)[b]
<0.03	820	1.00	1.00
0.03–<0.05	815	1.02 (0.92–1.12)	1.01 (0.91–1.11)
0.05–<0.06	788	1.01 (0.92–1.12)	0.99 (0.90–1.10)
0.06–<0.08	730	0.98 (0.88–1.08)	0.97 (0.88–1.07)
≥0.08	732	1.01 (0.91–1.12)	1.01 (0.91–1.12)
P_{trend}		0.97	0.99
n-6/n-3 fatty acid ratio			
<7.6	732	1.00	1.00
7.6–<8.3	807	1.13 (1.02–1.25)	1.12 (1.02–1.24)
8.3–<8.8	780	1.10 (1.00–1.22)	1.09 (0.98–1.20)
8.8–<9.6	729	1.02 (0.92–1.14)	1.01 (0.91–1.12)
≥9.6	837	1.13 (1.02–1.25)	1.10 (0.99–1.22)
P_{trend}		0.13	0.33
Cholesterol mg/1,000 kcal			
<68.6	821	1.00	1.00
68.6–<88.4	865	1.12 (1.01–1.23)	1.11 (1.01–1.23)
88.4–<106.7	769	1.03 (0.93–1.13)	1.02 (0.92–1.12)
106.7–<130.4	727	1.00 (0.91–1.11)	1.00 (0.90–1.11)
≥130.4	703	1.00 (0.90–1.11)	1.01 (0.90–1.12)
P_{trend}		0.41	0.50

[a]Adjusted for time on study, age at cohort entry, and ethnicity.

[b]Adjusted for time on study, age at cohort entry, ethnicity, family history of breast cancer, education, BMI, age atmenarche, age at first live birth, number of children, age at and type of menopause, hormone replacement therapy, smoking status, energy intake, and alcohol use.

Table 3

Associations between breast cancer and dietary fat according to race/ethnicity among 85,089 postmenopausal women in the Multiethnic Cohort study, 1993–2007

	African Americans		Native Hawaiians		Japanese Americans		Latinos		Whites		
	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	$P_{interaction}$[b]
Total fat (% energy)											
<23.4	111	1.00	62	1.00	318	1.00	87	1.00	216	1.00	0.71
23.4–<27.8	134	1.08 (0.84–1.39)	64	0.92 (0.65–1.30)	316	1.12 (0.95–1.31)	132	1.27 (0.97–1.67)	209	0.97 (0.80–1.18)	
27.8–<31.5	152	1.03 (0.80–1.31)	83	1.09 (0.78–1.53)	242	1.04 (0.88–1.23)	128	1.13 (0.86–1.48)	187	0.94 (0.77–1.15)	
31.5–<35.7	153	0.91 (0.71–1.16)	73	0.98 (0.70–1.39)	184	1.00 (0.83–1.20)	150	1.26 (0.97–1.65)	211	1.05 (0.87–1.28)	
>35.7	219	0.92 (0.73–1.16)	55	0.82 (0.57–1.19)	85	0.83 (0.65–1.06)	114	0.95 (0.71–1.26)	200	1.06 (0.87–1.29)	
P_{trend}		0.19		0.45		0.28		0.60		0.43	
Saturated fat (% energy)											
<6.4	106	1.00	62	1.00	414	1.00	63	1.00	186	1.00	0.94
6.4–<7.9	142	1.07 (0.83–1.37)	80	1.08 (0.77–1.51)	311	0.99 (0.86–1.15)	103	1.25 (0.91–1.71)	203	0.99 (0.81–1.21)	
7.9–<9.3	160	1.03 (0.81–1.32)	81	1.04 (0.74–1.46)	257	1.13 (0.97–1.33)	139	1.35 (1.00–1.82)	189	0.95 (0.77–1.16)	
9.3–<10.9	171	0.98 (0.76–1.25)	67	0.99 (0.69–1.40)	118	0.87 (0.71–1.08)	145	1.12 (0.83–1.51)	234	1.12 (0.92–1.36)	
>10.9	190	0.91 (0.71–1.16)	47	0.93 (0.63–1.37)	45	0.87 (0.64–1.19)	161	1.07 (0.79–1.43)	211	0.93 (0.76–1.14)	
P_{trend}		0.23		0.61		0.59		0.56		0.81	
Monounsaturated fat (% energy)											
<8.3	112	1.00	58	1.00	296	1.00	92	1.00	211	1.00	0.64
8.3–<10.0	129	1.02 (0.79–1.32)	64	0.97 (0.68–1.38)	307	1.13 (0.96–1.32)	142	1.40 (1.08–1.82)	219	1.07 (0.88–1.29)	
10.0–<11.5	152	1.07 (0.84–1.37)	81	1.13 (0.81–1.59)	234	1.02 (0.86–1.21)	127	1.19 (0.90–1.55)	194	1.00 (0.82–1.22)	
11.5–<13.1	155	0.94 (0.73–1.20)	75	1.04 (0.73–1.47)	201	1.04 (0.87–1.25)	132	1.20 (0.92–1.57)	194	1.06 (0.87–1.29)	
>13.1	221	0.94 (0.75–1.19)	59	0.83 (0.57–1.20)	107	0.91 (0.72–1.14)	118	1.09 (0.82–1.44)	205	1.17 (0.96–1.43)	
P_{trend}		0.39		0.44		0.51		0.93		0.18	
Polyunsaturated fat (% energy)											
<5.8	119	1.00	57	1.00	213	1.00	129	1.00	241	1.00	0.69
5.8–<6.9	138	1.00 (0.78–1.27)	49	0.77 (0.53–1.13)	233	0.99 (0.82–1.19)	134	1.05 (0.83–1.34)	229	1.11 (0.93–1.33)	
6.9–<7.8	149	0.97 (0.76–1.24)	76	1.04 (0.74–1.47)	254	1.06 (0.88–1.27)	129	1.05 (0.82–1.35)	211	1.15 (0.96–1.39)	
7.8–<9.0	163	0.92 (0.72–1.17)	84	1.14 (0.81–1.61)	257	1.10 (0.91–1.32)	128	1.12 (0.88–1.44)	173	1.06 (0.87–1.29)	

