

Adolescent Lifestyle Factors and Adult Breast Density in U.S. Chinese Immigrant Women

Marilyn Tseng

Temitope O. Olufade

Kathryn A. Evers

Celia Byrne

We examined recalled measures of adolescent diet, physical activity, and body size in relation to adult breast density in 201 U.S. Chinese immigrant women recruited in January 2002 to May 2003 from Philadelphia region screening programs. Mammographic images were classified into 1 of 4 categories ranging from “entirely fatty” to “extremely dense.” Questionnaires assessed diet and physical activity between ages 12–17, relative weight and height at age 10, and weight at age 18. To estimate odds ratios (ORs), we conducted logistic regression analyses using proportional odds models for polychotomous outcomes. Higher adult breast density was significantly associated with adolescent red meat intake (adjusted 3rd vs. 1st tertile OR = 3.0, 95% confidence interval (CI) 1.5–6.4, trend $P = 0.003$) but not with other adolescent factors. For the association of adult acculturation with breast density, adjustment for adolescent red meat intake attenuated the OR for the highest vs. lowest level of acculturation from 2.5 (95% CI 1.2–5.3) to 1.9 (95% CI 0.9–4.0). Greater adolescent red meat intake may have increased adult breast density and partly accounted for the strong association between acculturation and breast density in this sample of immigrant Chinese women. If confirmed by further study, dietary prevention efforts for breast cancer should be considered earlier in life.

INTRODUCTION

A growing literature in epidemiology suggests that childhood and adolescent exposures can affect susceptibility of breast tissue to cancer development in adulthood (1–4). Preadolescence and adolescence are characterized by rapid proliferation of incompletely differentiated breast epithelial cells, coupled with limited DNA repair (5). In addition, exposures during these time periods may affect the timing of breast epithelial cell differentiation (3) and the establishment of regular ovulatory cycles (5). While specific risk factors have yet to be established, adolescent body size (3,6), physical activity (2), and dietary intake (4) have received attention because of their possible effects on these mechanisms.

In a previous analysis (7), we found that the level of acculturation in a sample of U.S. Chinese immigrant women was significantly associated with breast density. While the distribution of several potential explanatory factors measured in adulthood differed by level of acculturation, none could completely explain the association of acculturation with breast density. To further investigate the factors involved in this association, we evaluated the contribution of factors occurring earlier in life. Studies among migrant populations offer a unique perspective on the role of adolescent exposures: Although adolescent and adult lifestyle factors such as diet are likely to be correlated in non-migrant populations (8,9), they are less likely to be correlated in women who migrate as adults, allowing for an assessment of adolescent exposures independent of adult exposures.

Objectives of this study were (1) to examine whether intake of selected dietary factors, physical activity, and body size during preadolescence and adolescence were associated with adult

breast density in a sample of U.S. Chinese immigrant women, 99% of whom migrated in adulthood; and (2) to determine the impact of preadolescent and adolescent factors on our previously observed association between the level of acculturation and breast density. Breast density, the percentage of total breast area with a mammographically dense appearance, is a useful indicator of breast cancer risk in epidemiologic studies (10) because of its strong association with breast cancer risk (11) in Asian women as well as in White women (12–14).

MATERIALS AND METHODS

Study Sample

A total of 250 participants were recruited between January 2002 and May 2003, from community organizations and contacts, mammography screening programs, and newspaper advertisements in the Philadelphia region. Women were eligible if they were of Chinese heritage, were ≥ 40 yr old, and had received a mammogram within the previous 3 mo. Exclusion criteria were a history of breast augmentation, breast reduction, prophylactic mastectomy, or any cancer except nonmelanoma skin cancer, current breast-feeding or breast-feeding within last 9 months, and current pregnancy. All participants gave their written, informed consent to participate in the research, and the study was approved by the Fox Chase Cancer Center Institutional Review Board.

Data Collection

At enrollment, participants completed health history and dietary questionnaires. To assess adolescent exposure history, women were asked the number of times per day, week, or month they consumed 5 items (beef, pork, tofu, green vegetables, fruits) between 12 and 17 yr old; how their weight and height compared with their peers at 10 yr old; and how much they weighed at 18 yr old. Participants also reported the number of hours per week, months per year, and total number of years of participation in any regular, strenuous physical activities between the ages of 12 and 17 yr. Activities were assigned a metabolic equivalent (MET) value (15), and total MET hours spent on strenuous physical activity between 12 and 17 yr old was calculated as MET \times hours/year \times number of years of participation, summed over all reported activities.

