Research Article

Cancer Epidemiology, Biomarkers & Prevention

Childhood Socioeconomic Position and Pubertal Onset in a Cohort of Multiethnic Girls: Implications for Breast Cancer

Robert A. Hiatt[1,2], Susan L. Stewart[3], Kristin S. Hoeft[1], Lawrence H. Kushi[4], Gayle C. Windham[5], Frank M. Biro[6], Susan M. Pinney[7], Mary S. Wolff[8], Susan L. Teitelbaum[8], and Dejana Braithwaite[1]

Abstract

Background: Higher socioeconomic position (SEP) has been associated with increased risk of breast cancer. Its relationship with earlier age of pubertal onset, a risk factor for breast cancer, is less clear.

Methods: We studied the relationship of SEP to pubertal onset in a multiethnic cohort of 1,237 girls ages 6 to 8 years at baseline. Girls in three U.S. cities were followed for 5 to 8 years with annual clinical examinations from 2004 to 2012. SEP measures were examined for associations with pubertal onset, assessed by breast budding (thelarche) and pubic hair development (adrenarche). Analyses were conducted with accelerated failure time models using a Weibull distribution, with left, right, and interval censoring.

Results: Higher body mass index percentage at entry to the study and black or Hispanic race/ethnicity were the strongest predictors of age at pubertal onset. An SEP index comprising household family income, mother's education, and home ownership was an independent predictor of thelarche in adjusted models for all girls together and for white and Latina, separately, but not black girls, and the relationship varied by study site. The SEP index was not related to adrenarche in adjusted models. Overall, girls from the lowest quintile of SEP entered puberty on average 6% earlier than girls from the highest quintile (time ratio = 0.94; 95% confidence interval 0.91–0.97) in adjusted models.

Conclusions: Our results suggest that early-life SEP may influence the timing of pubertal development.

Impact: Factors related to lower SEP in childhood can adversely affect early development in ways that may increase the risk of breast cancer. *Cancer Epidemiol Biomarkers Prev; 26(12); 1714–21. ©2017 AACR.*

Introduction

Socioeconomic position (SEP) at both an individual and population level has been repeatedly associated with increased breast cancer incidence in high-income countries (1, 2). The strongest explanation of this association is that women with higher SEP tend to have reproductive patterns and practices that are directly related to breast cancer incidence such as younger age at menarche (3, 4), older age at menopause (3, 5), older age at first full-term pregnancy (4, 5), lower parity (4, 6), and shorter duration of breast feeding (4, 6). Other breast cancer risk factors, such as use of hormone therapy and higher average alcohol intake, have also been linked to higher SEP (5, 7, 8). Among the reproductive risk factors, a younger age at menarche has been associated with a higher risk of breast cancer in multiple types of epidemiologic studies in many countries around the world (5). Earlier menarche is associated with early onset of ovulatory cycles with increased hormone exposures over a lifetime and has a long-lasting influence on breast cancer risk (9, 10). A meta-analysis of pooled data from studies of breast cancer and reproductive risk factors in Europe and North American estimated that breast cancer risk increases by 5% for each younger year of age at menarche (3).

Long-term trends in the average age of menarche from European countries over the past 100 years and from Korea in the past 50 years have shown a progressive drop in age of up to 5 years (11, 12). Causes for this striking downward trend are thought to be related to improved social circumstances, including better nutrition (13). Other possible influences on the downward trend of the age of menarche include environmental chemicals that disrupt hormone pathways (e.g., endocrine disrupting chemicals), lower physical activity, and psychosocial stressors (14–16).

Studies that examined SEP and age at menarche are inconsistent, with some finding lower SEP directly related to earlier menarche (17–20) and others the inverse (21–23). This inconsistency may be at least in part due to the changing relationship of SEP with body size over time (24, 25) and the association of obesity with race and ethnicity (26). The age of menarche is consistently related to increased subcutaneous fat and body mass

[1]Department of Epidemiology & Biostatistics, University of California, San Francisco, San Francisco, California. [2]Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, San Francisco, California. [3]Department of Public Health Sciences, University of California, Davis, Davis, California. [4]Division of Research, Kaiser Permanente, Oakland, California. [5]Division of Environmental and Occupational Disease Control, California Department of Public Health, Richmond, California. [6]Department of Adolescent Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio. [7]Department of Environmental Health, University of Cincinnati College of Medicine, Cincinnati, Ohio. [8]Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai, New York, New York.

Corresponding Author: Robert A. Hiatt, Department of Epidemiology & Biostatistics, University of California, San Francisco, 550 16th St, 2nd Floor, San Francisco, CA 94158. Phone: 415-514-8113; Fax: 415-514-8150; E-mail: robert.hiatt@ucsf.edu

doi: 10.1158/1055-9965.EPI-17-0496

in the prepubertal period (27), but the trends toward increased overweight and obesity in children (28–30) have been primarily among those of lower, rather than higher, SEP in more recent years (26, 28, 31), emphasizing the importance of considering the effects of SEP, race/ethnicity, and obesity together (32).

Although the age of menarche dropped substantially in the past century, the decrease has slowed. The age of pubertal onset, on the other hand, seems still to be decreasing (29, 33, 34). The reasons for the apparent drop in the age of pubertal onset have been a topic of intense concern and investigation (32, 33, 35), given earlier onset of female reproductive maturity is associated not only with increased breast cancer rates in adulthood, but also with more immediate negative consequences in adolescence, including sexual abuse, sexually transmitted diseases, and mental health issues such as depression (34, 36). Breast budding, or thelarche, is driven by activation of the hypothalamic–pituitary–ovarian axis and mediated by estrogen and is best measured by both observation and palpation, whereas the appearance of pubic hair and other secondary sexual characteristics, or adrenarche, is driven by androgen secretion from the adrenal cortex and assessed visually (29). In the current prospective cohort study, we sought to understand the relationship of SEP to pubertal onset in girls, which tends to precede menarche by about 2 years. The duration of time between pubertal onset and menarche is variable (33). The determinants of pubertal onset may be different from those of menarche and a more sensitive indicator of environmental and hormonal influences on pubertal maturation (33, 34). Menarche has been used in most epidemiologic studies, especially case–control studies, as it is an event more easily recalled by adult women. A subsequent report in our ongoing analyses will cover the relationship of SEP to menarche.