	African Americans		Native Hawaiians		Japanese Americans		Latinos		Whites		
	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	$P_{interaction}$[b]
>9.0	200	0.92 (0.73–1.16)	71	0.89 (0.62–1.26)	188	0.88 (0.72–1.07)	91	0.97 (0.74–1.28)	169	1.15 (0.94–1.41)	
P_{trend}		0.37		0.90		0.47		0.92		0.25	
Polyunsaturated/saturated fat ratio											
<0.69	157	1.00	32	1.00	62	1.00	178	1.00	253	1.00	0.66
0.69–<0.81	148	0.86 (0.69–1.08)	64	1.27 (0.83–1.95)	119	0.98 (0.72–1.33)	164	1.12 (0.91–1.39)	231	1.12 (0.94–1.34)	
0.81–<0.93	190	1.10 (0.89–1.35)	88	1.56 (1.04–2.34)	188	0.98 (0.73–1.30)	130	1.19 (0.95–1.50)	231	1.22 (1.02–1.46)	
0.93–<1.10	144	0.89 (0.71–1.11)	78	1.30 (0.86–1.96)	319	1.03 (0.79–1.36)	84	1.06 (0.82–1.38)	175	1.06 (0.88–1.29)	
>1.10	130	1.01 (0.80–1.28)	75	1.35 (0.89–2.05)	457	0.95 (0.73–1.24)	55	1.15 (0.85–1.56)	133	1.08 (0.87–1.33)	
P_{trend}		0.85		0.39		0.59		0.33		0.51	
Total n-3 fatty acids, g/1,000 kcal											
<0.68	144	1.00	41	1.00	186	1.00	141	1.00	257	1.00	0.42
0.68–<0.80	169	1.06 (0.85–1.33)	51	1.08 (0.71–1.63)	218	1.05 (0.87–1.28)	116	0.85 (0.66–1.09)	259	1.14 (0.95–1.35)	
0.80–<0.91	140	0.87 (0.69–1.09)	59	1.12 (0.75–1.68)	216	0.97 (0.80–1.18)	133	0.99 (0.78–1.26)	200	1.04 (0.87–1.26)	
0.91–<1.04	150	0.90 (0.71–1.13)	90	1.40 (0.96–2.03)	263	1.07 (0.88–1.29)	115	0.96 (0.75–1.24)	174	1.09 (0.90–1.32)	
>1.04	166	0.93 (0.75–1.17)	96	1.19 (0.82–1.73)	262	0.99 (0.82–1.20)	106	1.10 (0.85–1.42)	133	1.03 (0.84–1.28)	
P_{trend}		0.30		0.24		0.91		0.33		0.78	
α-Linolenic acid, 18:3, g/1,000 kcal											
<0.65	144	1.00	53	1.00	203	1.00	126	1.00	247	1.00	0.79
0.65–<0.76	170	1.06 (0.85–1.33)	50	0.83 (0.56–1.23)	218	1.02 (0.84–1.23)	111	0.87 (0.67–1.12)	262	1.19 (1.00–1.42)	
0.76–<0.86	156	0.98 (0.78–1.23)	67	1.00 (0.70–1.44)	231	0.99 (0.82–1.20)	126	0.96 (0.75–1.23)	185	1.01 (0.83–1.22)	
0.86–<0.99	148	0.94 (0.74–1.18)	85	1.15 (0.82–1.63)	253	1.05 (0.87–1.26)	133	1.04 (0.81–1.33)	191	1.21 (1.00–1.46)	
>0.99	151	0.94 (0.75–1.18)	82	0.97 (0.69–1.38)	240	0.93 (0.77–1.13)	115	1.00 (0.77–1.29)	138	1.02 (0.82–1.26)	
P_{trend}		0.35		0.63		0.52		0.62		0.71	
Eicosapentaenoic acid, 20:5, g/1,000 kcal											
<0.01	118	1.00	24	1.00	77	1.00	262	1.00	261	1.00	0.03
0.01–<0.01	151	1.01 (0.80–1.29)	35	0.95 (0.56–1.60)	171	1.06 (0.81–1.39)	160	0.91 (0.75–1.11)	238	1.09 (0.91–1.30)	
0.01–<0.02	166	0.98 (0.77–1.24)	57	1.11 (0.69–1.80)	268	1.20 (0.93–1.55)	96	0.87 (0.69–1.11)	192	0.98 (0.82–1.19)	
0.02–<0.03	175	0.98 (0.77–1.24)	100	1.40 (0.89–2.19)	310	1.12 (0.87–1.43)	57	0.83 (0.62–1.11)	180	1.15 (0.95–1.40)	
>0.03	159	0.87 (0.68–1.10)	121	1.29 (0.83–2.01)	319	1.10 (0.86–1.41)	36	0.84 (0.59–1.19)	152	1.18 (0.96–1.44)	
P_{trend}		0.15		0.11		0.89		0.15		0.09	

