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Title
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Permalink
https://escholarship.org/uc/item/3628d5kr

Journal
Cancer Causes & Control, 13(5)

ISSN
0957-5243

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Publication Date
2002-06-01

DOI
10.1023/a:1015786030864

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Cancer Causes and Control **13**: 407–415, 2002.
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Recent diet and breast cancer risk: the California Teachers Study (USA)

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Received 1 May 2001; accepted in revised form 15 January 2002

Key words: alcohol, antioxidants, breast cancer, diet, fat, phytoestrogens.

Abstract

Objective: The impact, if any, on breast cancer risk of modifying adult dietary intake is an area of much interest. We take the opportunity to address the relationship between recent adult diet and breast cancer risk during the first two years of follow-up of the large California Teachers Study cohort.

Methods: Of the 111,526 at-risk cohort members who resided in California and completed a baseline dietary assessment, 711 were diagnosed with invasive breast cancer after joining the cohort and before January 1998. Average daily nutrient intake was computed based on a food-frequency questionnaire assessing usual dietary intake and portion size during the year prior to joining the cohort. Incident breast cancers were identified through the California Cancer Registry and follow-up for death and confirmation of continued California residence utilized a variety of data sources. Cox proportional hazards models were used to calculate relative hazards.

Results: The following components of recent dietary intake were not associated with breast cancer risk: energy, fat, fiber, antioxidant vitamins, and phytoestrogens. Only recent average alcohol consumption of 20 or more grams per day (approximately two or more glasses of wine) was associated with increased risk (RR = 1.5, 95% CI: 1.2–2.0 compared to non-drinkers; $p_{\text{trend}} = 0.01$ across quintiles).

Conclusion: With the exception of alcohol consumption, this study provides no evidence that recent macro- or micronutrient composition of adult diet is likely to have a direct effect on breast cancer risk. Some reduction of alcohol consumption among those consuming more than one drink per day may be beneficial.

Introduction

Primary prevention of breast cancer through dietary modification is an area of much current interest, both scientifically and among the lay public. The behavior of many women is influenced by their beliefs about whether changing their diet as an adult will prevent the development of breast cancer; that is, whether dietary intake in the recent past can impact breast cancer risk. While intervention trials (such as the Women's Health Initiative [1] and the Canadian Diet and Breast Cancer Prevention Study [2]) directly address these questions, answers will not be available for some time yet and will be limited to certain aspects of diet. However, analyses of cohort studies, addressing different time periods and a wide variety of dietary components, can also be informative in this regard.

The incidence of breast cancer in California teachers and administrators is about 20% higher than the average incidence rate in the state, even when ethnic differences are taken into account [3, 4]. Dietary intake is reasonably heterogeneous in this population, as are most other lifestyle factors (see Table 1). Thus, we have taken the opportunity to address the issue of how recent dietary intake may impact breast cancer risk during the initial 2 years of follow-up in our cohort of over 133,000

Table 1. Selected characteristics of the California Teachers Study (CTS) cohort as included in the present analysis (n = 111,526)

Characteristics	n (%)	Mean	Percentile	
			20th	80th
Months of follow-up		23.9	20	26
Demographics				
Age at baseline (years)		52.5	41	65
<45	32,619 (29%)			
45–54	33,866 (30%)			
55–64	20,960 (19%)			
≥65	24,081 (22%)			
Race/ethnicity				
White	96,838 (87%)			
African American	2,796 (3%)			
Latina	4,777 (4%)			
Asian/Pacific Islander	3,921 (4%)			
Other/mixed	2,313 (2%)			
Not stated	881 (1%)			
Menstrual/reproductive factors				
Age at menarche (years)		12.5	11	14
≤10	7,800 (7%)			
11	16,970 (15%)			
12	30,135 (27%)			
13	32,411 (29%)			
14	13,802 (12%)			
≥15	8,823 (8%)			
Unknown/missing	1,585 (1%)			
Nulliparous	29.156 (26%)			
Age at first full-term pregnancy (years)		26.4	22	30
<20	4,057 (4%)			
20–24	24,414 (22%)			
25–29	32,435 (29%)			
30–34	14,251 (13%)			
≥35	4,487 (4%)			
Unknown/missing	2,726 (2%)			
Menopausal status at baseline				
Pre/perimenopausal	43,218 (39%)			
Postmenopausal	53,703 (48%)			
Unable to determine	14,605 (13%)			
Family history of breast cancer (first-degree relative)				
Yes	13,069 (12%)			
No	96,807 (87%)			
Unknown/missing	1,650 (1%)			
Body mass index		24.9	20.8	28.3
<20	11,848 (11%)			
20–24.9	53,470 (48%)			
25–29.9	26,391 (24%)			
≥30	15,018 (13%)			
Missing/unable to determine	4,799 (4%)			
Physical activity (hours of moderate or strenuous activity per week over the last 3 years)		2.9	0	5
Daily caloric intake (kcal)		1,559	1,096	1,960
Macronutrients				
Fat (g/day)		56	34	75
Saturated fat (g/day)		18	11	25
Linoleic acid (g/day)		11	6	16
Oleic acid (g/day)		21	13	29
Carbohydrates[a] (g/day)		187	128	240
Protein (g/day)		62	42	80