Materials and Methods

The purpose and study design of the Breast Cancer and the Environment Research Program (BCERP) have been described previously (14), and details of results from the BCERP Puberty Study have been published (34, 37–39). Briefly, the BCERP Puberty Study is a consortium of three collaborative prospective studies examining predictors of the onset of puberty in girls. Between 2004 and 2007, 1,239 socioeconomically and race/ethnically diverse girls, aged 6 to 8 years, were enrolled from three locations: the Greater San Francisco Bay Area, the Greater Cincinnati Area, and East Harlem in New York City, hereafter referred to as California, Ohio, and New York. The parent, legal guardian, or primary caregiver gave informed consent, and assent was obtained from the girl. Institutional review boards at each participating institution [Kaiser Permanente (Oakland, CA), Cincinnati Children's Hospital (Cincinnati, OH), Mount Sinai School of Medicine (New York, NY), and UCSF (San Francisco, CA)] approved the study protocols and procedures. Inclusion criteria were age (6–8 years), female sex, no underlying endocrine medical conditions, and in New York, black, or Hispanic race/ethnicity. The parents of 2 girls requested that data from their daughters not be included in the study. We followed 1,237 girls to the time of pubertal onset and included those with observed outcomes in this analysis.

Measurements

Data were obtained from questionnaires completed annually by a parent, legal guardian, or caregiver, either by in-person interviews (California and New York) or by self-administration for the first 5 years and then by interview (Ohio) for the 5- to 8-year duration of follow-up for this analysis, through March 2012. Interviews were conducted in English or Spanish according to the parent/guardian's preference. Anthropometry and assessment of pubertal signs were performed at annual visits in California and New York and semiannual visits in Ohio by clinical research assistants, nurse practitioners, or physicians trained with a standard protocol developed by expert pediatricians across the three sites (37).

Determination of SEP

We examined the following measures of SEP as well as parent/primary caregiver–reported race/ethnicity of the girl from the baseline questionnaire: education of the mother, household income, occupation of the primary financial provider, home ownership, and female as the head of household (defined as financial support only by one or more adult females). Household income combined the incomes of all wage earners and was recorded in categories as <$25,000, $25–$50,000, $50–$100,000, and >$100,000/year. Occupation of the primary financial provider was coded according to status categories as professional, nonmanual, and manual occupations for analyses (40). Mother's education was categorized as high school or less, some college or vocational school, bachelor's degree, and master's degree or higher. We constructed an SEP index that included household income, mother's education, and home ownership by standardizing each variable to mean zero and SD one and summing the standardized variables. Occupation of the primary financial provider had a substantial number of missing values and did not improve reliability of the SEP index (as measured by Cronbach alpha) and was not included.

Other independent variables

The girl's body mass index [weight (kg)/height $(m)^2$] percentile (BMI%) was based on age- and sex-specific growth charts from the Centers for Disease Control and Prevention for 2000 (41) at baseline (categorized as <50, 50–85, and ≥85th percentiles). BMI percentile was based on the baseline height and weight measurement for each girl using calibrated scales and stadiometers by research staff that had been trained and certified uniformly across all three sites. Race/ethnicity was categorized as black, white, Hispanic or Latino, and Asian American in hierarchical order following an algorithm that made each race/ethnic group mutually exclusive. Other variables examined included mother's place of birth (United States/Canada, Mexico, other Latin America/Puerto Rico/Virgin Islands, rest of the world), the study site, and mother's age at menarche (<12, 12–13, ≥14), which may reflect a genetic influence on pubertal development.

Pubertal onset

Girls' pubertal development was assessed using standard methods of Tanner staging conducted by trained staff at each in-person clinic visit using an established 5-stage classification scheme for describing the onset and progression of breast and pubic hair changes by inspection (29) and palpation (42). Details of training, certification, and assessment procedures are reported elsewhere (37). The outcomes were onset of signs of puberty as assessed both by observation and palpation of breast budding for stages B2 or higher (breast) and by observation of stages PH2 or higher (pubic hair).

Statistical analysis

Our *a priori* hypothesis about SEP and pubertal onset was that girls from lower SEP families would go through puberty earlier, and that relationship would be stronger among overweight or obese (BMI% > 85) girls. Race/ethnicity, which is known to be strongly related to pubertal onset independent of BMI (37, 43), was seen as a potential confounder in this relationship being related both to SEP and to pubertal onset. To explore this hypothesis, we first compared the characteristics of the girls in terms of the independent variables by site using χ^2 tests. We then computed a correlation matrix of multiple available SEP measures and assessed reliability using Cronbach alpha. The relationship of the SEP index with BMI was evaluated using polytomous logistic regression to model BMI percentile above the 85th percentile and between the 50th and 85th percentiles versus <50th percentile as a function of SEP quintile, first adjusted only for age at BMI measurement followed by adjustment for race/ethnicity. The relationship of the SEP index and other variables with age at onset of B2 and PH2 was then evaluated in unadjusted accelerated failure time models using a Weibull distribution (SAS PROC LIFEREG, SAS v. 9.3). Left and right censoring was used to account for pubertal transitions taking place outside the period of observation, and interval censoring accounted for pubertal transitions between examination visits. The number in each race/ethnic group was sufficient to allow estimation of interactions between race/ethnicity and other variables, and to produce stable estimates for black, white, and Hispanic girls. Subsequent models of the association between the SEP index and pubertal onset adjusted for BMI%, race/ethnicity, and interactions between BMI% and race/ethnicity, which were included to allow the association between pubertal onset and race/ethnicity to vary by BMI%. The effects of BMI%, race/ethnicity, and their interaction were modeled as the effect of BMI% for whites and the effect of race/ethnicity by BMI% category. We also estimated race/ethnicity–specific SEP effects in a model of the age at B2 to the SEP index, including a race/ethnicity–SEP interaction, and finally a site-specific model of age at B2 that included site–SEP, site–BMI%, and site–race/ethnicity interactions to estimate site-specific associations. Additional models were created to estimate trends across SEP levels.