Residential histories were used to calculate length of U.S. residence, age at migration, and proportion of life before age 18 spent in a rural location. Women also responded to questions on sociodemographic factors, breast cancer in first- or second-degree female relatives, pregnancy and breast-feeding history, menopausal status, and birth control and female hormone pill use. Level of acculturation was quantified using a scale (7) adapted from Hazuda et al. (16), based on 6 questions that assessed preferred language for speaking, reading, writing, and the ethnicity of neighbors, close friends, and coworkers. Scores could range from 6 to 24, with 24 representing the highest level of acculturation. Body mass index (BMI, in kg/m²) was

determined using self-reported weight and height. Adult dietary intake was assessed using an 88-item food frequency questionnaire designed for the target population that asked about intake over the past year (17).

Breast Density Assessment

Images were obtained from the hospitals where participants had recently received their screening mammogram. The median time between mammogram and interview was 12 days. Breast density was assessed by the study radiologist (K.A.E.), who was blinded to the identity and other personal characteristics of study subjects. Breast images were classified using the Breast Imaging Reporting and Data System (BI-RADS) categories (entirely fatty, having scattered fibroglandular tissue, heterogeneously dense, or extremely dense) (18). Results presented below are based on the cranial-caudal view of a randomly selected side, but assessments between left and right sides agreed in all but four (2%) women. Breast density assessments were highly reproducible when measured by the same radiologist in a separate study (19) ($\kappa = 0.97$ for left side, 0.89 for right side).

Statistical Analyses

Women were excluded from analysis if we were unable to obtain their mammographic images ($n = 32$) or if they were missing data on at least one of the adolescent exposure measures (dietary intake, physical activity, body size) or final model covariates (age, menopausal status, BMI, level of acculturation, family history of breast cancer, number of live births, age at first live birth, and dairy food intake) ($n = 17$). A comparison of the 201 women in our sample with the 49 excluded from analysis showed no difference with respect to age, BMI, or level of acculturation, or with respect to breast density category for the 17 women with assessments available.

To estimate odds ratios (ORs) for falling into a higher vs. lower density category, we performed logistic regression analyses using proportional odds models for polychotomous outcomes (20). When the score test (20) indicated a violation of the assumption of proportional odds, analyses were repeated using binary logistic regression with the upper two density (heterogeneously and extremely dense) categories as the outcome. All models were, at a minimum, adjusted for age (years) and menopausal status.

Adolescent red meat, tofu, and green vegetable intakes were modeled as continuous and categorical variables, with similar results. For ease of presentation, we show results for categorical variables, with ORs estimated for tertiles of intake relative to the lowest tertile. *P* values for linear trend were estimated by modeling an ordinal variable representing the scaled median value for each tertile. We created acculturation categories of approximately equal size to examine associations of low, middle, and high levels of acculturation with breast density.

We examined possible effect modification by menopausal status by estimating interaction *P* values in a model including variable \times menopausal status interaction terms. In analyses

stratified on menopausal status, only 1 premenopausal woman fell into the entirely fatty category, and she was included with women in the scattered fibroglandular tissue category for more stable estimates. Also, family history of breast cancer was excluded as a covariate in stratified models because none of the premenopausal women reported such a family history.

Multivariate models were adjusted for variables found to be significantly associated with breast density (7). In addition to age and menopausal status, these included level of acculturation (low, medium, high), BMI (kg/m²), having a first-degree relative with breast cancer (yes/no), a combined variable representing number of live births and age at first live birth (>2 children/age <25 yr, 0–2 children/age <25 yr, >2 children/age ≥25 yr, 0–2 children/age ≥25 yr), and adult weekly frequency of dairy food intake. Variables not associated with breast density (length of U.S. residence, age at migration, level of education, country of birth, residence in a rural location prior to age 18, age at menarche, having ever used hormonal contraceptives, having ever used hormone therapy, and adult intake of red meat, green vegetables, or tofu) were not included in final multivariate models.

To evaluate the extent to which an adolescent measure could explain the association between acculturation and breast density, we included the measure of interest in the model containing acculturation and other important predictors of breast density (7): BMI, having a first-degree relative with breast cancer, number of live births/age at first live birth, and adult dairy food intake, in addition to age and menopausal status. We then compared OR estimates for acculturation in the models with and without the adolescent measure.

