Dietary fat and breast cancer: comparison of results from food diaries and food-frequency questionnaires in the UK Dietary Cohort Consortium[1–4]

Timothy J Key, Paul N Appleby, Benjamin J Cairns, Robert Luben, Christina C Dahm, Tasnime Akbaraly, Eric J Brunner, Victoria Burley, Janet E Cade, Darren C Greenwood, Alison M Stephen, Gita Mishra, Diana Kuh, Ruth H Keogh, Ian R White, Amit Bhaniani, Gabor Borgulya, Angela A Mulligan, and Kay Tee Khaw

ABSTRACT

Background: Epidemiologic studies of dietary fat and breast cancer risk are inconsistent, and it has been suggested that a true relation may have been obscured by the imprecise measurement of fat intake.

Objective: We examined associations of fat with breast cancer risk by using estimates of fat intake from food diaries and food-frequency questionnaires (FFQs) pooled from 4 prospective studies in the United Kingdom.

Design: A total of 657 cases of breast cancer in premenopausal and postmenopausal women were matched on study, age, and recruitment date with 1911 control subjects. Nutrient intakes were estimated from food diaries and FFQs. Conditional logistic regression was used to estimate ORs for breast cancer associated with total, saturated, monounsaturated, and polyunsaturated fat intakes with adjustment for relevant covariates.

Results: Neither the food diaries nor the FFQs showed any positive associations between fat intake and overall breast cancer risk. ORs (95% CIs) for the highest compared with lowest quintiles of percentage of energy from total fat were 0.90 (0.66, 1.23) for food diaries and 0.80 (0.59, 1.09) for FFQs.

Conclusion: In this study, breast cancer risk was not associated with fat intake in middle-aged women in the United Kingdom, irrespective of whether diet was measured by food diaries or by FFQs. *Am J Clin Nutr* 2011;94:1043–52.

INTRODUCTION

In 1966 Lea (1) reported that breast cancer mortality in 23 countries was positively correlated with the supply of fat in those countries. Since then, numerous studies have investigated the hypothesis that high intakes of fat may increase breast cancer risk, but most of the results from prospective studies have been null (2, 3). In 2003 Bingham et al (4) suggested that FFQs[5] used to measure fat intake in most cohort studies were too imprecise to detect a relation between fat intake and breast cancer risk and supported this proposal by reporting results from a small prospective study in which breast cancer risk was significantly positively associated with fat intake as measured by 7-d food diaries but not with fat intake assessed by FFQs. A subsequent report from the control arm of the Women's Health Initiative trial also suggested that breast cancer risk in postmenopausal women was significantly positively associated with fat intake measured by 4-d food diaries but not with fat intake assessed by FFQs (5).

In the current study, we report an additional analysis of breast cancer risk in relation to fat intake estimated both by food diaries and FFQs in 4 prospective studies in the United Kingdom in the UK Dietary Cohort Consortium (6). The primary aim was to examine whether this extended study would confirm the results of

[1] From the Cancer Epidemiology Unit, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, United Kingdom (TJK, PNA, and BJC); the Medical Research Council Centre for Nutritional Epidemiology in Cancer Prevention and Survival, Department of Public Health and Primary Care (RHK, AB, GB, AAM, and KTK) and Department of Public Health and Primary Care (RL), University of Cambridge, Cambridge, United Kingdom; the Department of Cardiology, Aarhus University Hospital, Aalborg, Denmark (CCD); the Department of Epidemiology, School of Public Health, Aarhus University, Aarhus, Denmark (CCD); the Department of Epidemiology and Public Health, University College London, London, United Kingdom (TA and EJB); INSERM U1061, Montpellier, France (TA); the Centre for Epidemiology and Biostatistics, University of Leeds, Leeds, United Kingdom (VB, JEC, and DCG); the Medical Research Council Human Nutrition Research, Elsie Widdowson Laboratory, Cambridge, United Kingdom (AMS); the School of Population Health, University of Queensland, Herston, Australia (GM); the Medical Research Council Unit for Lifelong Health and Ageing, Department of Epidemiology and Public Health, University College London, London, United Kingdom (DK); the Medical Research Council Biostatistics Unit, Cambridge, United Kingdom (RHK and IRW); and the Medical Research Council Centre for Nutritional Epidemiology in Cancer Prevention and Survival (RHK, AB, GB, AAM, and KTK).

[2] The funders had no role in the design, implementation, analysis, or interpretation of data.

[3] Supported by the Medical Research Council and the Medical Research Council Population Health Sciences Research Network. The cohort studies included in this consortium received funding from the British Heart Foundation, Cancer Research UK, the Department of Health, United Kingdom, the Food Standards Agency, United Kingdom, the Medical Research Council, United Kingdom, the Stroke Association, United Kingdom, and the World Cancer Research Fund.

[4] Address correspondence to TJ Key, Cancer Epidemiology Unit, Nuffield Department of Clinical Medicine, University of Oxford, Richard Doll Building, Oxford OX3 7LF, United Kingdom. E-mail: tim.key@ceu.ox.ac.uk.

[5] Abbreviations used: EPIC, European Prospective Investigation into Cancer and Nutrition; FFQ, food-frequency questionnaire; UKWCS, UK Women's Cohort Study.

Received March 10, 2011. Accepted for publication July 7, 2011.

First published online August 24, 2011; doi: 10.3945/ajcn.111.015735.

Bingham et al (4). We also examined the association between fat and breast cancer in the subset of postmenopausal women who were not using hormone replacement therapy.

SUBJECTS AND METHODS

Subjects

We used data from the following 4 prospective cohort studies in the United Kingdom (**Table 1**): EPIC-Norfolk (7), EPIC-Oxford (8), the UKWCS (9), and Whitehall II study (10); data from a quintile study in the UK Dietary Cohort Consortium were not included because FFQs were not available in that study (the Medical Research Council National Survey of Health and Development). Participants gave informed consent, and each study was approved by the relevant ethics committee. Each cohort collected dietary information by using food diaries and FFQs. Information on demographic and lifestyle factors was collected either in interviews or in questionnaires administered before or at the same time as completion of the food diary.

Follow-up and ascertainment of cases of breast cancer

Follow-up for a diagnosis of breast cancer was through record linkage with the Office of National Statistics and local cancer registries. The 9th and 10th Revisions of the International Statistical Classification of Diseases, Injuries, and Causes of Death were used, and cancer of the breast was defined as codes 174 or C50, respectively. For each cohort in this study, closure dates of the study period were defined as the latest dates of complete follow-up for both cancer incidence and vital status and are given in Table 1.