For each model, time ratios (TRs) and estimated median age at onset for girls in the reference category of all variables in the model were computed, along with their 95% confidence intervals (CIs). The TR indicates how much earlier or later the estimated onset of puberty occurred relative to the reference category of a particular variable. For instance, if the median age at onset was 10 years in the reference category for a particular model, a TR of 0.95 indicates a 5% earlier onset, which corresponds to 6 months (i.e., 0.5 year). In a multivariable model, the number of months difference indicated by a TR depends on the levels of all independent variables in the model.

Results

All but 2 girls ($N = 1{,}235$) contributed to the assessment of the interval for the pubertal transition for breast development; 14% were left censored (B2 at baseline), 72% interval censored, and 13% right censored (still B1 when last observed). A pubertal transition interval for pubic hair development could be determined for 1,230 girls, with 12% left censored, 71% interval censored, and 17% right censored.

The study sample had a high degree of variability in SEP measures and covariates across sites (Table 1). All measures of SEP were highly skewed by site with lower SEP girls in New York and higher SEP level girls in the other two sites. Only black and Hispanic participants recruited in New York by design. Mothers of girls in New York were more likely to be first-generation immigrants from Mexico and Latin America, and more mothers of girls in New York had gone through menarche at ages less than 12 years than the other two sites. New York girls were also more likely to be obese (BMI% $\geq$ 85th percentile) at baseline compared with girls in other sites. Missing data ranged from 0.2% (BMI%) to 11.6% (occupation) of participants. All measures in the SEP indices were strongly correlated with each other except for occupational status.

In models adjusted only for age, BMI% above the 85th percentile was associated with lower SEP [quintile 1 (Q1) vs. Q5: OR = 2.6; 95% CI, 1.6–4.3; Q2 vs. Q5: OR = 2.6; 95% CI, 1.6–4.3; Q3 vs. Q5: OR = 1.8; 95% CI, 1.1–3.0; Q4 vs. Q5: OR = 1.8; 95% CI, 1.1–3.0]. BMI% above the 85th percentile was more common among black (OR = 2.1; 95% CI, 1.3–3.3) and Hispanic girls (OR = 2.9; 95% CI, 1.8–4.8) and less common among Asian (OR = 0.3; 95% CI, 0.1–0.9) girls compared with whites.

In unadjusted models, lower SEP index or any measure, except occupation, predicted earlier onset of B2 and PH2 by a substantial amount (Table 2). For example, a TR of 0.95 for girls with a household income of <$25K is equivalent to 5.8 months earlier onset of B2 compared with girls with household incomes >$100,000. For the SEP index, a TR of 0.94 for the lowest quintile of the SEP index is equivalent to 7.0 months earlier onset of B2 compared with girls in the highest quintile of SEP index. The unadjusted association of the SEP index with age at B2 and at PH2 was statistically significant ($P_{trend} < 0.0001$ for both). In adjusted models, the SEP index association was diminished only slightly after adjustment for race/ethnicity with race/ethnic–specific BMI% (interaction) effects; however, the association of SEP index with PH2 was not longer present (Table 3).

To further examine the impact of SEP on B2 by race/ethnicity, we estimated SEP effects separately among white, Hispanic, black, and Asian American girls (Table 4). After adjustment for BMI% and the interaction BMI% with race/ethnicity and with SEP, pubertal onset in Hispanic girls had the strongest association with SEP, although the trend for whites was also significant. No relationship was seen for black girls, and there were too few Asian girls to produce stable results. Finally, in stratified models, we found variation among the sites in the association of SEP with age at B2 adjusted for BMI% and race/ethnicity, with SEP significantly associated with age at B2 only in San Francisco (Table 5).

Discussion

To our knowledge, this is the first study to prospectively examine the influence of SEP on the onset of puberty determined by physical examinations in a multiethnic population of U.S. girls. In previously published analyses of this cohort of girls, we reported the median age of onset of breast budding (Tanner breast stage 2) to be at age 8.8, 9.3, 9.7, and 9.7 years for black, Latina, white, and Asian girls, respectively (34), compared with 8.9 and 10.0 years for black and white girls in the Pediatric Research in Office Settings (PROS; ref. 43), and BMI% predicted earlier puberty more strongly in the current study in the PROS performed 10 to 20 years earlier (43). In this analysis, we were interested in examining the interrelationship of social position with the age of

Table 1. Characteristics of sample of 1,237 girls ages 6–8 years at baseline by study site for household SEP variables, girl's race/ethnicity, mother's age at menarche and place of birth, and girl's BMI%, the BCERP