RESULTS

Among the 201 women in our analysis, mean (SD) age was 53.1 (10.2) yr, and 55% were premenopausal (Table 1). Mean length of residence in the United States was 11.7 (8.6) yr (range <1–45 yr), with mean age at migration to the United States of 41.3 (13.2) yr (range 11–69 yr). Only 3 women migrated before age 20. Most women (82%) were born in China or Hong Kong, and only 16% of women spent ≥10% of their lives prior to age 18 in a rural location. The level of acculturation in our sample was low, with a mean of 9.5 (range 6–20) out of a possible maximum score of 24. With respect to breast density, over half of the women fell into the extremely (37%) or heterogeneously (29%) dense categories, 27% were classified as having scattered fibroglandular tissue, and only 6% of women fell into the least dense (entirely fatty) category. Covariate distributions and associations with breast density are shown in Table 1. In these age- and menopausal status-adjusted analyses, breast density was significantly associated with level of acculturation, having a first-degree relative with breast cancer, fewer live births, and higher dairy food intake. It was inversely associated with age and BMI.

Reported intake of red meat between the ages of 12 and 17 was significantly associated with adult breast density in minimally and fully adjusted models (Table 2). Women who reported adolescent red meat intake in the highest tertile had a median intake frequency of once per day and a 3-fold greater odds of having denser breasts than women in the lowest tertile (OR = 3.0; 95% CI 1.5–6.4; trend $P = 0.003$). Positive associations of adolescent tofu and fruit intake with adult breast density were attenuated in multivariate models (Table 2), but also with adjustment only for adolescent red meat intake (OR = 1.4, 95% CI 0.7–2.7, trend $P = 0.39$, and OR = 1.6, 95% CI 0.7–3.7, trend $P = 0.39$, for highest vs. lowest tertiles of tofu and fruit intake, respectively), reflecting the moderate correlations of adolescent red meat with tofu ($r = 0.36$, $P < 0.0001$) and fruit ($r = 0.51$, $P < 0.0001$) intake in our sample. Adolescent intake of green vegetables was not associated with adult breast density. We also found no associations for adult breast density with weight at age 18, weight and height relative to peers at age 10, or regular, strenuous physical activity between ages 12–17 (Table 2).

In stratified analyses, the association of adolescent red meat intake with adult breast density was limited to postmenopausal women (Table 3). In fully adjusted models, the OR for higher adult breast density was 16.9 (95% CI 5.4–52.4, trend $P < 0.0001$) for postmenopausal women in the highest vs. lowest tertile of adolescent red meat intake, but it was 0.4 (95% CI 0.1–1.3) among premenopausal women (Table 3). Women with the highest red meat intake in adolescence were more likely to have had at least a college education, less likely to have lived in a rural area before age 18 yr, and more likely to have been born in Taiwan or Southeast Asia than in China (data not shown), suggesting the possibility of residual confounding. Additional adjustment for these factors in the model for postmenopausal women attenuated the OR from 16.9 to 10.8 (95% CI 3.1–37.9, trend $P = 0.0002$), but the strong association clearly persisted.

As reported previously (7), level of acculturation in our immigrant sample was significantly associated with breast density category. Age- and menopausal status-adjusted OR for highest vs. lowest acculturation category was 2.9 (95% CI 1.5–5.9), which was attenuated to 2.5 (95% CI 1.2–5.3) with further adjustment for breast density predictors and other potential explanatory factors (BMI, having a first-degree relative with breast cancer, number of live births/age at first live birth, and adult dairy food intake). Level of acculturation in adulthood was also strongly associated with adolescent red meat intake: Mean (SD) reported frequency of red meat intake (times/week) between ages 12–17 yr was 6.6 (4.8) among the most acculturated group of women vs. 2.8 (3.3) among the least acculturated ($P < 0.0001$). To examine the possible role of adolescent red meat intake to the association between acculturation and breast density in adulthood, we additionally adjusted for adolescent red meat intake in the model including the variables listed above. This attenuated the OR for highest vs. lowest acculturation category from 2.5 to 1.9 (95% CI 0.9–4.0). The attenuation was even

TABLE 1

Distributions of demographic characteristics and odds ratios* (OR) and corresponding 95% confidence intervals (CI) for higher breast density in 201 U.S. Chinese immigrant women