Case patients were individuals who were free of cancer (except for nonmelanoma skin cancer) at the time of diary completion and who developed breast cancer ≥12 mo later (6 mo in EPIC-Oxford) and before the end of the study period. In total there were 637 cases, of which 110 cases were premenopausal, 113 cases were perimenopausal, 424 cases were postmenopausal, and 10 cases were of unknown menopausal status at the time of diary completion.

Selection of matched control subjects

Each case was matched to control participants who were selected at random from all cohort members and were free of cancer (except for nonmelanoma skin cancer) at the date of diary completion and free of breast cancer at the end of follow-up within the appropriate stratum of matching criteria. Matching criteria included cohort, age at first day of diary completion, and calendar month of diary completion. There were some differences in the details of study design between cohorts because this work had started before the establishment of the UK Dietary Cohort Consortium. The differences were as follows: age matching was ±3 y except in EPIC-Oxford in which it was ±6 mo; the date of diary matching was ±3 mo except in EPIC-Oxford in which it was ±6 mo; the number of control subjects per case was ≤4 control subjects in the EPIC-Norfolk and Whitehall II studies, ≤5 control subjects in the UKWCS, and one control subject in EPIC-Oxford; and women (cases and control subjects) who were using hormone replacement therapy at the time of diary completion were excluded in EPIC-Oxford.

Measurement of food and nutrient intake

Food diaries (7-d diaries in the EPIC-Norfolk, EPIC-Oxford, and Whitehall II studies and 4-d diaries in the UKWCS) were completed at the time of recruitment (in the EPIC-Norfolk and Whitehall II study), ~6 mo after recruitment (in EPIC-Oxford), or ~4 y after recruitment (in the UKWCS). Participants were asked to record all foods and drinks they consumed within the times of day presented in the food diary (eg, before breakfast, breakfast, and midmorning) and, except for in the UKWCS, with photographs that showed servings of representative food items to aid in the estimation of portion sizes. Information from food diaries was coded to give nutrient intakes on the basis of national food table data as described previously (6); for the EPIC-Norfolk, EPIC-Oxford, and Whitehall II studies, diaries were coded with the Data Into Nutrients for Epidemiological Research program (11), and for the UKWCS, diaries were coded with the DANTE program (12).

FFQs were completed at the time of recruitment and were derived from the FFQ used in the Nurses' Health Study (13) and

TABLE 1
Characteristics of the 4 cohorts who participated in analyses of dietary fat and breast cancer risk in the UK Dietary Cohort Consortium[1]

Cohort	Participants	Years of food-diary completion	Years of food-frequency questionnaire completion	Last follow-up date	Time to diagnosis of cases	Cases	Control subjects	Age at first day of food-diary completion
					y	*n*	*n*	*y*
EPIC-Norfolk	General population in Norfolk, United Kingdom	1993–1998	1993–1998	31 December 2006	6.0 ± 3.0[2]	353	1252	59.3 ± 8.6
EPIC-Oxford	General population and vegetarians in the United Kingdom	1993–1999	1993–1999	31 December 2004	3.5 ± 1.9	194	194	53.3 ± 10.8
UKWCS	Middle-aged women in the United Kingdom	1999–2002	1995–1998	31 March 2006	2.4 ± 1.3	42	202	56.6 ± 9.1
Whitehall II study	Civil servants in the United Kingdom	1991–1993	1991–1993	30 September 2005	7.8 ± 3.2	68	263	50.5 ± 6.0

[1] EPIC, European Prospective Investigation into Cancer and Nutrition; UKWCS, UK Women's Cohort Study.
[2] Mean ± SD (all such values).

further developed for use in the United Kingdom. The EPIC version had 130 items and was validated by comparison with weighed intakes and biomarkers (14). The UKWCS FFQ was extended to 217 items, and its performance was assessed compared with food diaries and plasma nutrient concentrations (9). The Whitehall II FFQ had 127 items, and its performance was assessed compared with data from food diaries and serum and plasma nutrient concentrations (15).

Statistical methods

Conditional logistic regression was used to calculate ORs and 95% CIs for breast cancer according to quintiles of intake (on the basis of intakes across all studies) of each of total, saturated, monounsaturated, and polyunsaturated fats. Fat intakes were analyzed by using both the absolute intake and the relative intake expressed as a percentage of the total energy intake. To test for trends in breast cancer risk over the distribution of intakes, we calculated the ORs (95% CIs) for an increase in fat intake of 1 SD, and the *P* value was obtained by comparison of the ratio of the logarithm of the OR and its SE to the normal distribution.

Because the age matching between cases and control subjects was up to ±3 y, analyses were adjusted for age as a continuous variable. Analyses were also adjusted for height (<158, 158–162, 163–167, or ≥168 cm), weight (<60, 60–65, 66–71, or ≥72 kg), menopausal status at recruitment (premenopausal, postmenopausal, or other), parity (0, 1, 2, 3, or ≥4), current use of hormone replacement therapy (no or yes), physical activity (low, low-medium, medium-high, or high), alcohol intake (<1, 1–7, 8–19, or ≥20 g/d), and total energy intake. For some of these variables, a small number of values were unknown (15 missing values for height, 29 missing values for weight, 25 missing values for menopausal status, 11 missing values for parity, 52 missing values for current use of hormone replacement therapy, and 102 missing values for physical activity; in total, 70 cases and 136 control subjects had missing values for some of these covariates); these observations were included in the analyses by using a separate "missing" category for each of these variables. In addition to the calculation of ORs for all of the women in the current analysis, we also investigated breast cancer risks in the separate studies and in the following subsets: cases diagnosed ≥2 y after food-diary commencement and their matched control subjects (to reduce the possible effect of reverse causality) and women who were postmenopausal and not using hormone replacement therapy at food-diary completion.

Two-sided *P* values <0.05 were considered significant. All statistical analyses were performed with Stata (version 10; StataCorp LP) (16).

RESULTS

A total of 657 women diagnosed with breast cancer and 1911 matched control subjects without breast cancer were included in the analyses. The mean time from food-diary completion to case diagnosis ranged from 2.4 y in the UKWCS to 7.8 y in the Whitehall II study, with an average of 5.2 y (Table 1).