Variable	San Francisco area ($n = 444$) *n* (%)	Cincinnati area ($n = 377$) *n* (%)	New York City (East Harlem; $n = 416$) *n* (%)	All ($N = 1{,}237$) *n* (%)
SEP index				
Quintile 1 (lowest)	18 (4.2)	19 (6.8)	184 (51.8)	221 (20.8)
Quintile 2	63 (14.8)	32 (11.5)	116 (32.7)	211 (19.9)
Quintile 3	92 (21.5)	71 (25.4)	47 (13.2)	210 (19.8)
Quintile 4	119 (27.8)	83 (29.7)	7 (2.0)	209 (19.7)
Quintile 5	135 (31.6)	74 (26.5)	1 (0.3)	210 (19.8)
Total	427 (100)	279 (100)	355 (100)	1,061 (100)
Missing	17 (5.0)	98 (26.0)	61 (14.7)	176 (14.2)
Household income				
<$25,000	22 (3.8)	33 (11.1)	209 (54.4)	264 (23.6)
$25–50,000	72 (16.5)	57 (19.1)	116 (30.2)	245 (21.9)
$50–100,000	156 (35.7)	114 (38.3)	52 (13.5)	322 (28.8)
≥$100,000	187 (42.8)	94 (31.5)	7 (1.8)	288 (25.7)
Total	437 (100)	298 (100)	384 (100)	1,119 (100)
Missing	7 (1.6)	79 (21.0)	32 (7.7)	118 (9.5)
Education of mother				
≤High school	79 (18.1)	40 (12.3)	231 (60.8)	350 (30.6)
Some college or vocational	129 (29.6)	126 (38.7)	107 (28.2)	362 (31.7)
Bachelor's degree	136 (31.2)	106 (32.5)	30 (7.9)	272 (23.8)
Master's degree or higher	92 (21.1)	54 (16.6)	12 (3.2)	158 (13.8)
Total	436 (100)	326 (100)	380 (100)	1,142 (100)
Missing	8 (1.8)	51 (13.5)	36 (8.7)	95 (7.7)
Occupation of primary financial provider				
Manual	54 (12.3)	54 (17.1)	157 (46.4)	265 (24.2)
Nonmanual	207 (47.2)	123(38.9)	132 (39.1)	462 (42.3)
Professional	178 (40.5)	139 (44.0)	49 (14.5)	366 (33.5)
Total	439 (100)	316 (100)	338 (100)	1,093 (100)
Missing	5 (1.1)	61 (16.2)	78 (18.8)	144 (11.6)
Home ownership				
Rent	122 (27.6)	72 (23.1)	386 (94.4)	580 (49.9)
Other	320 (72.4)	240 (76.9)	23 (5.6)	583 (50.1)
Total	442 (100)	312 (100)	409 (100)	1,163 (100)
Missing	2 (0.5)	65 (17.2)	7 (1.7)	74 (6.0)
Female head of household				
Yes	54 (12.2)	63 (18.6)	121 (29.5)	238 (19.9)
No	390 (87.8)	276 (81.4)	289 (70.5)	955 (80.1)
Total	444 (100)	339 (100)	410 (100)	1,193 (100)
Missing	0 (0.0)	38 (10.1)	6 (1.4)	44 (3.6)
Mother's place of birth				
U.S. state/Canada	319 (72.0)	326 (95.9)	202 (49.8)	847 (71.2)
Mexico	47 (10.6)	3 (0.9)	112 (27.6)	162 (13.6)
Other Latin America/Puerto Rico/Virgin Islands	19 (4.3)	5 (1.5)	83 (20.4)	107 (9.0)
Rest of world	58 (13.1)	6 (1.8)	9 (2.2)	73 (6.1)
Total	443 (100)	340 (100)	406 (100)	1,189 (100)
Missing	1 (0.2)	37 (9.8)	10 (2.4)	48 (3.9)
Mother's age at menarche (years)				
<12	104 (23.7)	74 (22.1)	118 (30.3)	296 (25.5)
12–13	234 (53.3)	190 (56.7)	180 (46.3)	604 (51.9)
≥14	101 (23.0)	71 (21.2)	91 (23.4)	263 (22.6)
Total	439 (100)	335 (100)	389 (100)	1,163 (100)
Missing	5 (1.1)	42 (11.1)	27 (6.5)	74 (6.0)
Girl's race/ethnicity				
White	187 (42.1)	231 (61.3)	0 (0)	418 (33.8)
Black	97 (21.8)	126 (33.4)	167 (40.1)	390 (31.5)
Hispanic	108 (24.3)	15 (4.0)	249 (59.9)	372 (30.1)
Asian	52 (11.7)	5 (1.3)	0 (0)	57 (4.6)
Total	444 (100)	377 (100)	416 (100)	1,237 (100)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Girl's BMI (at baseline) BMI%				
BMI > 85th percentile	132 (29.7)	113 (30.0)	163 (39.4)	408 (33.0)
BMI 50–85th percentile	163 (36.7)	122 (32.4)	135 (32.6)	420 (34.0)
BMI < 50th percentile	149 (33.6)	142 (37.7)	116 (28.0)	407 (33.0)
Total	444 (100)	377 (100)	414 (100)	1,235 (100)
Missing	0 (0.0)	0 (0.0)	2 (0.5)	2 (0.2)

Note: $P < 0.0001$ for comparisons of all tabulated variables by site, except BMI% ($P < 0.01$).

Table 2. Unadjusted associations (TRs and 95% CIs) of SEP index, BMI%, and race/ethnicity to age at first signs of breast development (B2) or pubic hair development (PH2) in 1,235 girls ages 6–8 years at baseline, BCERP

Variable	Age at breast stage B2 ($n = 1,235$) (No.) TR (95% CI)	Age at pubic hair stage PH2 ($n = 1,230$) (No.) TR (95% CI)
SEP index[a]	1,059	1,054
Median age (y)	9.74 (9.54–9.94)	10.45 (10.23–10.67)
Quintile 1 (lowest)	0.94 (0.91–0.97)	0.95 (0.92–0.97)
Quintile 2	0.93 (0.91–0.96)	0.90 (0.87–0.93)
Quintile 3	0.96 (0.93–0.98)	0.93 (0.90–0.96)
Quintile 4	0.98 (0.95–1.00)	0.96 (0.93–0.99)
Quintile 5 (ref)	1.00	1.00
BMI%	1,233	1,228
Median[a]	9.83 (9.69–9.98)	10.44 (10.27–10.61)
>85th	0.89 (0.87–0.91)	0.90 (0.88–0.92)
50–85th	0.95 (0.94–0.97)	0.94 (0.92–0.96)
<50th (ref)	1.00	1.00
Race/ethnicity	1,235	1,230
Median[a]	9.58 (9.44–9.72)	10.27 (10.11–10.43)
Black	0.93 (0.92–0.95)	0.90 (0.88–0.92)
Hispanic	0.98 (0.96–1.00)	0.96 (0.94–0.99)
Asian	1.04 (1.00–1.08)	1.08 (1.04–1.13)
White (ref)	1.00	1.00

[a]Median of referent group
Abbreviation: ref, referent.