Table 1. (Continued)

Characteristics	n (%)	Mean	Percentile	
			20th	80th
Percentage of kcal from fat		32	25	38
Percentage of kcal from carbohydrates[a]		51	44	57
Percentage of kcal from protein		16	14	18
Fiber (g/day)		15	9	19
Ratios				
Fat:fiber		4.3	2.5	5.9
Carbohydrate:protein		3.1	2.5	3.7
Antioxidant vitamins				
β-carotene[b] (μg/day)		4,084	1,465	4,652
α-carotene[c] (μg/day)		494	157	766
Lycopene[c] (μg/day)		1,915	910	2,777
Lutein[c] (μg/day)		1,296	576	1,782
Cryptoxanthin[c] (μg/day)		95	27	154
Vitamin C[b] (mg/day)		390	79	653
Vitamin E[b] (α-TE/day)		94	8	204
Antioxidant index scores[d]				
Peroxyl radical absorbance capacity		4.8	2.1	6.9
Hydroxyl radical absorbance capacity		1.7	0.8	2.5
Antioxidant capacity against transition metals		0.8	0.4	1.1
Total score		17.7	8.3	25.0
Phytoestrogens (μg/day)				
Isoflavones		1,778	641	2,080
Genistein		919	290	1,100
Daidzein		801	301	906
Biochanin A		25	9	37
Formononetin		35	5	42
Coumestrol		114	64	157
Lignans		108	65	148
Matairesinol		23	12	33
Secoisolariciresinol		85	48	121
Total		2,001	821	2,343
Alcohol (g/day)				
Beer				
Non-drinkers	77,425 (69%)			
<5	24,667 (22%)			
5–19	2,547 (2%)			
≥20	496 (<1%)			
Wine				
Non-drinkers	42,241 (38%)			
<5	44,421 (40%)			
5–19	14,609 (13%)			
≥20	3,864 (3%)			
Liquor				
Non-drinkers	71,511 (64%)			
<5	27,613 (25%)			
5–19	4,660 (4%)			
≥20	1,351 (1%)			
Total		11.4[e]	3.3[e]	15.6[e]
Non-drinkers	35,004 (31%)			
<5	20,367 (18%)			
5–9	18,029 (16%)			
10–14	13,990 (13%)			
15–19	8,912 (8%)			
≥202	8,833 (8%)			
Unknown/missing	6,391 (6%)			

Table 1. (Continued)

[a] Not including carbohydrates from alcohol.
[b] From food and supplements.
[c] From food only.
[d] Specific antioxidant scores are based on values in vegetables; total score includes values from fruits and vegetables.
[e] Among consumers only.

California teachers. In addition to addressing many of the commonly studied nutrients we also examine the effects of specific nutrient ratios, indices of antioxidant intake, and the intake of specific phytoestrogenic compounds.

Materials and methods

Study population

The California Teachers Study (CTS) cohort was established in 1995–1996 when 133,479 active and retired female teachers and administrators participating in the California State Teachers Retirement System returned a 16-page, mailed, optically scannable questionnaire [4]. The questionnaire covered a wide variety of issues related to breast cancer risk and women's health. Included were questions on demographics; menstrual and reproductive events; use of exogenous estrogens, vitamins, and medications; personal and family history of cancer and chronic diseases; screening behaviors; physical activity; height and weight; dietary intake; use of alcohol and tobacco; and indications of exposure to potential environmental hazards. Whenever possible, phrasing of questions was drawn from established and validated instruments. At baseline the cohort ranged in age from 21 to 103 years.