Characteristics of cases and control subjects are presented in **Table 2**. The mean age at diary completion in cases was 56.4 y compared with 57.2 y in control subjects. A total of 65.5% of cases were postmenopausal at recruitment compared with 71.7% of control subjects. The mean height was 1.63 m in cases compared with 1.62 m in control subjects. The other nondietary characteristics did not differ significantly between cases and control subjects. For dietary characteristics, food-diary estimates of energy, alcohol, and monounsaturated and polyunsaturated fats were higher in cases than in control subjects, whereas for estimates from FFQs, the only significant difference was that alcohol intake was significantly higher in cases than in control subjects. Apart from alcohol, mean nutrient intakes in cases and control subjects, which were estimated from both the food diary and FFQ, did not differ by >5%.

Correlations between fat intakes as a percentage of energy estimated from food diaries and FFQs were 0.51 for total fat, 0.61 for saturated fat, 0.40 for monounsaturated fat, and 0.37 for polyunsaturated fat. Mean intakes of total fat as a percentage of energy as estimated from the food diaries were 32.9% in EPIC-Norfolk, 33.3% in EPIC-Oxford, 32.5% in the UKWCS, and 33.6% in the Whitehall II study. Corresponding estimates for FFQs were 32.0% in EPIC-Norfolk, 31.0% in EPIC-Oxford, 31.6% in the UKWCS, and 31.9% in the Whitehall II study.

Associations between fat intake and overall breast cancer risk are presented in **Table 3**. Median total fat intakes in the lowest and highest quintiles of intake were 41.0 and 94.7 g/d, respectively, on the basis of estimates from food diaries and 40.0 and 108.5 g/d, respectively, on the basis of estimates from FFQs. As a percentage of energy, median total fat intakes in the lowest and highest quintile of intake were 25.7% and 40.3%, respectively, on the basis of estimates from food diaries, and 24.2% and 39.3%, respectively, on the basis of estimates from FFQs. There was no evidence that total fat intake was positively associated with breast cancer risk; ORs (95% CIs) in the top quintile of fat intake were 0.87 (0.54, 1.41) and 0.80 (0.50, 1.30) for the food diary and FFQ, respectively, and corresponding values for the percentage of energy from fat were 0.90 (0.66, 1.23) and 0.80 (0.59, 1.09), respectively.

Median saturated fat intakes in the lowest and highest quintile of intake were 14.1 and 37.2 g/d, respectively, on the basis of estimates from food diaries, and 13.7 and 43.0 g/d, respectively, on the basis of estimates from FFQs. As a percentage of energy, median saturated fat intakes in the lowest and highest quintile of intake were 8.5% and 16.5%, respectively, on the basis of estimates from food diaries, and 7.9% and 16.4%, respectively, on the basis of estimates from FFQs. There was no evidence that saturated fat intake was positively associated with breast cancer risk; ORs (95% CIs) in the top quintile of saturated fat intake were 0.86 (0.57, 1.30) and 0.67 (0.44, 1.02) for the food diary and FFQ, respectively, and corresponding values for the percentage of energy from saturated fat were 0.81 (0.60, 1.10) and 0.81 (0.60, 1.09), respectively. There was also no evidence that intakes of monounsaturated or polyunsaturated fat were associated with breast cancer risk (Table 3).

ORs for breast cancer associated with an increase of 1 SD in the intake of fats estimated from food diaries and FFQs overall and in the 4 contributing studies, together with the tests for heterogeneity between studies, are shown in **Table 4**. For all women combined, breast cancer risk was not significantly associated with an SD increase in any of the fat components, either estimated from food diaries or FFQs. For food-diary estimates, there was a significant heterogeneity between studies for saturated fat as grams and the percentage of energy, and for polyunsaturated fat as the percentage

TABLE 2
Characteristics of cases and control subjects[1]

Characteristic	Control subjects	Cases	*P* for difference
n	1911	657	
Age at first day of diary completion (y)	57.2 ± 9.2[2]	56.4 ± 9.7	0.046
Age at menarche (y)[3]	12.9 ± 1.7	12.8 ± 1.5	0.251
Parity [*n* (%)][3]			
0	366 (19.2)	148 (22.6)	
1	249 (13.1)	84 (12.8)	
2	752 (39.5)	266 (40.6)	
3	361 (19.0)	112 (17.1)	
≥4	174 (9.1)	45 (6.9)	0.148
Menopausal status [*n* (%)][3]			
Premenopausal	344 (18.1)	110 (17.0)	
Perimenopausal	192 (10.1)	113 (17.5)	
Postmenopausal	1360 (71.7)	424 (65.5)	<0.001
Height (m)[3]	1.62 ± 0.06	1.63 ± 0.07	<0.001
Weight (kg)[3]	67.3 ± 12.2	67.9 ± 11.6	0.274
BMI (kg/m^2)[3]	25.8 ± 4.5	25.7 ± 4.5	0.688
Physical activity [*n* (%)][3]			
Inactive	495 (26.7)	176 (28.7)	
Moderately inactive	629 (33.9)	211 (34.4)	
Moderately active	416 (22.5)	139 (22.7)	
Active	313 (16.9)	87 (14.2)	0.426
Hormone replacement therapy use [*n* (%)][3]			
Never	1291 (69.0)	457 (71.0)	
Previous	232 (12.4)	69 (10.7)	
Current	349 (18.6)	118 (18.3)	0.489
Nutrient intake estimated from food diaries			
Energy intake (MJ/d)	7.36 ± 1.68	7.58 ± 1.65	0.004
Alcohol consumption (g/d)	8.9 ± 13.0	10.4 ± 13.7	0.008
Total fat consumption (g/d)	66.4 ± 21.2	68.3 ± 20.8	0.051
Total fat consumption (% of energy)	33.0 ± 5.7	33.0 ± 5.7	0.984
Saturated fat consumption (g/d)	25.1 ± 9.6	25.5 ± 9.4	0.334
Saturated fat consumption (% of energy)	12.4 ± 3.1	12.3 ± 3.2	0.450
Monounsaturated fat consumption (g/d)	22.7 ± 7.4	23.6 ± 7.5	0.014
Monounsaturated fat consumption (% of energy)	11.3 ± 2.2	11.4 ± 2.2	0.404
Polyunsaturated fat consumption (g/d)	12.6 ± 4.8	13.2 ± 5.1	0.007
Polyunsaturated fat consumption (% of energy)	6.3 ± 1.8	6.4 ± 1.8	0.272
Nutrient intake estimated from FFQs			
Energy intake (MJ/d)	8.23 ± 2.42	8.38 ± 2.69	0.175
Alcohol consumption (g/d)[3]	6.0 ± 8.8	7.4 ± 10.2	0.001
Total fat consumption (g/d)	71.7 ± 27.7	72.6 ± 30.5	0.493
Total fat consumption (% of energy)	31.9 ± 5.9	31.6 ± 6.1	0.293
Saturated fat consumption (g/d)	27.0 ± 12.3	27.1 ± 13.2	0.867
Saturated fat consumption (% of energy)	12.0 ± 3.3	11.7 ± 3.5	0.131
Monounsaturated fat consumption (g/d)	23.6 ± 9.7	24.0 ± 10.4	0.358
Monounsaturated fat consumption (% of energy)	10.5 ± 2.3	10.4 ± 2.4	0.852
Polyunsaturated fat consumption (g/d)	14.1 ± 6.4	14.3 ± 6.9	0.331
Polyunsaturated fat consumption (% of energy)	6.3 ± 2.1	6.3 ± 2.1	0.946