Demographic Characteristic	All Women (N = 201)		Premenopausal Women (n = 91)		Postmenopausal Women (n = 110)	
	Distribution	OR*	Distribution	OR*	Distribution	OR*
Mean (SD) age (yr)	53.1 (10.2)	0.6 (0.5–0.8)**	44.6 (4.1)	0.7 (0.4–1.1)**	60.1 (8.1)	0.6 (0.5–0.8)**
Postmenopausal (%)	55	0.5 (0.2–1.1)				
Mean (SD) length of US residence (yr) [†]	11.7 (8.6)	1.0 (0.8–1.1)**	11.1 (6.4)	0.7 (0.5–1.0)**	12.2 (10.1)	1.1 (0.9–1.3)**
Mean (SD) age at migration (yr) [†]	41.3 (13.2)	1.0 (0.9–1.2)**	33.5 (6.8)	1.4 (1.0–2.0)**	47.8 (13.8)	0.9 (0.8–1.1)**
Acculturation score (%)						
6–8	40	1.0	43	1.0	37	1.0
>8–10	33	1.7 (0.9–3.2)	29	1.1 (0.4–3.0)	37	2.3 (1.0–5.3)
>10	27	2.9 (1.5–5.9)	29	2.5 (0.8–7.4)	25	3.6 (1.4–9.1)
Level of education (%)						
<HS	39	1.0	41	1.0	37	1.0
HS graduate ≤ college	37	1.6 (0.9–3.1)	40	1.2 (0.5–3.1)	35	2.2 (0.9–5.0)
College graduate +	24	1.8 (0.9–3.6)	20	1.6 (0.5–5.2)	28	2.1 (0.9–5.2)
Place of birth (%)						
China	82	1.0	80	1.0	84	1.0
Southeast Asia	10	1.3 (0.5–3.2)	11	0.5 (0.1–1.7)	9	3.4 (1.0–11.7)
Taiwan	8	2.0 (0.7–5.6)	9	5.0 (0.6–44.4)	7	1.2 (0.3–4.6)
Proportion of life up to age 18 yr lived in rural area (%)						
<10%	84	1.0	85	1.0	83	1.0
10–90%	6	0.7 (0.2–2.3)	4	2.8 (0.3–30.2)	7	0.3 (0.1–1.5)
>90%	10	0.6 (0.2–1.5)	10	1.7 (0.4–7.5)	10	0.2 (0.1–0.9)
Mean (SD) BMI (kg/m ²)	24.1 (3.4)	0.8 (0.8–0.9)	24.0 (3.2)	0.8 (0.7–1.0)	24.1 (3.6)	0.8 (0.8–0.9)
First degree relative with breast cancer (%)	6	5.3 (1.5–18.7)	4	— [‡]	7	4.4 (1.1–17.2)
Mean (SD) age at menarche (yr)	14.4 (1.8)	1.0 (0.5–2.1)**	14.3 (1.8)	1.6 (0.5–2.1)**	14.5 (1.9)	0.8 (0.3–2.0)**
Number of live births/age at first live birth (%)						
>2/<25 yr	17	1.0	8	1.0	25	1.0
0–2/<25 yr	24	2.6 (1.1–6.1)	26	2.0 (0.4–11.0)	22	2.3 (0.8–6.8)
>2/≥25 yr	11	2.1 (0.8–5.7)	8	0.4 (0.1–2.9)	15	4.2 (1.3–13.9)
0–2/≥25 yr	48	2.6 (1.2–5.7)	58	1.5 (0.3–7.0)	39	3.3 (1.3–8.3)
Ever used hormonal contraceptives (%) [†]	12	1.7 (0.7–4.0)	13	2.3 (0.6–9.8)	12	1.4 (0.5–4.2)
Ever used estrogens (%) [†]	12	1.9 (0.8–4.4)	2	2.3 (0.1–43.7)	20	1.9 (0.8–4.6)
Median weekly dairy food intake						
Tertile 1	0.2	1.0	0.1	1.0	0.2	1.0
Tertile 2	7	1.7 (0.9–3.4)	4	2.8 (1.0–7.6)	7	1.2 (0.5–3.1)
Tertile 3	10	2.5 (1.2–4.9)	11	1.7 (0.6–4.8)	9	2.8 (1.1–6.9)
Breast density category (%)		—		—		—
Entirely fatty	6		1		11	
Scattered fibroglandular tissue	27		11		40	

(Continued on next page)

TABLE 1

Distributions of demographic characteristics and odds ratios* (OR) and corresponding 95% confidence intervals (CI) for higher breast density in 201 U.S. Chinese immigrant women (*Continued*)

Demographic Characteristic	All Women (<i>N</i> = 201)		Premenopausal Women (<i>n</i> = 91)		Postmenopausal Women (<i>n</i> = 110)	
	Distribution	OR*	Distribution	OR*	Distribution	OR*
Heterogeneously dense	29		26		31	
Extremely dense	37		60		18	

*Analyses including all women were adjusted for age and menopausal status. Stratified analyses were adjusted for age only.

**OR for 5-yr increment.

†Due to missing data, *N* = 198 for length of U.S. residence and age at migration (*n* = 90 premenopausal, *n* = 108 postmenopausal); *N* = 197 for hormonal contraceptives (*n* = 88 premenopausal, *n* = 109 postmenopausal); *N* = 199 for estrogens (*n* = 89 premenopausal, *n* = 110 postmenopausal).