For purposes of this analysis we excluded women (in a hierarchical manner) who were not residing in California at baseline (n = 9700), had joined the cohort after 1997 (n = 34), reported having been diagnosed with breast cancer prior to completing the baseline questionnaire, or were identified by the California Cancer Registry as having had a previous breast cancer (n = 7027), had not completed the dietary questionnaire (n = 3070), or whose self-report of food consumption was judged to be overreported (*i.e.* >5000 calories/day) or underreported (*i.e.* <600 calories/day) (n = 78 and 2044, respectively) based on estimated daily caloric intake. Of the 111,526 women included in this analysis, 711 were diagnosed with invasive breast cancer and 143 with *in-situ* breast cancer a month or more after joining the cohort and before 1 January 1998. Less than 1% of the 111,526 women had moved out of California or died prior to 1 January 1998; these women contributed person-months to the analysis up to the date of these events.

Dietary assessment

Dietary intake was assessed using an early version of the 1995 food-frequency questionnaire (FFQ) developed and validated by Dr Gladys Block [5–8]. The dietary assessment focused on the year prior to baseline (for most women this was 1995) and included questions on the frequency of consumption and portion size of 103 food and beverage items/groups; assessments of vitamin supplement use and alcohol consumption; and several ancillary questions on cooking practices. The original Block nutrient database was updated using data from various sources [9–11] and values of antioxidant indices (*i.e.* the antioxidant activity of a variety of vegetables against peroxyl radicals, hydroxyl radicals, and those produced by the oxidation of transition metals and a total score based on the antioxidant capacity of fruits and vegetables [12, 13]) and seven phytoestrogenic compounds (*i.e.* the isoflavones: genistein, daidzein, biochanin A, and formononetin; the coumestan: coumestrol; and the lignans: matairesinol and secoisolariciresinol [14]) per 100 g of food were added. Daily intake of calories, macro- and micronutrients, fiber, phytoestrogens, alcohol, and the four antioxidant index scores were calculated for each woman.

Follow-up

The cohort is followed annually for cancer diagnosis, death, and change of address. Annual linkage between the California Cancer Registry (CCR) and the cohort membership is used to identify incident cancer cases and to obtain information on the characteristics of the tumor, including site and stage, and for cancers of the breast, estrogen receptor (ER) status. The CCR is a population-based cancer registry, is anchored in legislation that mandates reporting, covers the entire state of California, has interstate agreements with 13 other states for casesharing purposes, and is estimated to be over 97% complete. The San Francisco Bay Area, Santa Clara–Monterey Bay Area, and Los Angeles County registries have been part of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program for many years and the remainder of the state has recently been included in this program. Thus, the CCR maintains the high-quality standards set

by the SEER program. Linkage between the CTS cohort and the CCR database is based on full name, date of birth, address, and social security number, and includes manual review of possible matches. Mortality files as well as reports from relatives are used to ascertain date and cause of death. Changes of address are obtained by annual mailings, responses from participants, and record linkages with multiple sources, including the California Department of Motor Vehicles and the US Postal Service National Change of Address database.

Data analysis

Follow-up time was calculated as the number of months between joining the cohort (*i.e.* the date the baseline questionnaire was completed) and either the date of breast cancer diagnosis, the date of death, the date (or estimated date) the woman moved out of California, or 31 December 1997, whichever came first. Relative risks and 95% confidence intervals were estimated for each dietary component of interest individually using Cox proportional hazards models adjusting for age, race/ethnicity, and other potentially confounding factors (*i.e.* caloric intake, physical activity, and established breast cancer risk factors) as noted in the footnotes of the tables [15, 16]. Effect modification under a multiplicative model was formally assessed using methods described by Walter and Holford [17]. Tests for trend were calculated across quintiles treating the quintiles as an ordinal variable. To minimize biases associated with the recent use of supplements by individuals who perceive themselves to be in ill-health, multivariate analyses of β-carotene and vitamins C and E are limited to non-supplement users and long-term (defined as two or more years) multivitamin users or users of the supplement being evaluated; short-term users of that supplement or multivitamins are excluded [18].