	African Americans		Native Hawaiians		Japanese Americans		Latinos		Whites		
	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	$P_{interaction}$[b]
Docosahexaenoic acid, 22:6, g/1,000 kcal											
<0.02	111	1.00	30	1.00	106	1.00	234	1.00	255	1.00	0.04
0.02–<0.03	120	0.89 (0.69–1.16)	46	1.07 (0.67–1.70)	200	1.11 (0.87–1.40)	175	1.05 (0.86–1.28)	241	1.10 (0.93–1.32)	
0.03–<0.04	164	0.95 (0.75–1.21)	63	1.16 (0.75–1.80)	259	1.16 (0.93–1.46)	99	0.87 (0.69–1.10)	195	1.04 (0.86–1.25)	
0.04–<0.06	180	0.89 (0.70–1.13)	84	1.17 (0.77–1.78)	288	1.11 (0.89–1.39)	64	0.88 (0.66–1.16)	185	1.18 (0.97–1.42)	
>0.06	194	0.84 (0.67–1.06)	114	1.30 (0.86–1.95)	292	1.11 (0.89–1.39)	39	0.82 (0.58–1.15)	147	1.15 (0.94–1.41)	
P_{trend}		0.17		0.14		0.75		0.10		0.14	
Total n-6 fatty acids, g/1,000 kcal											
<5.7	122	1.00	57	1.00	213	1.00	130	1.00	224	1.00	0.46
5.7–<6.9	132	0.97 (0.76–1.24)	54	0.79 (0.54–1.15)	238	1.03 (0.85–1.24)	135	1.06 (0.83–1.34)	236	1.18 (0.98–1.42)	
6.9–<7.9	159	1.04 (0.82–1.32)	78	1.10 (0.78–1.55)	250	1.05 (0.88–1.27)	134	1.10 (0.86–1.40)	198	1.12 (0.92–1.35)	
7.9–<9.1	168	0.94 (0.74–1.19)	71	0.98 (0.69–1.40)	249	1.06 (0.88–1.27)	116	1.04 (0.81–1.34)	189	1.15 (0.94–1.40)	
>9.1	188	0.87 (0.69–1.10)	77	0.97 (0.69–1.37)	195	0.91 (0.75–1.11)	96	1.06 (0.81–1.38)	176	1.15 (0.94–1.40)	
P_{trend}		0.19		0.78		0.47		0.72		0.23	
Linoleic acid, 18:2, g/1,000 kcal											
<5.7	117	1.00	59	1.00	212	1.00	127	1.00	226	1.00	0.68
5.7–<6.8	132	0.99 (0.77–1.28)	52	0.79 (0.54–1.15)	239	1.04 (0.86–1.25)	142	1.13 (0.89–1.44)	228	1.13 (0.94–1.36)	
6.8–<7.8	161	1.06 (0.84–1.35)	74	1.01 (0.71–1.42)	254	1.07 (0.89–1.29)	129	1.09 (0.85–1.39)	205	1.15 (0.95–1.39)	
7.8–<9.0	163	0.93 (0.73–1.19)	75	1.01 (0.72–1.43)	245	1.07 (0.89–1.29)	116	1.07 (0.83–1.38)	184	1.09 (0.90–1.33)	
>9.0	196	0.94 (0.74–1.18)	77	0.95 (0.68–1.34)	195	0.92 (0.76–1.13)	97	1.10 (0.84–1.44)	180	1.15 (0.94–1.40)	
P_{trend}		0.41		0.79		0.54		0.63		0.24	
Arachidonic acid, 20:4, g/1,000 kcal											
<0.03	88	1.00	63	1.00	258	1.00	127	1.00	284	1.00	0.53
0.03–<0.05	90	0.83 (0.62–1.12)	81	1.24 (0.89–1.72)	296	1.08 (0.92–1.28)	130	1.06 (0.83–1.36)	218	0.90 (0.76–1.08)	
0.05–<0.06	116	0.85 (0.65–1.13)	72	0.91 (0.65–1.29)	257	1.02 (0.86–1.22)	135	1.08 (0.84–1.38)	208	1.00 (0.83–1.20)	
0.06–<0.08	149	0.77 (0.59–1.01)	67	0.92 (0.65–1.31)	215	1.03 (0.86–1.24)	114	0.93 (0.72–1.20)	185	1.10 (0.91–1.32)	
>0.08	326	0.94 (0.74–1.19)	54	1.05 (0.73–1.52)	119	1.02 (0.82–1.27)	105	0.89 (0.69–1.16)	128	1.05 (0.85–1.30)	
P_{trend}		0.59		0.66		0.99		0.21		0.28	
n-6/n-3 fatty acid ratio											
<7.6	90	1.00	92	1.00	284	1.00	102	1.00	164	1.00	0.44