[1] *P* values were based on independent samples *t* tests for continuous variables and chi-square tests of association for categorical variables. FFQs, food-frequency questionnaires.
[2] Mean ± SD (all such values).
[3] Unknown for some participants.

energy. This heterogeneity was due to the results from the UKWCS, for which there were significant reductions in risk associated with an increase in the intake of saturated fat and a significant increase in risk associated with an increase in the intake of polyunsaturated fat. For FFQ estimates, there was significant heterogeneity between studies for polyunsaturated fat as a percentage of energy, which was due to the results from EPIC-Norfolk in which there was a significant reduction in risk in association with an increase in the intake of polyunsaturated fat as the percentage energy. Analyses of food-diary estimates of fat intake and breast cancer risk were repeated without the UKWCS. ORs (95% CIs) for a 1-SD increase in percentage of energy from fat were 0.97 (0.87, 1.07) for total fat, 1.00 (0.91, 1.11) for saturated fat, 0.98 (0.89, 1.09) for monounsaturated fat, and 0.93 (0.84, 1.03) for polyunsaturated fat.

ORs for breast cancer associated with an increase of 1 SD in the intake of fats estimated from food diaries and FFQs for 2 subsets of women are shown in **Table 5**. There were no

TABLE 3
Associations between fat intake and overall breast cancer risk[1]

	Quintile of fat intake					
	1 (referent)	2	3	4	5	*P*-trend
Nutrient intake estimated from food diaries						
Total fat (g/d)						
Median (g/d)	41.0	54.7	65.8	76.6	94.7	—
No. of cases/control subjects	116/397	124/391	141/371	131/383	145/369	—
OR (95% CI)	1.00	1.02 (0.74, 1.41)	1.10 (0.79, 1.54)	0.94 (0.64, 1.39)	0.87 (0.54, 1.41)	0.392
Total fat (% of energy)						
Median (% of energy)	25.7	30.3	33.2	35.8	40.3	—
No. of cases/control subjects	132/382	132/382	139/374	123/391	131/382	—
OR (95% CI)	1.00	1.00 (0.75, 1.35)	1.01 (0.75, 1.36)	0.88 (0.65, 1.20)	0.90 (0.66, 1.23)	0.504
SFA (g/d)						
Median (g/d)	14.1	19.8	24.3	29.0	37.2	—
No. of cases/control subjects	122/391	128/387	135/378	133/381	139/374	—
OR (95% CI)	1.00	0.97 (0.72, 1.33)	1.02 (0.73, 1.40)	0.92 (0.64, 1.32)	0.86 (0.57, 1.30)	0.224
SFA (% of energy)						
Median (% of energy)	8.5	10.8	12.3	13.7	16.5	—
No. of cases/control subjects	139/375	139/375	119/394	137/377	123/390	—
OR (95% CI)	1.00	0.99 (0.73, 1.32)	0.80 (0.59, 1.08)	1.01 (0.75, 1.35)	0.81 (0.60, 1.10)	0.343
MUFA (g/d)						
Median (g/d)	13.8	18.6	22.5	26.3	32.7	—
No. of cases/control subjects	116/398	120/394	146/366	122/393	153/360	—
OR (95% CI)	1.00	0.99 (0.71, 1.37)	1.23 (0.88, 1.73)	0.91 (0.62, 1.34)	1.03 (0.65, 1.62)	0.697
MUFA (% of energy)						
Median (% of energy)	8.6	10.3	11.4	12.4	14.1	—
No. of cases/control subjects	124/390	139/375	134/379	120/394	140/373	—
OR (95% CI)	1.00	1.13 (0.83, 1.53)	1.05 (0.77, 1.43)	0.87 (0.63, 1.19)	1.06 (0.78, 1.44)	0.813
PUFA (g/d)						
Median (g/d)	7.3	9.9	12.0	14.5	19.1	—
No. of cases/control subjects	126/388	116/398	129/384	141/372	145/369	—
OR (95% CI)	1.00	0.83 (0.61, 1.14)	0.88 (0.63, 1.21)	0.90 (0.64, 1.27)	0.77 (0.53, 1.13)	0.667
PUFA (% of energy)						
Median	4.3	5.3	6.1	7.0	8.6	—
No. of cases/control subjects	129/385	122/392	135/378	126/388	145/368	—
OR (95% CI)	1.00	0.87 (0.64, 1.19)	1.01 (0.75, 1.36)	0.84 (0.62, 1.14)	0.97 (0.71, 1.31)	0.565
Nutrient intake estimated from FFQs						
Total fat (g/d)						
Median (g/d)	40.0	54.9	67.7	82.7	108.5	—
No. of cases/control subjects	138/375	123/392	123/390	134/380	139/374	—
OR (95% CI)	1.00	0.83 (0.61, 1.13)	0.81 (0.58, 1.13)	0.78 (0.54, 1.12)	0.80 (0.50,1.30)	0.525
Total fat (% of energy)						
Median (% of energy)	24.2	28.7	32.0	34.9	39.3	—
No. of cases/control subjects	151/363	137/377	108/405	132/382	129/384	—
OR (95% CI)	1.00	0.94 (0.70, 1.26)	0.68 (0.50, 0.92)	0.85 (0.63, 1.14)	0.80 (0.59, 1.09)	0.366
SFA (g/d)						
Median (g/d)	13.7	19.7	24.8	31.2	43.0	—
No. of cases/control subjects	148/366	125/388	117/396	135/380	132/381	—
OR (95% CI)	1.00	0.79 (0.58, 1.06)	0.72 (0.52, 0.98)	0.78 (0.55, 1.11)	0.67 (0.44, 1.02)	0.606
SFA (% of energy)						
Median (% of energy)	7.9	10.1	11.7	13.3	16.4	—
No. of cases/control subjects	155/359	127/387	129/384	118/396	128/385	—
OR (95% CI)	1.00	0.76 (0.57, 1.03)	0.84 (0.63, 1.13)	0.76 (0.56, 1.03)	0.81 (0.60, 1.09)	0.434
MUFA (g/d)						
Median (g/d)	12.7	17.8	22.2	27.4	36.0	—
No. of cases/control subjects	131/383	132/382	121/392	133/381	140/373	—
OR (95% CI)	1.00	1.04 (0.76, 1.41)	0.84 (0.60, 1.16)	0.85 (0.59, 1.22)	0.91 (0.58, 1.43)	0.725
MUFA (% of energy)						
Median (% of energy)	7.5	9.2	10.5	11.6	13.4	—
No. of cases/control subjects	139/375	137/377	114/399	134/380	133/380	—
OR (95% CI)	1.00	1.05 (0.79, 1.40)	0.79 (0.58, 1.07)	0.97 (0.72, 1.30)	0.91 (0.67, 1.24)	0.705