Results

Table 1 describes the 111,526 members of the cohort included in this analysis in terms of demographics, established breast cancer risk factors, physical activity level, and dietary intake. Relative risk analyses (Tables 2–5) are based on 222,249 person-years of follow-up contributed by these 111,526 women. During the two-year follow-up period, 711 women developed invasive breast cancer. Excluded from relative risk analyses are 143 women (contributing 162 person-years of follow-up) who developed *in-situ* breast carcinoma during the follow-up period.

The relationship between breast cancer risk and recent energy, macronutrient, and fiber intake is presented in Table 2, along with associations for various types of fat (*i.e.* saturated fat, linoleic acid – the most commonly consumed polyunsaturated fatty acid, and oleic acid – the most commonly consumed monounsaturated fatty acid), and the ratio of fat-to-fiber and carbohydrate-to-protein intake. None of these dietary components were related to risk, nor were the associations modified by menopausal status.

Table 3 presents the associations between breast cancer risk and recent consumption of antioxidant micronutrients and specific indices of antioxidant activity. Only α-carotene was associated with risk. However, while there was a significant trend of increasing risk with increasing consumption of α-carotene, the point estimate for the highest quintile was not statistically significant.

Table 2. Relative risks[a] and 95% confidence intervals quantifying the relationship between breast cancer risk and recent dietary intake of calories, macronutrients, and fiber in the California Teachers Study cohort

Nutrient	Quintile					*p*-Value for trend
	1	2	3	4	5	
Calories	1.0	0.9 (0.7–1.2)	1.1 (0.8–1.3)	1.1 (0.8–1.3)	1.0 (0.8–1.3)	0.7
Total fat	1.0	1.0 (0.8–1.3)	1.0 (0.8–1.3)	0.9 (0.7–1.3)	0.8 (0.6–1.2)	0.4
Saturated fat	1.0	1.1 (0.8–1.4)	1.0 (0.8–1.4)	0.8 (0.6–1.1)	0.8 (0.6–1.2)	0.2
Linoleic acid	1.0	0.8 (0.7–1.1)	0.9 (0.7–1.1)	1.0 (0.7–1.3)	0.9 (0.7–1.3)	0.9
Oleic acid	1.0	1.0 (0.8–1.2)	0.9 (0.7–1.1)	1.0 (0.7–1.3)	0.9 (0.6–1.2)	0.5
Carbohydrate	1.0	0.9 (0.7–1.2)	1.0 (0.7–1.3)	1.0 (0.8–1.4)	0.8 (0.5–1.2)	0.8
Protein	1.0	0.9 (0.7–1.1)	0.9 (0.7–1.1)	0.9 (0.6–1.2)	0.9 (0.6–1.4)	0.6
Fiber	1.0	1.0 (0.8–1.2)	0.9 (0.7–1.1)	0.9 (0.7–1.2)	0.9 (0.7–1.2)	0.3
Fat:fiber	1.0	1.2 (1.0–1.5)	1.0 (0.8–1.3)	0.9 (0.7–1.2)	1.1 (0.8–1.4)	0.7
Carbohydrate:protein	1.0	0.8 (0.7–1.1)	1.1 (0.9–1.4)	0.9 (0.7–1.2)	1.0 (0.8–1.2)	1.0

[a] Adjusted for age, race, daily caloric intake, family history of breast cancer, age at menarche, nulliparity/age at first full-term pregnancy, physical activity, and an interaction term for body mass index and menopausal status.

Table 3. Relative risks[a] and 95% confidence intervals quantifying the relationship between breast cancer risk and recent dietary intake of antioxidants in the California Teachers Study cohort