	African Americans		Native Hawaiians		Japanese Americans		Latinos		Whites		
	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	$P_{interaction}$[b]
7.6–<8.3	118	1.08 (0.82–1.42)	87	1.13 (0.84–1.52)	275	1.10 (0.93–1.30)	146	1.26 (0.97–1.62)	181	1.14 (0.92–1.41)	
8.3–<8.8	164	1.22 (0.94–1.58)	66	0.96 (0.70–1.32)	244	1.15 (0.97–1.37)	122	1.00 (0.77–1.30)	184	1.05 (0.85–1.30)	
8.8–<9.6	175	1.05 (0.82–1.36)	51	0.83 (0.58–1.17)	174	0.95 (0.79–1.15)	124	1.05 (0.81–1.37)	205	1.07 (0.87–1.32)	
>9.6	222	1.13 (0.88–1.45)	41	0.82 (0.57–1.19)	168	1.04 (0.86–1.26)	117	1.13 (0.87–1.48)	289	1.20 (0.99–1.45)	
P_{trend}		0.54		0.14		0.99		0.79		0.11	
Cholesterol, mg/1,000 kcal											
<68.6	113	1.00	64	1.00	314	1.00	100	1.00	230	1.00	0.82
68.6–<88.4	108	0.83 (0.64–1.08)	75	1.09 (0.78–1.53)	318	1.28 (1.09–1.49)	126	1.10 (0.85–1.43)	238	1.07 (0.90–1.29)	
88.4–<106.7	142	0.89 (0.69–1.14)	66	0.90 (0.64–1.27)	240	1.13 (0.95–1.34)	133	1.08 (0.83–1.40)	188	0.94 (0.77–1.14)	
106.7–<130.4	168	0.85 (0.67–1.08)	75	1.04 (0.74–1.46)	167	1.05 (0.87–1.27)	129	0.99 (0.76–1.30)	188	0.99 (0.81–1.20)	
>130.4	238	0.86 (0.68–1.08)	57	0.99 (0.68–1.42)	106	1.00 (0.80–1.25)	123	0.98 (0.75–1.28)	179	1.10 (0.90–1.34)	
P_{trend}		0.36		0.86		0.85		0.55	216	0.62	