(Continued)

TABLE 3 (*Continued*)

	Quintile of fat intake					
	1 (referent)	2	3	4	5	*P*-trend
PUFA (g/d)						
Median (g/d)	7.2	10.2	12.7	16.1	22.8	—
No. of cases/control subjects	124/390	138/375	134/380	123/391	138/375	—
OR (95% CI)	1.00	1.11 (0.83, 1.49)	1.01 (0.74, 1.37)	0.80 (0.57, 1.12)	0.91 (0.63, 1.31)	0.603
PUFA (% of energy)						
Median (% of energy)	4.0	5.0	5.9	7.0	9.1	—
No. of cases/control subjects	137/377	130/384	126/387	125/389	139/374	—
OR (95% CI)	1.00	0.93 (0.69, 1.24)	0.86 (0.64, 1.16)	0.83 (0.62, 1.11)	0.94 (0.71, 1.26)	0.546

[1] Conditional logistic regression was adjusted for age, alcohol consumption, parity, menopausal status, current hormone replacement therapy use, physical activity, height, weight, and energy intake. Analyses were based on 657 cases and 1911 matched control subjects. *P* values relate to tests for trend obtained by using the continuous intake variable. FFQs, food-frequency questionnaires; SFA, saturated fatty acid.

significant associations of fat with breast cancer risk in the subset of 548 cases (and 1620 matched control subjects) diagnosed ≥2 y after completing their food diaries. In the subset of women who were postmenopausal and not using hormone replacement therapy at the time of completing the food diary (286 cases and 699 matched control subjects), fat intake was inversely associated with risk, and this inverse association was significant for several fat-intake variables estimated from food diaries.

DISCUSSION

In this analysis, overall breast cancer risk was not associated with intakes of dietary total or saturated fat as estimated from food diaries or FFQs. Thus, we did not confirm the previous findings of Bingham et al (4) and Freedman et al (5), who reported that breast cancer risk was significantly associated with some measures of fat intakes from food diaries but not from FFQs. Although both Bingham et al (4) and Freedman et al (5) reported significant associations with diary estimates of fat, their results differed. In Bingham et al (4), the association was not significant for total fat but was significant for saturated fat, whereas in Freedman et al (5), the association was significant for total fat but not for saturated fat. Furthermore, although these authors highlighted differences in their results between food diaries and FFQs, their results for total fat from FFQs were in the

TABLE 4
Breast cancer associated with a 1-SD increase in fat intake as estimated from food diaries and FFQs overall and subdivided by cohort[1]

Nutrient intake (1 SD)	All women[2]	EPIC-Norfolk[3]	EPIC-Oxford[4]	UKWCS[5]	Whitehall II study[6]	*P*-heterogeneity between cohorts
Estimated from food diaries						
Total fat (21.1 g/d)	0.92 (0.77, 1.11)	0.83 (0.65, 1.05)	1.00 (0.67, 1.50)	1.01 (0.50, 2.05)	1.31 (0.73, 2.36)	0.622
Total fat (5.7% of energy)	0.97 (0.88, 1.07)	0.92 (0.81, 1.05)	0.99 (0.79, 1.24)	0.97 (0.67, 1.42)	1.29 (0.91, 1.83)	0.201
SFA (9.6 g/d)	0.92 (0.80, 1.06)	0.96 (0.78, 1.17)	0.84 (0.62, 1.13)	0.41 (0.22, 0.77)*	1.37 (0.89, 2.10)	0.015
SFA (3.2% of energy)	0.95 (0.87, 1.05)	0.98 (0.86, 1.12)	0.89 (0.72, 1.10)	0.53 (0.34, 0.83)*	1.31 (0.96, 1.78)	0.002
MUFA (7.5 g/d)	0.97 (0.82, 1.14)	0.84 (0.67, 1.05)	1.03 (0.72, 1.46)	0.98 (0.56, 1.74)	1.59 (0.93, 2.71)	0.476
MUFA (2.2% of energy)	0.99 (0.89, 1.09)	0.92 (0.81, 1.05)	1.00 (0.80, 1.25)	0.97 (0.69, 1.37)	1.48 (1.04, 2.09)*	0.081
PUFA (4.9 g/d)	0.97 (0.86, 1.10)	0.84 (0.70, 1.01)	1.27 (0.97, 1.66)	1.97 (1.18, 3.28)*	0.66 (0.42, 1.03)	0.101
PUFA (1.8% of energy)	0.97 (0.88, 1.07)	0.88 (0.77, 1.01)	1.19 (0.96, 1.46)	1.60 (1.10, 2.33)*	0.77 (0.54, 1.10)	0.009
Estimated from FFQs						
Total fat (28.5 g/d)	0.94 (0.76, 1.15)	0.85 (0.65, 1.12)	1.00 (0.62, 1.61)	0.85 (0.38, 1.92)	1.28 (0.70, 2.35)	0.529
Total fat (6.0% of energy)	0.96 (0.87, 1.05)	0.93 (0.82, 1.06)	0.93 (0.75, 1.15)	0.86 (0.53, 1.39)	1.16 (0.85, 1.57)	0.423
SFA (12.5 g/d)	0.96 (0.82, 1.12)	1.02 (0.82, 1.25)	0.76 (0.53, 1.10)	0.77 (0.41, 1.43)	1.16 (0.78, 1.75)	0.742
SFA (3.4% of energy)	0.96 (0.87, 1.06)	1.01 (0.88, 1.15)	0.80 (0.63, 1.00)*	0.71 (0.43, 1.18)	1.14 (0.86, 1.51)	0.116
MUFA (9.9 g/d)	0.97 (0.81, 1.16)	0.87 (0.68, 1.12)	1.23 (0.82, 1.84)	0.96 (0.49, 1.87)	1.20 (0.65, 2.20)	0.450
MUFA (2.3% of energy)	0.98 (0.89, 1.08)	0.94 (0.82, 1.08)	1.02 (0.83, 1.25)	1.00 (0.64, 1.56)	1.18 (0.84, 1.64)	0.428
PUFA (6.5 g/d)	0.97 (0.85, 1.10)	0.83 (0.69, 0.99)*	1.30 (0.95, 1.78)	1.16 (0.70, 1.90)	1.06 (0.71, 1.59)	0.056
PUFA (2.1% of energy)	0.97 (0.88, 1.07)	0.86 (0.76, 0.98)*	1.19 (0.95, 1.49)	1.17 (0.77, 1.78)	1.09 (0.82, 1.46)	0.033