‡No premenopausal women reported a first-degree relative with breast cancer.

more pronounced in postmenopausal women, for whom the OR for the highest vs. lowest acculturation category decreased from 2.9 (95% CI 1.1–7.6) to 1.5 (95% CI 0.5–4.1). The association of adolescent red meat intake with adult breast density, in contrast, remained statistically significant with adjustment for acculturation (Tables 2 and 3).

DISCUSSION

In our sample of Chinese immigrant women, adolescent red meat intake was a significant predictor of breast density in adulthood. Indeed, it emerged as a possible explanatory factor for the association between level of acculturation and breast density that we observed previously (7). None of our measures of adolescent body size or physical activity were associated with later breast density, nor was adolescent intake of tofu, green vegetables, or fruit.

Red meats may increase cancer risk because bioavailable iron in meat can catalyze the generation of free radicals, which cause oxidative damage, and/or because certain, high-temperature cooking methods produce carcinogenic substances—namely, heterocyclic amines and polycyclic aromatic hydrocarbons (21). In recent work, the heterocyclic amine 2-amino-3-methylimidazo[4,5-b]pyridine (PhIP) stimulated the proliferation of estrogen-responsive cells, suggesting that at least one red meat-derived compound can induce mitogenesis and cell growth (22,23), with implications for both breast density and breast cancer. Studies of adolescent diet and breast cancer risk have not yielded consistent results (24), but 3 studies observed associations of breast cancer with high-fat meat intake at ages 12–13 yr (25) and with red meat intake during high school (4,26). The only other study, to our knowledge, that examined adolescent diet in relation to mammographic breast density found no association for any recalled dietary factors at ages 12–13 yr, including high-fat meats (27).

Because of the rapid proliferation of undifferentiated epithelial cells occurring during this period, adolescence may be

a period of increased susceptibility. In fact, we saw no association with breast density for red meat intake in adulthood, which was not correlated with adolescent red meat intake in our immigrant sample ($r = 0.15$, $P = 0.13$). In their study of adolescent diet and breast cancer, Linos et al. (26) also reported a positive association for red meat intake during adolescence but not in adulthood. Why we observed an association only among postmenopausal women is unclear, but breast density among premenopausal women had limited variability, with 60% in the extremely dense category and only one person in the entirely fatty category.

An association with adolescent red meat intake was apparent in our sample despite their low level of intake compared with Western populations. Median consumption frequency was seven servings per week in the highest tertile for our sample and 0.2 servings per week in the lowest tertile. In contrast, median high school intake of red meat among Nurses' Health Study II participants was 2.49 servings per day in the highest quintile and 0.71 servings per day in the lowest (26). We evaluated potential residual confounding by adjusting for sociodemographic factors that were associated with adolescent red meat intake in our sample, including birthplace, residence in a rural area during childhood or adolescence, level of education, and current level of acculturation, but the association persisted. Although the potential for residual confounding still exists, our current results suggest that adolescent intake of red meats has an effect on breast density that continues into adulthood.

A second notable finding was that red meat intake emerged as a partial explanatory factor for our previously observed association between level of acculturation and breast density in adulthood (7). An association between level of acculturation and breast density in a foreign-born immigrant sample has implications for understanding whether acculturation-related lifestyle changes in adulthood affect breast cancer risk. However, indicators of acculturation may also be correlated with social or cultural differences established before migration. In an earlier

TABLE 2
Distributions of preadolescent and adolescent characteristics, adjusted odds ratios (OR), and corresponding 95% confidence intervals (CI) for higher breast density ($N = 201$)

Preadolescent and Adolescent Characteristics	Distribution	Age- and Menopausal Status-Adjusted OR (95% CI)	Fully Adjusted* OR (95% CI)
Frequency of intake (times/wk) ages 12–17 yr			
Median red meat intake			
Tertile 1	0.2	1.0	1.0
Tertile 2	3	1.7 (0.9–3.3)	1.4 (0.7–2.8)
Tertile 3	7	3.3 (1.7–6.4)	3.0 (1.5–6.4)
Trend <i>P</i>		0.0004	0.003
Median tofu intake			
Tertile 1	0	1.0	1.0
Tertile 2	1	1.5 (0.8–3.0)	1.3 (0.6–2.5)
Tertile 3	3	2.0 (1.0–3.8)	1.5 (0.7–3.1)
Trend <i>P</i>		0.06	0.30
Median green vegetable intake			
Tertile 1	1	1.0	1.0
Tertile 2	7	0.8 (0.3–1.9)	0.8 (0.3–2.1)
Tertile 3	14	0.9 (0.4–2.0)	1.0 (0.4–2.5)
Trend <i>P</i>		0.96	0.77
Median fruit intake			
Tertile 1	0	1.0	1.0
Tertile 2	2	1.8 (1.0–3.6)	1.7 (0.8–3.3)
Tertile 3	7	2.6 (1.3–5.1)	1.8 (0.9–3.8)
Trend <i>P</i>		0.01	0.16
Any strenuous physical activity ages 12–17 yr (%)	20	1.1 (0.6–2.2)	0.8 (0.4–1.7)
Mean (SD) weight at age 18 (kg)	48.3 (7.2)	0.9 (0.7–1.0) [†]	0.9 (0.7–1.1) [†]
Weight compared to other girls at age 10 (%)			
Thinner	28	1.0 (0.6–2.0)	1.0 (0.5–1.9)
About the same	57	1.0	1.0
Heavier	15	0.7 (0.3–1.4)	1.1 (0.5–2.5)
Height compared to other girls at age 10 (%)			
Shorter	13	1.1 (0.5–2.6)	1.2 (0.5–2.9)
About the same	60	1.0	1.0
Taller	27	1.0 (0.5–2.0)	1.1 (0.6–2.2)
Mean adult height (m)	1.58 (0.05)	1.0 (0.6–1.7) [†]	0.9 (0.5–1.5) [†]