Table 3. Relationship of SEP index to age at Tanner breast stage B2 and Tanner stage PH2 adjusted for BMI%, race/ethnicity, and BMI%-race/ethnicity interaction in 1,059 girls ages 6–8 years of age at baseline, BCERP

Variable	Age at B2 ($n = 1,059$) TR (95% CI)	Age at PH2 ($n = 1,054$) TR (95% CI)
SEP index		
Median[a]	10.19 (9.92–10.46)	10.87 (10.58–11.18)
Quintile 1 (lowest)	0.94 (0.91–0.97)	1.00 (0.97–1.04)
Quintile 2	0.95 (0.92–0.98)	0.96 (0.93–1.00)
Quintile 3	0.96 (0.94–0.99)	0.97 (0.94–1.00)
Quintile 4	0.98 (0.96–1.01)	0.98 (0.95–1.01)
Quintile 5 (ref)	1.00	1.00
BMI%: White (ref)		
≥85th	0.92 (0.89–0.95)	0.94 (0.90–0.97)
50–85th	0.94 (0.91–0.97)	0.94 (0.90–0.97)
<50th (ref)	1.00	1.00
Race/ethnicity		
BMI% ≥ 85th:		
Black	0.91 (0.87–0.95)	0.88 (0.84–0.92)
Hispanic	1.00 (0.96–1.04)	0.97 (0.93–1.01)
Asian	0.99 (0.88–1.11)	0.99 (0.88–1.12)
White (ref)	1.00	1.00
BMI% 50–85th:		
Black	0.98 (0.94–1.02)	0.91 (0.88–0.95)
Hispanic	1.05 (1.01–1.09)	0.99 (0.95–1.03)
Asian	1.10 (1.03–1.17)	1.11 (1.04–1.19)
White (ref)	1.00	1.00
BMI% < 50th:		
Black	1.00 (0.96–1.04)	0.92 (0.89–0.96)
Hispanic	1.02 (0.98–1.06)	0.97 (0.93–1.01)
Asian	0.99 (0.94–1.04)	1.05 (0.99–1.11)
White (ref)	1.00	1.00

NOTE: Race/ethnicity–BMI% interaction: $P < 0.001$ (B2), $P = 0.31$ (PH2). SEP trend: $P = 0.0002$ (B2); $P = 0.8633$ (PH2).
Abbreviations: B2, breast stage 2; ref, referent.
[a]Median of referent group for all variables in model.

pubertal onset, which is viewed as a window of susceptibility in the life course perspective of breast cancer etiology (44, 45). We found that a prepubertal girl's SEP as measured by multiple variables, but especially by a lower SEP index, which was comprised of household income, mother's education, and home ownership, was associated with earlier age at the onset of pubertal signs of breast but not pubic hair development in models adjusted for BMI%, race/ethnicity, and their interaction. Specifically, girls in the lowest SEP index quintile developed pubertal signs of breast budding a full 7 months earlier than girls in the highest SEP quintile. Adjustment for BMI%, with or without race/ethnicity and their interaction, somewhat attenuated but did not substantially change the relationship of SEP with the onset of breast development compared with the unadjusted model. We did not find a statistically significant relationship of the SEP index to adrenarche as assessed by pubic hair development. This relationship deserves further exploration, but it may be that influences on pubertal development associated with social disadvantage act more strongly on the hypothalamic–pituitary–ovarian axis than that on the development of the adrenal cortex.

Our *a priori* concept was that the effect of SEP on age at puberty worked through, or was mediated by, its association with obesity. Whereas the decreasing age of menarche internationally has long been associated with higher standards of living and better nutrition, many countries are now experiencing an epidemic of pediatric obesity, which is associated with earlier age at puberty and is more prevalent in lower, not higher, SEP groups (28, 31). In our study population, although lower SEP was associated with earlier onset of B2, it was relatively independent of obesity (i.e., BMI%) and of race/ethnicity as well. This is consistent with the findings from the National Longitudinal Study of Youth (20) and suggests that there may be other pathways through which SEP influences early pubertal development. For example, one such pathway relates to psychosocial stress in early childhood (46). There is evidence that the absence of fathers is associated with earlier pubertal onset, at least in higher SEP girls (47, 48). Other factors may relate to exposures to environmental chemicals (38, 39) and to the built environment (49) associated with higher levels of pollution and to obesity, food insecurity, fewer playgrounds, and less opportunities for physical activity that were not examined in this analysis.

Consistent with the hypothesis, in addition to BMI, race/ethnicity was a strong predictor of the age of pubertal onset, with black girls entering puberty substantially before girls in other groups. In a model with race/ethnicity–specific SEP effects, a lower SEP index was related to earlier onset of puberty measured by breast budding in Hispanic and white girls, but not in black girls. For black girls, BMI% proved a strong predictor of pubertal onset, whereas SEP did not. The absence of a relationship between SEP and pubertal onset among black girls has also been observed by Braithwaite and colleagues (18) in the National Growth and Health Study and by Krieger and colleagues examining long terms trends in the National Health and Nutritional Examination Survey (32), although it was not seen in the National Longitudinal Study of Youth (20).

Our results are consistent with one other recent prospective study of SEP and puberty in a large Australian cohort of both girls and boys that relied on parental self-report of pubertal onset (50). In 1,770 girls assessed at age 10 to 11 years, the rate of early puberty was increased 2-fold (OR = 1.96; 95% CI, 1.08–3.56) for girls with low household SEP. In other studies of pubertal onset as measured by menarche, our results are compatible with Windham and colleagues (17), Braithwaite and colleagues (18), James-Todd

Table 4. Relationship of SEP index to age at Tanner B2 by race/ethnicity in 1,059 girls ages 6–8 years of age at entry to study with adjustment for BMI%, BCERP

	White $n = 371$ TR (95% CI)	Hispanic $n = 321$ TR (95% CI)	Black $n = 315$ TR (95% CI)	Asian $n = 52$ TR (95% CI)
SEP index[a]				
Quintile 1 (low)	0.91 (0.77–1.07)	0.93 (0.87–1.00)	0.98 (0.91–1.06)	0.84 (0.71–1.01)
Quintile 2	0.93 (0.88–1.00)	0.92 (0.85–0.99)	0.99 (0.91–1.06)	1.22 (0.95–1.58)
Quintile 3	0.97 (0.93–1.00)	1.00 (0.92–1.08)	0.95 (0.88–1.03)	0.93 (0.85–1.02)
Quintile 4	0.97 (0.94–1.00)	1.04 (0.96–1.14)	0.95 (0.88–1.03)	1.05 (0.96–1.15)
Quintile 5 (ref)	1.00	1.00	1.00	1.00
BMI%				
≥85	0.92 (0.89–0.95)	0.90 (0.87–0.93)	0.84 (0.81–0.88)	0.94 (0.83–1.06)
50–85	0.94 (0.91–0.97)	0.97 (0.93–1.01)	0.92 (0.89–0.96)	1.06 (0.96–1.14)
<50 (ref)	1.00	1.00	1.00	1.00

NOTE: Median at referent levels of all variables in the model = 10.25 (95% CI, 9.97–10.54). Race/ethnicity–BMI% interaction: $P < 0.001$; race/ethnicity–SEP interaction: $P < 0.0001$. SEP trend: white: $P = 0.007$; Hispanic: $P < 0.0001$; black: $P = 0.33$; Asian: $P = 0.51$.