[a]Adjusted for time on study, age at cohort entry, family history of breast cancer, education, BMI, age at menarche, age at first live birth, number of children, age at and type of menopause, hormone replacement therapy, smoking status, energy intake, and alcohol use.

[b]Interaction test is based on the Wald test.

Table 4

Associations between breast cancer and dietary fat according to hormone receptor status among 85,089 postmenopausal women in the Multiethnic Cohort study, 1993–2007

	ER^+/PR^+		ER^+/PR^-		ER^-/PR^-		
	Cases	**HR (95% CI)**[a]	**Cases**	**HR (95% CI)**[a]	**Cases**	**HR (95% CI)**[a]	$P_{interaction}$[b]
Total fat (% energy)							
<23.4	374	1.00	66	1.00	105	1.00	0.46
23.4–<27.8	417	1.12 (0.98–1.29)	73	1.13 (0.81–1.58)	100	0.94 (0.71–1.23)	
27.8–<31.5	364	1.02 (0.88–1.18)	76	1.25 (0.89–1.74)	94	0.88 (0.66–1.16)	
31.5–<35.7	326	0.96 (0.82–1.12)	76	1.31 (0.93–1.83)	97	0.89 (0.67–1.18)	
>35.7	283	0.90 (0.77–1.06)	59	1.12 (0.78–1.61)	103	0.92 (0.69–1.23)	
P_{trend}		0.08		0.32		0.54	
Saturated fat (% energy)							
<6.4	395	1.00	65	1.00	109	1.00	0.33
6.4–<7.9	405	1.07 (0.93–1.23)	82	1.33 (0.96–1.84)	98	0.88 (0.67–1.16)	
7.9–<9.3	377	1.05 (0.91–1.22)	66	1.16 (0.82–1.64)	91	0.82 (0.62–1.09)	
9.3–<10.9	328	0.99 (0.85–1.15)	79	1.47 (1.04–2.07)	95	0.84 (0.63–1.12)	
>10.9	259	0.83 (0.71–0.99)	58	1.15 (0.79–1.67)	106	0.92 (0.69–1.22)	
P_{trend}		0.03		0.36		0.56	
Monounsaturated fat (% energy)							
<8.3	353	1.00	61	1.00	102	1.00	0.44
8.3–<10.0	424	1.21 (1.05–1.40)	76	1.28 (0.91–1.79)	100	0.97 (0.73–1.28)	
10.0–<11.5	369	1.10 (0.95–1.28)	74	1.32 (0.94–1.86)	98	0.96 (0.72–1.27)	
11.5–<13.1	323	1.00 (0.86–1.17)	84	1.56 (1.12–2.18)	84	0.81 (0.60–1.09)	
>13.1	295	0.98 (0.83–1.15)	55	1.11 (0.76–1.62)	115	1.08 (0.82–1.42)	
P_{trend}		0.29		0.27		0.92	
Polyunsaturated fat (% energy)							
<5.8	355	1.00	72	1.00	90	1.00	0.52
5.8–<6.9	355	0.99 (0.86–1.15)	64	0.90 (0.64–1.26)	110	1.21 (0.91–1.59)	
6.9–<7.8	403	1.14 (0.99–1.32)	77	1.12 (0.81–1.56)	94	1.02 (0.76–1.37)	
7.8–<9.0	359	1.05 (0.90–1.22)	73	1.11 (0.80–1.54)	108	1.17 (0.88–1.56)	
>9.0	292	0.88 (0.75–1.03)	64	1.03 (0.73–1.45)	97	1.05 (0.78–1.41)	
P_{trend}		0.24		0.55		0.88	
Polyunsaturated/saturated fat ratio							
<0.69	296	1.00	66	1.00	94	1.00	0.85
0.69–<0.81	334	1.11 (0.95–1.30)	70	1.06 (0.76–1.49)	101	1.08 (0.81–1.43)	
0.81–<0.93	356	1.14 (0.98–1.34)	74	1.11 (0.79–1.55)	105	1.13 (0.85–1.50)	
0.93–<1.10	385	1.14 (0.97–1.33)	66	0.93 (0.66–1.33)	103	1.10 (0.83–1.47)	
>1.10	393	1.07 (0.91–1.26)	74	0.98 (0.69–1.40)	96	1.05 (0.78–1.43)	
P_{trend}		0.58		0.67		0.76	
Total n-3 fatty acids, g/1,000 kcal							