*Odds ratios for higher vs. lower breast density estimated from polychotomous logistic regression, adjusted for age, menopausal status, BMI, family history of breast cancer, level of acculturation, combined variable representing number of live births and age at first live birth, and adult weekly frequency of dairy food intake.

[†]OR for weight at age 18 yr is per 5 kg change; OR for adult height is per 0.1 m change.

study of Asian American women (28), breast cancer risk among women born in the East was partly determined by whether their communities before migration were rural or urban, with a 30% higher risk for migrants from urban areas. In our sample, the more acculturated women had a higher level of education, lower age at menarche, stronger family history of breast cancer; were less likely to have lived in a rural area before age 18; and were more likely to be from Taiwan or Southeast Asian than from China. The more acculturated women also tended to have higher red meat intake as adolescents, and this appears to have

accounted in part for their higher breast density measured in adulthood.

We did not see associations for tofu, green vegetable, or fruit consumption, physical activity, height, or weight in adolescence. Findings from studies of adolescent soy food intake with breast cancer risk have been mixed (29–31). Our null finding with respect to physical activity is consistent with the only other study to have examined this issue (27), but null findings with respect to body size are at odds with previous work (1,3,6,27,32–34). In addition to a true lack of association, possible explanations

TABLE 3
Odds ratios (OR) and corresponding 95% confidence intervals (CI) for adolescent red meat intake, stratified on menopausal status ($N = 201$)

Adolescent Red Meat Intake	Age-Adjusted		Fully Adjusted*	
	Premenopausal ($n = 91$)	Postmenopausal ($n = 110$)	Premenopausal ($n = 91$)	Postmenopausal ($n = 110$)
Times per week	1.0 (0.9–1.1)	1.2 (1.1–1.3)	0.9 (0.8–1.0)	1.3 (1.1–1.4)
Interaction P value**	0.002	0.009		
Tertiles				
Tertile 1	1.0	1.0	1.0	1.0
Tertile 2	1.1 (0.4–3.3)	2.1 (0.9–5.1)	0.7 (0.2–2.3)	2.4 (0.9–6.1)
Tertile 3	0.9 (0.3–2.3)	10.5 (4.0–27.3)	0.4 (0.1–1.3)	16.9 (5.4–52.4)
Trend P	0.70	< 0.0001	0.12	< 0.0001
Interaction P value	0.0005		0.01	

*Odds ratios for higher vs. lower breast density estimated from polychotomous logistic regression, adjusted for age, BMI, level of acculturation, combined variable representing number of live births and age at first live birth, and adult weekly frequency of dairy food intake.

** P value for trend was estimated using an ordinal variable representing the scaled median value for each category.

for our failure to detect these associations include poor recall of these measures, limited variability in our sample, and our use of qualitative rather than quantitative estimates of density, all of which would make it more difficult to detect an association.

Our study population of Chinese immigrant women offered a unique perspective on adolescent exposures potentially associated with adult breast density. Adolescent exposures such as diet in this study population are less likely to track into adulthood, providing an opportunity to study these exposures with less potential for confounding by more recent exposures. However, given the relatively small sample size of this study and its associated limitations (e.g., wide confidence intervals), our provocative findings warrant confirmation in larger, similarly informative samples of immigrant women.