Abbreviations: B2, breast stage 2; ref, referent.

[a]SEP index – Household income, mother's education, own/rent home.

and colleagues (19), and Deardorff and colleagues (20), where lower SEP was associated with an earlier age at menarche. For example, in the National Growth and Health Study, Braithwaite and colleagues found that higher SEP (measured by household income) white girls were more likely to go through menarche later than lower SEP white girls. In contrast, black girls of higher SEP went through menarche earlier than lower SEP black girls.

Our study has the advantage of a prospective design and repeated direct examination of girls as they entered the pubertal transition. Most of the literature relates to SEP and age of menarche obtained retrospectively (3, 4), as menarche is more easily recalled by adult women in epidemiologic studies than pubertal onset. Inferences in this study were strengthened by its longitudinal design and annual (or semiannual in Ohio) data collection, including physical examination with breast palpation. Breast palpation is preferred as it reduces errors in assessment from observation alone where there may appear to be breast development in overweight and obese girls (51). The study participants were also race/ethnically and socioeconomically diverse and more than 80% of the girls showed signs of pubertal development before the end of the data collection period or loss to follow-up.

Limitations of the study include fairly long (usually annual) intervals between observations and left censoring of a proportion of pubertal transitions. Cincinnati girls were examined every 6 months, and thus, the dating of pubertal onset was more precise at this site. That the other two sites examined girls annually could be considered a limitation, but it is not clear how serious an effect this was as mean pubertal onset in Cincinnati was estimated at a time intermediate between the other two sites (Table 3). It should be noted that we assessed the onset of signs of puberty in this study, but are aware that these signs, breast budding and pubic hair growth, may not be reflections of true pubertal onset. Rather, they may reflect changes in body phenotype due to external environmental exposures, such as those potentially brought on by endocrine-disrupting chemicals that may also vary by SEP (52, 53). Also, these results may not be generalizable to the entire U.S. population, even though we used data from an integrated cohort in three national geographic locations; participants were selected primarily from urban areas and were a selected sample in the sense that they agreed to participate for multiple visits over many years.

The relevance of these findings to breast cancer incidence in adulthood is a matter of speculation, as previously conducted longitudinal studies on the relationship are inconsistent. Higher childhood SEP, as measured by either father's occupation or education, was not related to breast cancer incidence in a large Dutch study (54), but, as measured by higher early family income, it was associated with greater risk of breast cancer in the Wisconsin Longitudinal Study (55). In the future, the increasing prevalence of pediatric obesity in the United States (and other industrialized countries; ref. 56) may play a role in the relationship of SEP and breast cancer (57). Higher obesity may increase breast cancer risk by reducing the age of puberty, and thus lifelong exposure to estrogen. This hypothesis is not supported by data from the Nurse's Health Study where recalled childhood obesity was associated with lower, not higher, risk of breast cancer (58), but that was a cohort of women who grew up in the early part of the last century, and the assessment of obesity is subject to recall bias. If current shifts in the association of SEP with pubertal onset and menarche reverse the traditional relationship such that higher childhood SEP is associated with lower rates of breast cancer, the currently understood pattern of reproductive risk factors for breast cancer could be altered in future decades.

Table 5. Relationship of SEP index to age at Tanner B2 by site in 1,059 girls ages 6–8 years of age at entry to study with adjustment for BMI% and race/ethnicity, BCERP

	San Francisco area $n = 427$ TR (95% CI)	Cincinnati area $n = 278$ TR (95% CI)	New York City (East Harlem) $n = 354$ TR (95% CI)
SEP index[a]			
Quintile 1 (low)	0.93 (0.87–1.00)	0.97 (0.90–1.04)	1.01 (0.97–1.06)
Quintile 2	0.96 (0.91–1.00)	1.05 (0.99–1.11)	0.99 (0.94–1.03)
Quintile 3	0.99 (0.95–1.02)	0.96 (0.92–1.00)	1.00 (ref)
Quintile 4	1.00 (0.97–1.04)	0.96 (0.92–1.00)	
Quintile 5	1.00 (ref)	1.00 (ref)	
BMI%			
≥85	0.95 (0.92–0.98)	0.82 (0.79–0.85)	0.85 (0.82–0.88)
50–85	0.98 (0.95–1.01)	0.90 (0.87–0.93)	0.93 (0.90–0.97)
<50	1.00 (ref)	1.00 (ref)	1.00 (ref)
Race/ethnicity			
Black	0.93 (0.90–0.96)	0.94 (0.90–0.98)	0.99 (0.96–1.02)
Hispanic	1.02 (0.98–1.05)	0.93 (0.84–1.03)	1.00 (ref)
Asian	0.99 (0.95–1.03)	1.24 (1.09–1.42)	
White	1.00 (ref)	1.00 (ref)	

NOTE: Median at referent levels of all variables in the model = 10.21 (95% CI 9.91–10.51). Site–race/ethnicity interaction: $P = 0.0002$; site–BMI% interaction: $P < 0.0001$; site–SEP interaction: $P = 0.001$. SEP trend: San Francisco: $P = 0.019$; Cincinnati: $P = 0.79$; New York City: $P = 0.39$. New York SEP quintile 3 includes 8 girls in quintiles 4 and 5.

Abbreviations: B2, breast stage 2; ref, referent;

[a]SEP index – Household income, mother's education, own/rent home.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Disclaimer

The contents of this article are solely the responsibility of the authors and do not necessarily represent the official views of the NIEHS or NCI, the NIH, the Centers for Disease Control and Prevention, or the California Department of Public Health.