Antioxidants	Quintile					*p*-Value for trend
	1	2	3	4	5	
Carotenoids						
β-Carotene	1.0	1.0 (0.7–1.3)	0.9 (0.7–1.2)	1.1 (0.9–1.4)	1.1 (0.9–1.4)	0.2
α-Carotene	1.0	0.8 (0.6–1.0)	1.0 (0.8–1.3)	1.0 (0.8–1.3)	1.2 (0.9–1.5)	0.03
Lycopene	1.0	1.0 (0.8–1.3)	1.0 (0.8–1.2)	1.0 (0.8–1.3)	0.9 (0.7–1.1)	0.5
Lutein	1.0	1.1 (0.8–1.4)	1.1 (0.8–1.4)	1.0 (0.8–1.3)	1.2 (0.9–1.6)	0.3
Cryptoxanthin	1.0	1.0 (0.8–1.2)	0.9 (0.7–1.1)	0.9 (0.7–1.1)	1.0 (0.8–1.3)	0.7
Vitamin C	1.0	0.8 (0.6–1.1)	1.1 (0.8–1.4)	0.9 (0.7–1.2)	1.1 (0.8–1.3)	0.5
Vitamin E	1.0	1.0 (0.8–1.3)	1.0 (0.8–1.3)	1.0 (0.8–1.3)	1.1 (0.9–1.4)	0.4
Antioxidant indices						
Peroxyl radical absorbance capacity	1.0	1.1 (0.8–1.4)	1.0 (0.8–1.3)	1.1 (0.9–1.4)	1.0 (0.8–1.3)	0.8
Hydroxyl radical absorbance capacity	1.0	1.1 (0.8–1.4)	1.1 (0.8–1.4)	1.1 (0.9–1.5)	1.1 (0.8–1.4)	0.6
Antioxidant capacity against transition metals	1.0	1.1 (0.8–1.4)	1.1 (0.8–1.4)	1.2 (0.9–1.5)	1.1 (0.8–1.4)	0.4
Total score	1.0	1.1 (0.8–1.4)	1.0 (0.7–1.2)	1.1 (0.8–1.4)	1.0 (0.7–1.2)	0.8

[a] Adjusted for age, race, daily caloric intake, family history of breast cancer, age at menarche, nulliparity/age at first full-term pregnancy, physical activity, and an interaction term for body mass index and menopausal status.

Table 4. Relative risks[a] and 95% confidence intervals quantifying the relationship between breast cancer risk and recent dietary intake of phytoestrogens in the California Teachers Study cohort

Phytoestrogens	Quintile					*p*-Value for trend
	1	2	3	4	5	
Isoflavones						
Genistein	1.0	1.0 (0.8–1.3)	1.0 (0.8–1.3)	1.1 (0.8–1.4)	1.0 (0.7–1.3)	0.9
Daidzein	1.0	1.0 (0.8–1.2)	1.0 (0.8–1.3)	1.0 (0.8–1.3)	0.9 (0.7–1.2)	0.6
Biochanin A	1.0	0.9 (0.7–1.2)	1.0 (0.8–1.3)	0.9 (0.7–1.1)	1.0 (0.8–1.3)	0.7
Formononetin	1.0	1.3 (1.0–1.7)	1.2 (1.0–1.6)	1.0 (0.7–1.2)	1.1 (0.8–1.4)	0.4
Coumestrol	1.0	1.3 1.0–1.6)	1.1 (0.8–1.4)	1.2 (0.9–1.5)	1.1 (0.9–1.5)	0.7
Lignans						
Matairesinol	1.0	0.8 (0.7–1.1)	1.0 (0.8–1.3)	1.0 (0.8–1.3)	1.1 (0.8–1.4)	0.2
Secoisolariciresiniol	1.0	1.2 (0.9–1.5)	1.1 (0.9–1.5)	1.3 (1.0–1.7)	1.4 (1.0–1.8)	0.02

[a] Adjusted for age, race, daily caloric intake, family history of breast cancer, age at menarche, nulliparity/age at first full-term pregnancy, physical activity, and an interaction term for body mass index and menopausal status.

The effects of recent phytoestrogen consumption on breast cancer risk were equally null (Table 4). Only the primary lignan, secoisolariciresinol, was associated with increased risk but this association was substantially reduced after adjustment for consumption of wine, an important source of secoisolariciresinol. After wine adjustment the relative risk for the highest quintile of secoisolariciresinol was 1.2 (95% CI: 0.9–1.6), suggesting that the originally observed risk elevation is likely to be due to confounding by alcohol consumption. There were no substantial differences in the effects of phytoestrogens by the estrogen receptor (ER) status of the tumor or by menopausal status. However, the level of consumption of phytoestrogens was rather low in this population, with the highest quintile of exposure being equivalent to only one or more servings of tofu per week.