Measurement error due to inaccurate recall of exposures from adolescence may have attenuated associations. As noted above, residual confounding is also possible, for example from other unmeasured dietary exposures or sociodemographic indicators. In addition, quantitative estimates of percent of breast density and size of dense area would have given us greater precision in our analyses than a qualitative, 4-category assessment of breast density. Indeed, indirect evidence suggests that quantitative estimates of dense breast area may be more relevant to breast cancer risk in Asian American women than estimates of percent of density: Despite being at lower risk for breast cancer, Asian American women have higher percent of breast density than White women in the United States (35–37). Nevertheless, breast density on a relative scale remains a significant predictor of breast cancer risk in Asian American women as it does in white women (12,13).

In summary, in our sample of Chinese immigrant women in the United States, reported adolescent red meat intake was significantly associated with higher breast density in adulthood, suggesting that adolescent dietary exposures have persisting ef-

fects on adult breast cancer risk. Adolescent red meat intake also partially explained an association between participants' level of acculturation as U.S. immigrants and their breast density. The current findings suggest that preventive measures for breast cancer should begin early in life and that adolescent factors should be considered in studies of breast cancer etiology and risk.

ACKNOWLEDGMENTS

The authors are indebted to Ms. Yun Song for her crucial work in the collection and management of data for this study. The authors also thank Andrew Balshem and the Fox Chase Cancer Center Population Studies Facility for their assistance in data entry. Finally, for their generous assistance in participant recruitment, the authors are deeply grateful to Dr. Philip Siu, Dr. Catherine Piccoli, Kin Lam, and Lih-Yuh Chen of Thomas Jefferson University Hospital, and Nancy Liao and Viki Chen of the American Cancer Society. This work was supported by grants CRTG-01-018-01-CCE from the American Cancer Society and P30 CA006927 from the National Institutes of Health.

REFERENCES

1. Berkey CS, Frazier AL, Gardner JD, and Colditz GA: Adolescence and breast carcinoma risk. *Cancer* **85**, 2400–2409, 1999.
2. Wyshak G and Frisch RE: Breast cancer among former college athletes compared to non-athletes: a 15-year follow-up. *Br J Cancer* **82**, 726–730, 2000.
3. Hilakivi-Clarke L, Forsen T, Eriksson JG, Luoto R, Tuomilehto J, et al.: Tallness and overweight during childhood have opposing effects on breast cancer risk. *Br J Cancer* **85**, 1680–1684, 2001.
4. Frazier AL, Li L, Cho E, Willett WC, and Colditz GA: Adolescent diet and risk of breast cancer. *Cancer Causes Control* **15**, 73–82, 2004.
5. Colditz GA and Frazier AL: Models of breast cancer show that risk is set by events of early life: prevention efforts must shift focus. *Cancer Epidemiol Biomarkers Prev* **4**, 567–571, 1995.