[1] All values are ORs; 95% CIs in parentheses. Conditional logistic regression was adjusted for age, alcohol consumption, parity, menopausal status and current hormone replacement therapy use when applicable, physical activity, height, weight, and energy intake. *$P < 0.05$ (*P* values relate to tests for trend obtained by using the continuous intake variable). EPIC, European Prospective Investigation into Cancer and Nutrition; FFQs, food-frequency questionnaires; SFA, saturated fatty acid; UKWCS, United Kingdom Women's Cohort Study.

[2] Analyses were based on 657 cases and 1911 matched control subjects.

[3] Analyses were based on 353 cases and 1252 matched control subjects.

[4] Analyses were based on 194 cases and 194 matched control subjects.

[5] Analyses were based on 42 cases and 202 matched control subjects.

[6] Analyses were based on 68 cases and 263 matched control subjects.

TABLE 5
Breast cancer associated with a 1-SD increase in fat intake as estimated from food diaries and FFQs in subsets of follow-up and menopausal status[1]

Nutrient intake (1 SD)	Cases diagnosed ≥2 y after diary commencement[2]	Women who were postmenopausal and not using hormone replacement therapy at diary commencement[3]
Estimated from the food diaries		
Total fat (21.1 g/d)	0.93 (0.76, 1.14)	0.70 (0.52, 0.95)*
Total fat (5.7% of energy)	0.98 (0.87, 1.09)	0.81 (0.69, 0.95)*
SFA (9.6 g/d)	1.00 (0.85, 1.17)	0.81 (0.64, 1.02)
SFA (3.2% of energy)	1.01 (0.91, 1.13)	0.85 (0.73, 1.00)*
MUFA (7.5 g/d)	0.93 (0.77, 1.12)	0.76 (0.58, 1.01)
MUFA (2.2% of energy)	0.97 (0.87, 1.09)	0.83 (0.71, 0.98)*
PUFA (4.9 g/d)	0.88 (0.76, 1.02)	0.87 (0.71, 1.07)
PUFA (1.8% of energy)	0.91 (0.81, 1.02)	0.89 (0.76, 1.04)
Estimated from the FFQs		
Total fat (28.5 g/d)	0.94 (0.75, 1.17)	0.78 (0.56, 1.08)
Total fat (6.0% of energy)	0.95 (0.85, 1.06)	0.89 (0.76, 1.03)
SFA (12.5 g/d)	0.99 (0.84, 1.17)	0.84 (0.66, 1.07)
SFA (3.4% of energy)	0.98 (0.88, 1.10)	0.90 (0.78, 1.05)
MUFA (9.9 g/d)	0.96 (0.79, 1.17)	0.82 (0.62, 1.09)
MUFA (2.3% of energy)	0.97 (0.87, 1.08)	0.89 (0.76, 1.05)
PUFA (6.5 g/d)	0.93 (0.81, 1.07)	0.98 (0.81, 1.19)
PUFA (2.1% of energy)	0.93 (0.84, 1.03)	0.96 (0.83, 1.11)

[1] All values are ORs; 95% CIs in parentheses. Conditional logistic regression was adjusted for age, alcohol consumption, parity, menopausal status and current hormone replacement therapy use when applicable, physical activity, height, weight, and energy intake. $^*P < 0.05$ (P values relate to tests for trend obtained by using the continuous intake variable). FFQs, food-frequency questionnaires; SFA, saturated fatty acid.

[2] Analyses were based on 548 cases and 1620 matched control subjects.

[3] Analyses were based on 286 cases and 699 matched control subjects.

same direction as their results from diaries. We cannot identify any reason why our results were somewhat different from those of Bingham et al (5); the results of Bingham et al (4) were based on 168 breast cancer cases out of 657 cases included in the current analysis, and because the current results were based on nearly 4 times as many cases, the results should be more reliable.

The main strength of the current study is that it was a moderately large study with data on fat intakes from food diaries and FFQs and was designed to examine the possibility that food diaries are better able to detect the putative association between fat and breast cancer. Weaknesses are that the sample size was not large enough to exclude small associations of dietary fat with breast cancer risk, and although the research in the 4 cohorts was standardized in the analysis phase, there were some differences between contributing cohorts in study design (the format of food diaries and FFQs, eligibility, and control selection). An examination of results from the individual studies showed no evidence of heterogeneity for total fat intake, but there was some heterogeneity for subtypes of fat. The largest departures from overall estimates were for food-diary estimates in the UKWCS, in which risk was inversely associated with saturated fat but positively associated with polyunsaturated fat. We were not able to identify any reason for this heterogeneity, which could have been due to chance, a real difference between the cohorts, or perhaps related to the different method of coding food diaries in the UKWCS. The exclusion of the data from this cohort had no material effect on the overall results.

Validation studies that used biomarkers have shown that the food diary used in these British cohorts was more accurate than the FFQ for estimating absolute intakes of some nutrients, particularly of nitrogen and potassium, and it has been argued that is a better method overall (14, 17). However, for total fat, there is no direct biomarker, and it cannot be assumed that the diary is better than the FFQ. Compared with 16 d of weighed food intakes, the correlations of total fat intake (as a percentage of energy) with estimates from the 7-d food diary and FFQ were 0.77 and 0.64, respectively (14). Some information on the validity of estimates of the intake of saturated fat can be gained by examining its association with plasma LDL cholesterol; in EPIC-Norfolk, the percentage of energy from saturated fat was positively associated with plasma LDL cholesterol for both the food diary (P-trend < 0.001) and FFQ (P-trend = 0.011) (17). For polyunsaturated fat, a validation study in women in the Whitehall II study (15) showed almost identical correlations between serum cholesteryl ester PUFAs and dietary PUFAs as a percentage of total dietary fatty acids as measured by the food diary (0.49) or FFQ (0.50). Thus, the available evidence from validation studies suggested that both of the methods used in these British cohorts provided reasonably valid estimates of the intake of fat but did not show that either method was better than the other method.