	ER+/PR+		ER+/PR−		ER−/PR−		
	Cases	**HR (95% CI)[a]**	**Cases**	**HR (95% CI)[a]**	**Cases**	**HR (95% CI)[a]**	***P* interaction[b]**
<0.68	355	1.00	68	1.00	108	1.00	0.74
0.68–<0.80	383	1.08 (0.93–1.25)	67	1.00 (0.71–1.40)	95	0.87 (0.66–1.15)	
0.80–<0.91	338	0.97 (0.83–1.12)	87	1.35 (0.98–1.86)	97	0.90 (0.68–1.18)	
0.91–<1.04	361	1.04 (0.90–1.21)	58	0.94 (0.66–1.34)	103	0.96 (0.73–1.26)	
>1.04	327	0.95 (0.82–1.11)	70	1.19 (0.85–1.68)	96	0.92 (0.69–1.22)	
P_{trend}		0.45		0.41		0.78	
α-Linolenic acid, 18:3, g/1,000 kcal							
<0.65	360	1.00	65	1.00	109	1.00	0.51
0.65–<0.76	383	1.07 (0.92–1.23)	79	1.23 (0.89–1.72)	91	0.82 (0.62–1.09)	
0.76–<0.86	348	0.98 (0.84–1.14)	63	1.02 (0.72–1.45)	102	0.93 (0.71–1.22)	
0.86–<0.99	363	1.05 (0.91–1.22)	76	1.30 (0.93–1.82)	105	0.97 (0.74–1.27)	
>0.99	310	0.90 (0.77–1.05)	67	1.21 (0.85–1.71)	92	0.87 (0.66–1.15)	
P_{trend}		0.19		0.29		0.63	
Eicosapentaenoic acid, 20:5, g/1,000 kcal							
<0.01	338	1.00	86	1.00	93	1.00	0.18
0.01–<0.01	330	0.96 (0.82–1.12)	68	0.78 (0.56–1.07)	106	1.16 (0.88–1.54)	
0.01–<0.02	361	1.02 (0.87–1.18)	66	0.73 (0.53–1.02)	97	1.07 (0.80–1.43)	
0.02–<0.03	352	0.96 (0.82–1.13)	67	0.74 (0.53–1.03)	102	1.14 (0.85–1.53)	
>0.03	383	1.05 (0.90–1.23)	63	0.70 (0.50–0.99)	101	1.17 (0.86–1.57)	
P_{trend}		0.37		0.10		0.44	
Docosahexaenoic acid, 22:6, g/1,000 kcal							
<0.02	339	1.00	81	1.00	97	1.00	0.25
0.02–<0.03	358	1.03 (0.89–1.20)	77	0.94 (0.69–1.29)	99	1.03 (0.78–1.37)	
0.03–<0.04	328	0.94 (0.80–1.09)	61	0.74 (0.53–1.04)	97	1.02 (0.76–1.35)	
0.04–<0.06	358	1.00 (0.85–1.16)	66	0.80 (0.57–1.12)	104	1.09 (0.82–1.45)	
>0.06	381	1.07 (0.92–1.25)	65	0.80 (0.57–1.12)	102	1.08 (0.81–1.45)	
P_{trend}		0.35		0.18		0.55	
Total n-6 fatty acids, g/1,000 kcal							
<5.7	347	1.00	72	1.00	88	1.00	0.60
5.7–<6.9	366	1.04 (0.90–1.20)	67	0.94 (0.67–1.31)	108	1.21 (0.91–1.61)	
6.9–<7.9	390	1.13 (0.97–1.30)	70	1.01 (0.73–1.41)	96	1.07 (0.80–1.43)	
7.9–<9.1	354	1.04 (0.89–1.21)	77	1.14 (0.83–1.58)	111	1.22 (0.92–1.62)	
>9.1	307	0.93 (0.79–1.08)	64	1.01 (0.71–1.42)	96	1.06 (0.79–1.42)	
P_{trend}		0.35		0.65		0.79	
Linoleic acid, 18:2, g/1,000 kcal							
<5.7	348	1.00	70	1.00	85	1.00	0.50
5.7–<6.8	360	1.02 (0.88–1.19)	69	1.00 (0.71–1.39)	109	1.27 (0.95–1.68)	
6.8–<7.8	397	1.14 (0.99–1.32)	73	1.08 (0.78–1.51)	95	1.09 (0.81–1.46)	
7.8–<9.0	343	1.01 (0.87–1.17)	74	1.13 (0.81–1.58)	112	1.28 (0.96–1.70)	
>9.0	316	0.95 (0.81–1.11)	64	1.04 (0.73–1.46)	98	1.11 (0.83–1.50)	