6. Ahlgren M, Melbye M, Wohlfahrt J, and Sorensen TI: Growth patterns and the risk of breast cancer in women. *N Engl J Med* **351**, 1619–1626, 2004.
7. Tseng M, Byrne C, Evers KA, London WT, and Daly MB: Acculturation and breast density in foreign-born, U.S. Chinese women. *Cancer Epidemiol Biomarkers Prev* **15**, 1301–1305, 2006.
8. Frazier AL, Willett WC, and Colditz GA: Reproducibility of recall of adolescent diet: Nurses' Health Study (United States). *Cancer Causes Control* **6**, 499–506, 1995.
9. Barnekow-Bergkvist M, Hedberg G, Janlert U, and Jansson E: Physical activity pattern in men and women at the ages of 16 and 34 and development of physical activity from adolescence to adulthood. *Scand J Med Sci Sports* **6**, 359–370, 1996.
10. Byrne C: Studying mammographic density: implications for understanding breast cancer. *J Natl Cancer Inst* **89**, 531–533, 1997.
11. Boyd NF, Lockwood GA, Byng JW, Tritchler DL, and Yaffe MJ: Mammographic densities and breast cancer risk. *Cancer Epidemiol Biomarkers Prev* **7**, 1133–1144, 1998.
12. Maskarinec G and Meng L: A case-control study of mammographic densities in Hawaii. *Breast Cancer Res Treat* **63**, 153–161, 2000.
13. Ursin G, Ma H, Wu AH, Bernstein L, Salane M, et al.: Mammographic density and breast cancer in three ethnic groups. *Cancer Epidemiol Biomarkers Prev* **12**, 332–338, 2003.
14. Cummings SR, Tice JA, Bauer S, Browner WS, Cuzick J, et al.: Prevention of breast cancer in postmenopausal women: approaches to estimating and reducing risk. *J Natl Cancer Inst* **101**, 384–398, 2009.
15. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, et al.: Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc* **32**, S498–S504, 2000.
16. Hazuda HP, Stern MP, and Haffner SM: Acculturation and assimilation among Mexican Americans: scales and population-based data. *Soc Sci Q* **69**, 687–706, 1988.
17. Tseng M and Hernandez T: Comparison of intakes of US Chinese women based on food frequency and 24-hour recall data. *J Am Diet Assoc* **105**, 1145–1148, 2005.
18. American College of Radiology: *Breast Imaging Reporting and Data System (BI-RADS)*, 2nd ed. American College of Radiology, Reston, VA, 1995.
19. Tseng M, Byrne C, Evers KA, and Daly MB: Dietary intake and breast density in high-risk women: a cross-sectional study. *Breast Cancer Res* **9**, R72, 2007.
20. Stokes ME, Davis CS, and Koch GG: *Categorical Data Analysis Using the SAS System*. SAS Institute, Inc., Cary, NC, 1995.
21. World Cancer Research Fund/American Institute for Cancer Research: *Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective*. American Institute for Cancer Research, Washington, DC, 2007.
22. Gooderham NJ, Creton S, Lauber SN, and Zhu H: Mechanisms of action of the carcinogenic heterocyclic amine PhIP. *Toxicol Lett* **168**, 269–277, 2007.
23. Lauber SN, Ali S, and Gooderham NJ: The cooked food derived carcinogen 2-amino-1-methyl-6-phenylimidazo[4,5-b] pyridine is a potent oestrogen: a mechanistic basis for its tissue-specific carcinogenicity. *Carcinogenesis* **25**, 2509–2517, 2004.
24. Okasha M, McCarron P, Gunnell D, and Smith GD: Exposures in childhood, adolescence and early adulthood and breast cancer risk: a systematic review of the literature. *Breast Cancer Res Treat* **78**, 223–276, 2003.
25. Potischman N, Weiss HA, Swanson CA, Coates RJ, Gammon MD, et al.: Diet during adolescence and risk of breast cancer among young women. *J Natl Cancer Inst* **90**, 226–233, 1998.
26. Linos E, Willett WC, Cho E, Colditz G, and Frazier LA: Red meat consumption during adolescence among premenopausal women and risk of breast cancer. *Cancer Epidemiol Biomarkers Prev* **17**, 2146–2151, 2008.
27. Sellers TA, Vachon CM, Pankratz VS, Janney CA, Fredericksen Z, et al.: Association of childhood and adolescent anthropometric factors, physical activity, and diet with adult mammographic breast density. *Am J Epidemiol* **166**, 456–464, 2007.
28. Ziegler RG, Hoover RN, Pike MC, Hildesheim A, Nomura AM, et al.: Migration patterns and breast cancer risk in Asian-American women. *J Natl Cancer Inst* **85**, 1819–1827, 1993.
29. Shu XO, Jin F, Dai Q, Wen WQ, Potter JD, et al.: Soyfood intake during adolescence and subsequent risk of breast cancer among Chinese women. *Cancer Epidemiol Biomarkers Prev* **10**, 483–488, 2001.
30. Wu AH, Wan PC, Hankin JH, Tseng C, Yu MC, et al.: Adolescent and adult soy intake and risk of breast cancer in Asian-Americans. *Carcinogenesis* **23**, 1491–1496, 2002.
31. Maskarinec G, Takata Y, Franke AA, Williams AE, and Murphy SP: A 2-year soy intervention in premenopausal women does not change mammographic densities. *J Nutr* **134**, 3089–3094, 2004.
32. Heng D, Gao F, Jong R, Fishell E, Yaffe M, et al.: Risk factors for breast cancer associated with mammographic features in Singaporean Chinese women. *Cancer Epidemiol Biomarkers Prev* **13**, 1751–1758, 2004.
33. Saftlas A, Wolfe J, Hoover R, Brinton L, Schairer C, et al.: Mammographic parenchymal patterns as indicators of breast cancer risk. *Am J Epidemiol* **129**, 518–526, 1989.
34. Bardia A, Vachon CM, Olson JE, Vierkant RA, Wang AH, et al.: Relative weight at age 12 and risk of postmenopausal breast cancer. *Cancer Epidemiol Biomarkers Prev* **17**, 374–378, 2008.
35. Maskarinec G, Meng L, and Ursin G: Ethnic differences in mammographic densities. *Int J Epidemiol* **30**, 959–965, 2001.
36. El-Bastawissi AY, White E, Mandelson MT, and Taplin S: Variation in mammographic breast density by race. *Ann Epidemiol* **11**, 257–263, 2001.
37. Chen Z, Wu AH, Gauderman J, Bernstein L, Ma H, et al.: Does mammographic density reflect ethnic differences in breast cancer incidence rates? *Am J Epidemiol* **159**, 140–147, 2004.