Authors' Contributions

Conception and design: R.A. Hiatt, S.L. Stewart, L.H. Kushi, G.C. Windham, F.M. Biro, S.M. Pinney, M.S. Wolff, S.L. Teitelbaum, D. Braithwaite
Development of methodology: R.A. Hiatt, L.H. Kushi, G.C. Windham, F.M. Biro, S.M. Pinney, M.S. Wolff, S.L. Teitelbaum, D. Braithwaite
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): K.S. Hoeft, L.H. Kushi, G.C. Windham, F.M. Biro, S.M. Pinney, M.S. Wolff, S.L. Teitelbaum
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): R.A. Hiatt, S.L. Stewart, L.H. Kushi, S.M. Pinney, M.S. Wolff, D. Braithwaite
Writing, review, and/or revision of the manuscript: R.A. Hiatt, S.L. Stewart, K.S. Hoeft, L.H. Kushi, G.C. Windham, F.M. Biro, S.M. Pinney, M.S. Wolff, S.L. Teitelbaum, D. Braithwaite
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): K.S. Hoeft
Study supervision: R.A. Hiatt, F.M. Biro, S.L. Teitelbaum
Other (obtained funding for the project): D. Braithwaite

Acknowledgments

This work was supported by a NCIRO3 CA143936-01 awarded to D. Braithwaite and made possible by the Breast Cancer and the Environment Research Program award numbers U01ES012770 (to F.M. Biro and S.M. Pinney), U01ES012771 (to M.S. Wolff and S.L. Teitelbaum), U01ES012800 and U01ES012801 (to R.A. Hiatt, S.L. Stewart, L.H. Kushi, and G.C. Windham), U01ES019435 (to L.H. Kushi and G.C. Windham), U01ES019453 (to F.M. Biro and S.M. Pinney), U01ES019454 (to M.S. Wolff and S.L. Teitelbaum), and U01ES019457 (to R.A. Hiatt and S.L. Stewart) from the National Institute of Environmental Health Sciences (NIEHS) and the NCI; P01ES009584 and P30ES006096 from NIEHS; UL1RR024131, UL1RR029887, and UL1RR026314 from the National Center for Research Resources; and F31 DE023282 from NIDCR (to K. S. Hoeft).

We gratefully acknowledge support of the Avon Foundation for community outreach and education.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received June 7, 2017; revised August 3, 2017; accepted September 18, 2017; published OnlineFirst September 22, 2017.

References

1. Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. Epidemiol Rev 1993;15:36–47.
2. Robert SA, Strombom I, Trentham-Dietz A, Hampton JM, McElroy JA, Newcomb PA, et al. Socioeconomic risk factors for breast cancer: distinguishing individual- and community-level effects. Epidemiology 2004; 15:442–50.
3. Collaborative Group on Hormonal Factors in Breast Cancer. Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies. Lancet Oncol 2012;13:1141–51.
4. Ma H, Bernstein L, Pike MC, Ursin G. Reproductive factors and breast cancer risk according to joint estrogen and progesterone receptor status: a meta-analysis of epidemiological studies. Breast Cancer Res 2006; 8:R43.
5. McPherson K, Steel CM, Dixon JM. ABC of breast diseases. Breast cancer-epidemiology, risk factors, and genetics. BMJ 2000;321:624–8.
6. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. Lancet 2002;360: 187–95.
7. Chen WY, Rosner B, Hankinson SE, Colditz GA, Willett WC. Moderate alcohol consumption during adult life, drinking patterns, and breast cancer risk. JAMA 2011;306:1884–90.
8. Ravdin PM, Cronin KA, Howlader N, Berg CD, Chlebowski RT, Feuer EJ, et al. The decrease in breast-cancer incidence in 2003 in the United States. N Engl J Med 2007;356:1670–4.
9. Bernstein L. Epidemiology of endocrine-related risk factors for breast cancer. J Mammary Gland Biol Neoplasia 2002;7:3–15.
10. Apter D, Vihko R. Early menarche, a risk factor for breast cancer, indicates early onset of ovulatory cycles. J Clin Endocrinol Metab 1983;57:82–6.
11. Cho GJ, Park HT, Shin JH, Hur JY, Kim YT, Kim SH, et al. Age at menarche in a Korean population: secular trends and influencing factors. Eur J Pediatr 2010;169:89–94.
12. Tanner JM. Growth at adolescence. Springfield, Ill: Thomas; 1962.
13. Ly D, Forman D, Ferlay J, Brinton LA, Cook MB. An international comparison of male and female breast cancer incidence rates. Int J Cancer 2013;132:1918–26.
14. Hiatt RA, Haslam SZ, Osuch J. The breast cancer and the environment research centers: transdisciplinary research on the role of the environment in breast cancer etiology. Environ Health Perspect 2009;117:1814–22.
15. Mishra GD, Cooper R, Tom SE, Kuh D. Early life circumstances and their impact on menarche and menopause. Womens Health 2009;5:175–90.
16. Forman MR, Mangini LD, Thelus-Jean R, Hayward MD. Life-course origins of the ages at menarche and menopause. Adolescent Health Med Ther 2013;4:1–21.
17. Windham GC, Bottomley C, Birner C, Fenster L. Age at menarche in relation to maternal use of tobacco, alcohol, coffee, and tea during pregnancy. Am J Epidemiol 2004;159:862–71.
18. Braithwaite D, Moore DH, Lustig RH, Epel ES, Ong KK, Rehkopf DH, et al. Socioeconomic status in relation to early menarche among black and white girls. Cancer Causes Control 2009;20:713–20.
19. James-Todd T, Tehranifar P, Rich-Edwards J, Titievsky L, Terry MB. The impact of socioeconomic status across early life on age at menarche among a racially diverse population of girls. Ann Epidemiol 2010;20:836–42.
20. Deardorff J, Abrams B, Ekwaru JP, Rehkopf DH. Socioeconomic status and age at menarche: an examination of multiple indicators in an ethnically diverse cohort. Ann Epidemiol 2014;24:727–33.
21. Graber JA, Brooks-Gunn J, Warren M. The antecedents of menarcheal age: heredity, family environment, and stressful life events. Child Dev 1995;66:346–59.
22. Moisan J, Meyer F, Gingras S. A nested case-control study of the correlates of early menarche. Am J Epidemiol 1990;132:953–61.
23. Windham GC, Zhang L, Longnecker MP, Klebanoff M. Maternal smoking, demographic and lifestyle factors in relation to daughter's age at menarche. Paed Perinat Epidemiol 2008;22:551–61.
24. Baum CL II, Ruhm CJ. Age, socioeconomic status and obesity growth. J Health Econ 2009;28:635–48.
25. Murasko JE. Socioeconomic status, height, and obesity in children. Econ Hum Biol 2009;7:376–86.
26. Singh GK, Siahpush M, Kogan MD. Rising social inequalities in US childhood obesity, 2003-2007. Ann Epidemiol 2010;20:40–52.
27. Kaplowitz PB. Link between body fat and the timing of puberty. Pediatrics 2008;121:S208–17.
28. Popkin BM, Gordon-Larsen P. The nutrition transition: worldwide obesity dynamics and their determinants. Int J Obes Relat Metab Disord 2004; 28:S2–9.