The only dietary component associated with breast cancer risk was alcohol consumption (Table 5). Relative to non-drinkers, consumers of 20 or more grams of alcohol per day (approximately equivalent to two or more glasses of wine per day) were at a 50% increased risk of breast cancer (95% CI: 1.2–2.0); the relative risk per 10 g/day was 1.12 (95% CI: 1.05–1.20). These associations were similar for wine and liquor and for pre- and postmenopausal women.

Limiting analyses to the 355 (50%) of women who developed their breast cancer more than one year after joining the cohort (and for women not developing breast cancer, to those with more than one year of follow-up)

Table 5. Relative risks[a] and 95% confidence intervals for the relationship between breast cancer risk and recent alcohol consumption California Teachers Study cohort

Alcohol	Non-drinkers	g/day					*p*-Value for trend
		<5	5–9	10–14	15–19	≥20	
Total	1.0 [217][b]	0.9 (0.7–1.2) [125]	0.9 (0.7–1.2) [94]	1.2 (0.9–1.6) [96]	1.0 (0.8–1.4) [60]	1.5 (1.2–2.0) [89]	0.01
Beer	1.0 [536]	0.9 (0.7–1.1) [131]		0.9 (0.5–1.6) [14]			0.2
Wine	1.0 [253]	1.0 (0.9–1.2) [269]		1.3 (1.0–1.6) [116]		1.7 (1.2–2.4) [43]	0.002
Liquor	1.0 [439]	1.1 (0.9–1.3) [170]		1.6 (1.2–2.1) [53]		1.7 (1.0–2.8) [19]	0.002

[a] Adjusted for age, race, daily caloric intake, family history of breast cancer, age at menarche, nulliparity/age at first full-term pregnancy, physical activity, and an interaction term for body mass index and menopausal status.

[b] Figures in square brackets indicate no. of cases.

⌒ demarcation represents collapsed categories.

did not substantially change any of these observations. For example, the relative risk for 20 or more grams of alcohol per day was 1.5 (95% CI: 1.0–2.1).

Discussion

This research examined the proximal effects of recent adult diet (in the preceding 1–2 year period) on the diagnosis of breast cancer. A wide variety of dietary components were examined. Only average alcohol consumption of 20 or more grams per day (*i.e.* equivalent to two or more glasses of wine per day) was associated with risk.

The elevation in risk associated with alcohol consumption we observed is consistent with pooled analyses of cohort and case–control studies and with two meta-analyses [19–22]. As in the present study there was no evidence that the effect of alcohol was modified by menopausal status [19, 22], and no beverage-specific effects were observed [20, 22]. In the present study, risk was significantly elevated among women consuming 20 or more grams of alcohol per day, in the pooled analysis of cohort studies it was 30 or more g/day, and in the pooled analysis of case–control studies it was more than 40 g/day of alcohol [19, 20]. In the meta-analysis of 38 case–control and cohort studies, there were statistically significant elevations in risk of 11%, 24%, and 38% for one, two, and three drinks per day, respectively, using random effects models incorporating the observed heterogeneity between studies into the estimates of risk [21]. Both meta-analyses have suggested that, within cohort studies, the association between alcohol consumption and breast cancer risk is stronger in studies with shorter follow-up periods [21, 22]. This may be related to changes in exposure over time, thus the longer ago the baseline measure was taken, the less representative it is of the relevant etiologic period [21], consistent with a proximal effect of this exposure on breast cancer development.

The lack of association observed for dietary fat consumption and breast cancer risk is consistent with a pooled analysis of cohort studies, with most case–control studies, and with the conclusions of several recent reviews [23–25]. In addition, in the present study no associations were seen for the ratios of fat-to-fiber or carbohydrate-to-protein consumption, which have been more strongly associated with the metabolism of estrogens, sex hormone binding globulin (SHBG), or insulin than any of these individual nutrients alone [26–29].