	ER+/PR+		ER+/PR−		ER−/PR−		
	Cases	**HR (95% CI)[a]**	**Cases**	**HR (95% CI)[a]**	**Cases**	**HR (95% CI)[a]**	**$P_{interaction}$[b]**
P_{trend}		0.47		0.64		0.57	
Arachidonic acid, 20:4, g/1,000 kcal							
<0.03	391	1.00	74	1.00	90	1.00	0.26
0.03–<0.05	371	0.97 (0.84–1.12)	87	1.21 (0.88–1.65)	100	1.12 (0.84–1.49)	
0.05–<0.06	367	0.98 (0.85–1.14)	71	1.04 (0.75–1.45)	98	1.10 (0.83–1.47)	
0.06–<0.08	333	0.96 (0.83–1.11)	61	0.95 (0.67–1.34)	105	1.19 (0.89–1.58)	
>0.08	302	0.95 (0.81–1.11)	57	0.93 (0.65–1.34)	106	1.12 (0.83–1.50)	
P_{trend}		0.64		0.39		0.49	
n-6/n-3 fatty acid ratio							
<7.6	343	1.00	72	1.00	83	1.00	0.88
7.6–<8.3	357	1.08 (0.93–1.25)	67	0.95 (0.68–1.32)	115	1.35 (1.02–1.79)	
8.3–<8.8	347	1.07 (0.92–1.24)	73	1.05 (0.75–1.45)	103	1.17 (0.87–1.56)	
8.8–<9.6	345	1.07 (0.92–1.24)	58	0.82 (0.58–1.17)	76	0.83 (0.61–1.14)	
>9.6	372	1.10 (0.95–1.28)	80	1.07 (0.77–1.48)	122	1.28 (0.96–1.70)	
P_{trend}		0.28		0.85		0.56	
Cholesterol, mg/1,000 kcal							
<68.6	395	1.00	71	1.00	100	1.00	0.68
68.6–<88.4	387	1.05 (0.91–1.21)	83	1.26 (0.91–1.73)	106	1.08 (0.82–1.42)	
88.4–<106.7	353	1.00 (0.86–1.15)	77	1.23 (0.89–1.71)	95	0.97 (0.73–1.29)	
106.7–<130.4	324	0.97 (0.83–1.12)	63	1.06 (0.75–1.50)	90	0.91 (0.68–1.22)	
>130.4	305	0.97 (0.83–1.14)	56	1.00 (0.69–1.44)	108	1.07 (0.80–1.42)	
P_{trend}		0.51		0.75		0.94	

[a]Adjusted for time on study, age at cohort entry, ethnicity, family history of breast cancer, education, BMI, age at menarche, age at first live birth, number of children, age at and type of menopause, hormone replacement therapy, smoking status, energy intake, and alcohol use. ER^-/PR^+ breast cancers were not analyzed separately because of the small number of cases (n = 59).

[b]Interaction test is based on competing risk techniques.