We conducted 2 subset analyses. In the first analysis, we examined associations of fat with breast cancer risk in cases (and their matched control subjects) who had completed their food diary ≥2 y before diagnosis to exclude any effects of prediagnostic events on diet; this analysis provided similar results to the overall analysis. We also examined the subset of women who were postmenopausal and not using hormone replacement therapy at the time that they completed their food diaries. This subset was of interest because, in the NIH-AARP study, the positive associations of total, saturated, and monounsaturated fats with breast cancer risk were confined to women in this subset (18), and the adverse effect of obesity (which might be

TABLE 6
Prospective studies of total fat, saturated fat, and breast cancer risk

Reference	Study	No. of cases	Dietary assessment	Exposure category and model	Total fat	Saturated fat
Pooled analysis						
Smith-Warner et al, 2001 (2)	Pooled analysis of 8 prospective studies, 7 studies of which were included in Boyd et al, 2003 (20)	7329	Food-frequency questionnaires	5% increase in energy from fat, adjusted for total energy	1.00 (0.98, 1.03)[1]	1.03 (0.95, 1.10)
Meta-analysis						
Boyd et al, 2003 (20)	Meta-analysis of 14 prospective studies, 7 of which were included in Smith-Warner et al, 2001 (2)	8735	10 studies with food-frequency questionnaires; 4 studies with food record, recall, or diet history	Highest compared with lowest tertiles, quartiles or quintiles of fat, various models	1.11 (0.99, 1.25)	1.15 (1.02, 1.30)
Individual studies since 2003						
Löf et al, 2007 (21)	Swedish Women's Lifestyle and Health Cohort	974	Food-frequency questionnaire	Highest compared with lowest quintiles of fat, adjusted for energy	1.02 (0.72, 1.45)	1.12 (0.69, 1.81)
Thiébaut et al, 2007 (18)	NIH-AARP Diet and Health Study	3501	Food-frequency questionnaire	Highest compared with lowest quintiles of percentage of energy from fat, adjusted for energy	1.11 (1.00, 1.26)	1.18 (1.06, 1.31)
Sieri et al, 2008 (22)	European Prospective Investigation into Cancer and Nutrition	7119	Mostly food-frequency questionnaires	Highest compared with lowest quintiles of percentage of energy from fat, adjusted for energy	1.04 (0.96, 1.13)	1.10 (1.01, 1.19)
Studies with food records and food-frequency questionnaires						
Freedman et al, 2006 (5)	Women's Health Initiative USA, nonintervention group	603	Food record Food-frequency questionnaire	Highest compared with lowest quintiles of fat, adjusted for energy	2.09 (1.21, 3.61) 1.71 (0.70, 4.18)	1.51 (0.94, 2.43) 1.00 (0.49, 2.02)
Current study	Pooled analysis of 4 British prospective studies	657	Food record Food-frequency questionnaire	Highest compared with lowest quintiles of percentage of energy from fat, adjusted for energy	0.90 (0.66, 1.23) 0.80 (0.59, 1.09)	0.81 (0.60, 1.10) 0.81 (0.60, 1.09)
Randomized controlled trials						
Prentice et al, 2006 (23)	Women's Health Initiative	1727	Intervention trial	Low-fat dietary pattern intervention compared with control subjects	0.91 (0.83, 1.01)	Not applicable
Martin et al, 2011 (24)	Canadian dietary intervention trial	220	Intervention trial	Low-fat dietary pattern intervention compared with control subjects	1.19 (0.91, 1.55)	Not applicable

[1] RR; 95% CI in parentheses (all such values).

associated with fat intake) on breast cancer risk is also largely seen in this subset (19). However, in our analysis, the point estimates of the association of fat with breast cancer risk in this subset were all less than one and nearly all were lower than the corresponding point estimates for all women, and for several fat intake variables estimated from the food diary, the association was significantly inverse. Thus, in our analysis there was no evidence that fat intake was positively associated with breast cancer risk in the subset of postmenopausal women who were not taking hormone replacement therapy.

The results of other prospective studies of dietary fat intakes in adult women and breast cancer risk are summarized in **Table 6**. In a pooled analysis of 8 studies that all used FFQs, there was no association of the total or saturated fat intake with breast cancer risk (2). In a subsequent meta-analysis of 14 prospective studies published up to 2003, which included 4 studies that used food-record or interview-based methods for assessments of diets and also 7 of 8 studies in the pooled analysis (2), RRs (95% CIs) were 1.11 (0.99, 1.25) and 1.15 (1.02, 1.30) for the highest compared with lowest amounts of total fat and saturated fat, respectively (20). In subsequent studies that used FFQs, there was no association of total or saturated fat intakes with breast cancer risk in a Swedish cohort (21), whereas in the NIH-AARP study (18), both total and saturated fats were weakly but significantly positively associated with risk [RRs (95% CIs) for high intake of 1.11 (1.00, 1.26) and 1.18 (1.06, 1.31), respectively]. In the largest single study that used data from women in 10 European countries (22) that were mostly based on FFQs (with some data from diet-history methods and food records), total fat was not associated with risk, whereas there was a small but significant positive association of risk with the intake of saturated fat [RR (95% CI) for a high intake of saturated fat: 1.10 (1.01, 1.19)]; there was some overlap between this study and the current study because the FFQ data from EPIC-Norfolk and EPIC-Oxford were included in both analyses. In an analysis of data from food records and FFQs for women in the control arm of the Women's Health Initiative (5), there was a large and significant association of the total fat intake estimated from food records with risk [RR (95% CI): 2.09 (1.21, 3.61)] but no other significant associations. In 2 randomized controlled trials, a reduction in the total fat intake did not significantly affect breast cancer risk (23, 24). Overall, prospective studies on fat intake in adult women and breast cancer risk suggested either no association or, at most, a small positive association. The earlier report of Bingham et al (4) and the study of Freedman et al (5) suggested that data from food diaries and records might give larger associations than those observed by using FFQs, but the current study did not support this result and suggested that any inconsistencies in the literature on the association between dietary fat and breast cancer risk were not likely to be explained simply by differences between dietary assessment methods.