Recent consumption of antioxidant vitamins was not associated with breast cancer risk in this cohort. In addition to examining these antioxidant micronutrients directly, we incorporated recent work on the development of antioxidant indices which also take into account antioxidant activity in plant foods from compounds other than vitamins C, E, and β-carotene [12, 13]. We assessed a total antioxidant score and three specific indices reflecting the absorbance capacity of peroxyl and hydroxyl radicals, respectively, and the antioxidant capacity against transition metals. The index measuring antioxidant capacity against peroxyl radicals, commonly found in the human body, reflects the activity of vitamins C and E and β-carotene as well as glutathione, melatonin, flavonoids, and other antioxidants. The

index measuring antioxidant activity against hydroxyl radicals reflects the activity of glucose, proteins, uric acid, and other compounds. The third index reflects both antioxidant activity and the transition metal-initiated prooxidant activity of compounds such as ascorbic acid and flavonoids [12]. None of these indices indicated protective effects of recent dietary antioxidant consumption on breast cancer risk. These findings are consistent with those for antioxidant micronutrients in the few cohort studies which have examined those associations and many of the case–control studies, albeit not the pooled analysis of case–control studies addressing this issue [23, 30]. However, in the case–control analyses the possibility of recall bias cannot be ruled out.

Phytoestrogens are weak estrogens found in plants or derived from plant precursors. They consist of several classes of compounds (*i.e.* isoflavones, coumestans, and lignans) which are structurally similar to endogenous estrogens but which have been shown to have both estrogenic and antiestrogenic effects on breast tissue [31–36]. Despite the reduction in breast cancer risk observed in some Asian populations associated with higher levels of consumption of phytoestrogen-rich soy-based foods or soy protein [37–39], the present study, as well as a recent case–control study of non-Asian women, found no apparent association between phytoestrogen consumption and breast cancer risk [40]. However, in both these American studies the lack of an association may well have been due to the low level of consumption of phytoestrogens in these populations, with the highest quintile of exposure being equivalent to only one or more servings of tofu per week. Neither study showed effect modification by menopausal status or the ER status of the tumor.

Apropos the interest in whether adult diet (and changes in adult diet) affect breast cancer risk, our interest here was to examine *recent* dietary intake. In the context of a cohort study evaluating only incident cancer diagnoses, the possibility of recall biases in our dietary assessment should be low even though we included women who completed the dietary assessment as little as a month prior to diagnosis. To determine whether such biases might have been introduced, we repeated our analyses excluding women diagnosed within a year of completing the baseline survey. While our statistical power was somewhat reduced in these analyses, no differences in effect were observed. Another potential limitation of our analyses, as with virtually all dietary assessments that rely on using food-frequency questionnaires to assess dietary intake, is the possibility of misclassification of exposure due to inaccuracies in reporting. While food-frequency questionnaires similar to the instrument we administered to our cohort have been used extensively in epidemiologic studies, and validated in a number of populations [6, 8, 41–43], we are in the process of conducting a validation/calibration study specific to our cohort which in the future may help improve our estimates of dietary intake.

In summary, the findings of this study suggest that, with the exception of alcohol consumption, recent adult diet (at least in terms of the dietary components studied here) does not influence, beneficially or detrimentally, the development of breast cancer. Thus, to the extent that adult diet is fairly constant over time, this and other studies (while not directly addressing the issue of dietary change), lend some support to the idea that, as adults, changes in dietary composition (other than in alcohol consumption or in very substantial ways) may be unlikely to have much of a direct impact on breast cancer risk. However: (1) the effects of diet during earlier periods of life, such as during puberty, adolescence, or early adulthood, and indirect effects, such as through obesity resulting from chronic excess intake of calories or fat, may still be important; and (2) further investigation of the effects of genetic variation in the metabolism of various nutrients and phytochemical compounds may prove promising in elucidating the nature of the diet–disease relationship and in identifying subgroups of women who may benefit from changes in the intake of specific dietary components. At present the only public health recommendation regarding dietary intake and breast cancer risk that seems appropriate is some reduction of alcohol consumption among those consuming more than one drink a day. Abstinence or reduction in alcohol consumption below one drink per day are not necessarily recommended due to the protective effects of moderate alcohol consumption against myocardial infarction, a major cause of morbidity and mortality in women.

Acknowledgements

This research was supported by grants 4JB-0116 from the Breast Cancer Research Program, University of California; R01 CA77398 from the National Cancer Institute; and contract 97-10500 from the California Breast Cancer Research Fund. The authors thank the following people for technical or administrative support: Gretchen Agha, Mark Allen, Alison Canchola, Subo Chang, Susan Hurley, Jocelyn Koo, Jan Schaefer, Amy Shiau, Erin Silva, Jane Sullivan-Halley, and Orawan Takaki.

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