In conclusion, this study showed no evidence that breast cancer risk was associated with fat intake in middle-aged women in the United Kingdom, irrespective of whether the diet was measured by food diaries or by FFQs.

We thank the participants in the cohort studies for their contributions to this research. Sheila Rodwell (also known professionally as Sheila Bingham), who died in 2009, established the UK Dietary Cohort Consortium as part of the Medical Research Council Centre for Nutritional Epidemiology and Cancer of which she was director.

The authors' responsibilities were as follows—TJK, EJB, VB, JEC, AMS, DK, RHK, and KTK, designed the research; TJK, EJB, VB, JEC, AAM, and KTK: acquired data; PNA, RL, RHK, and IRW: performed statistical analyses; TJK: wrote the manuscript; and all authors: interpreted data, contributed to and reviewed the manuscript, and read and approved the final manuscript. None of the authors had a personal or financial conflict of interest.

REFERENCES

1. Lea AJ. Dietary factors associated with death-rates from certain neoplasms in man. Lancet 1966;2:332–3.
2. Smith-Warner SA, Spiegelman D, Adami HO, et al. Types of dietary fat and breast cancer: a pooled analysis of cohort studies. Int J Cancer 2001;92:767–74.
3. Gerber M. Background review paper on total fat, fatty acid intake and cancers. Ann Nutr Metab 2009;55:140–61.
4. Bingham SA, Luben R, Welch A, Wareham N, Khaw K-T, Day N. Are imprecise methods obscuring a relation between fat and breast cancer. Lancet 2003;362:212–4.
5. Freedman LS, Potischman N, Kipnis V, Midthune O, Schatzkin A, Thompson FE, Troiano RP, Prentice R, Patterson R, Carroll R, et al. A comparison of two dietary instruments for evaluating the fat-breast cancer relationship. Int J Epidemiol 2006;35:1011–21.
6. Dahm CC, Keogh RH, Spencer EA, Greenwood DC, Key TJ, Fentiman IS, Shipley MJ, Brunner EJ, Cade JE, Burley VJ, et al. Dietary fiber and colorectal cancer risk: a nested case-control study using food diaries. J Natl Cancer Inst 2010;102:614–26.
7. Day N, Oakes S, Luben R, Khaw KT, Bingham S, Welch A, Wareham N. EPIC-Norfolk: study design and characteristics of the cohort. European Prospective Investigation of Cancer. Br J Cancer 1999;80(suppl 1):95–103.
8. Davey GK, Appleby PN, Spencer EA, Key TJ. EPIC-Oxford: lifestyle characteristics and nutrient intakes in a cohort of 33883 meat-eaters and 31546 non meat-eaters in the UK. Public Health Nutr 2003;6:259–68.
9. Cade JE, Burley VJ, Greenwood DC; UK Women's Cohort Study Steering Group. The UK Women's Cohort Study: comparison of vegetarians, fish-eaters and meat-eaters. Public Health Nutr 2004;7:871–8.
10. Marmot M, Brunner E. Cohort profile: the Whitehall II study. Int J Epidemiol 2005;34:251–6.
11. Welch AA, McTaggart A, Mulligan AA, Luben R, Walker N, Khaw KT, Day NE, Bingham SA. DINER (Data Into Nutrients for Epidemiological Research) - a new data-entry program for nutritional analysis in the EPIC-Norfolk cohort and the 7-day diary method. Public Health Nutr 2001;4:1253–65.
12. Cade JE, Frear L, Greenwood DC. Assessment of diet in young children with an emphasis on fruit and vegetable intake: using CADET–Child and Diet Evaluation Tool. Public Health Nutr 2006;9:501–8.
13. Willett WC, Sampson L, Stampfer MJ, Rosner B, Bain C, Witschi J, Hennekens CH, Speizer FE. Reproducibility and validity of a semiquantitative food frequency questionnaire. Am J Epidemiol 1985;122:51–65.
14. Bingham SA, Gill C, Welch A, Cassidy A, Runswick SA, Oakes S, Lubin R, Thurnham DI, Key TJ, Roe L, Khaw KT, Day NE. Validation of dietary assessment methods in the UK arm of EPIC using weighed records, and 24-hour urinary nitrogen and potassium and serum vitamin C and carotenoids as biomarkers. Int J Epidemiol 1997;26(suppl 1):S137–51.
15. Brunner E, Stallone D, Juneja M, Bingham S, Marmot M. Dietary assessment in Whitehall II: comparison of 7 d diet diary and food-frequency questionnaire and validity against biomarkers. Br J Nutr 2001;86:405–14.
16. StataCorp. Stata Statistical Software: release 10. College Station, TX: StataCorp LP, 2007.
17. Bingham S, Luben R, Welch A, Low YL, Khaw KT, Wareham N, Day N. Associations between dietary methods and biomarkers, and between fruits and vegetables and risk of ischaemic heart disease, in the EPIC Norfolk Cohort Study. Int J Epidemiol 2008;37:978–87.
18. Thiébaut AC, Kipnis V, Chang SC, Subar AF, Thompson FE, Rosenberg PS, Hollenbeck AR, Leitzmann M, Schatzkin A. 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.
19. Lahmann PH, Hoffmann K, Allen N, van Gils CH, Khaw KT, Tehard B, Berrino F, Tjønneland A, Bigaard J, Olsen A, et al. Body size and breast

cancer risk: findings from the European Prospective Investigation into Cancer And Nutrition (EPIC). Int J Cancer 2004;111:762–71.
20. 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.
21. Löf M, Sandin S, Lagiou P, Hilakivi-Clarke L, Trichopoulos D, Adami HO, Weiderpass E. Dietary fat and breast cancer risk in the Swedish women's lifestyle and health cohort. Br J Cancer 2007;97: 1570–6.
22. Sieri S, Krogh V, Ferrari P, Berrino F, Pala V, Thiébaut AC, Tjønneland A, Olsen A, Overvad K, Jakobsen MU, 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.
23. Prentice RL, Caan B, Chlebowski RT, Patterson R, Kuller LH, Ockene JK, Margolis KL, Limacher MC, Manson JE, Parker LM, 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.
24. Martin LJ, Li Q, Melnichouk O, Greenberg C, Minkin S, Hislop G, Boyd NF. A randomized trial of dietary intervention for breast cancer prevention. Cancer Res 2011;71:123–33.