29. Biro FM, Huang B, Crawford PB, Lucky AW, Striegel-Moore R, Barton BA, et al. Pubertal correlates in black and white girls. J Pediatr 2006;148: 234–40.
30. Lee JM, Appugliese D, Kaciroti N, Corwyn RF, Bradley RH, Lumeng JC. Weight status in young girls and the onset of puberty. Pediatrics 2007;119: e624–30.
31. Wang Y. Disparities in pediatric obesity in the United States. Adv Nutr 2011;2:23–31.
32. Krieger N, Kiang MV, Kosheleva A, Waterman PD, Chen JT, Beckfield J. Age at menarche: 50-year socioeconomic trends among US-born black and white women. Am J Public Health 2015;105:388–97.
33. Euling SY, Herman-Giddens ME, Lee PA, Selevan SG, Juul A, Sorensen TI, et al. Examination of US puberty-timing data from 1940 to 1994 for secular trends: panel findings. Pediatrics 2008;121:S172–91.
34. Biro F, Greenspan L, Galvez M, Pinney S, Teitelbaum S, Windham G, et al. Onset of breast development in a longitudinal cohort. Pediatrics 2013; 132:1019–27.
35. Euling SY, Selevan SG, Pescovitz OH, Skakkebaek NE. Role of environmental factors in the timing of puberty. Pediatrics 2008;121: S167–71.
36. Downing J, Bellis MA. Early pubertal onset and its relationship with sexual risk taking, substance use and anti-social behaviour: a preliminary cross-sectional study. BMC Public Health 2009;9:446.
37. Biro FM, Galvez MP, Greenspan LC, Succop PA, Vangeepuram N, Pinney SM, et al. Pubertal assessment method and baseline characteristics in a mixed longitudinal study of girls. Pediatrics 2010;126: e583–90.
38. Windham GC, Pinney SM, Voss RW, Sjodin A, Biro FM, Greenspan LC, et al. Brominated flame retardants and other persistent organohalogenated compounds in relation to timing of puberty in a longitudinal study of girls. Environ Health Perspect 2015;123:1046–52.
39. Wolff MS, Teitelbaum SL, McGovern K, Pinney SM, Windham GC, Galvez M, et al. Environmental phenols and pubertal development in girls. Environ Int 2015;84:174–80.
40. Erikson R, Goldthorpe JH. The constant flux: a study of class mobility in industrial societies. Oxford, England: Oxford University Press; 1992.
41. Centers for Disease Control and Prevention NCfHS. CDC growth charts. 2000. [cited 2000 May 30]. Available from: https://www.cdc.gov/growthcharts/cdc_charts.htm.
42. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. Arch Dis Child 1969;44:291–303.
43. Herman-Giddens ME, Slora EJ, Wasserman RC, Bourdony CJ, Bhapkar MV, Koch GG, et al. Secondary sexual characteristics and menses in young girls seen in office practice: a study from the Pediatric Research in Office Settings Network. Pediatrics 1997;99:505–12.
44. Ben-Shlomo Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. Int J Epidemiol 2002;31:285–93.
45. Michels K, Willett WC. Breast cancer- early life matters. N Engl J Med. 2004;351:1679–81.
46. Belsky J, Steinberg L, Draper P. Childhood experience, interpersonal development, reproductive strategy: an evolutionary theory of socialization. Child Dev 1991;62:647–70.
47. Comings DE, Muhleman D, Johnson JP, MacMurray JP. Parent-daughter transmission of the androgen receptor gene as an explanation of the effect of father absence on age of menarche. Child Dev 2002;73:1046–51.
48. Deardorff J, Ekwaru JP, Kushi LH, Ellis BJ, Greenspan LC, Mirabedi A, et al. Father absence, body mass index, and pubertal timing in girls: differential effects by family income and ethnicity. J Adolescent Health 2011;48: 441–7.
49. Hoyt LT, Kushi LH, Leung CW, Nickleach DC, Adler N, Laraia BA, et al. Neighborhood influences on girls' obesity risk across the transition to adolescence. Pediatrics 2014;134:942–9.
50. Sun Y, Mensah FK, Azzopardi P, Patton GC, Wake M. Childhood social disadvantage and pubertal timing: a national birth cohort from Australia. Pediatrics 2017;139:e20164099.
51. Desmangles JC, Lappe JM, Lipaczewski G, Haynatzki G. Accuracy of pubertal Tanner staging self-reporting. J Pediatr Endocrinol Metab 2006;19:213–21.
52. Borrell LN, Factor-Litvak P, Wolff MS, Susser E, Matte TD. Effect of socioeconomic status on exposures to polychlorinated biphenyls (PCBs) and dichlorodiphenyldichloroethylene (DDE) among pregnant African-American women. Arch Environ Health 2004;59:250–5.
53. Tyrrell J, Melzer D, Henley W, Galloway TS, Osborne NJ. Associations between socioeconomic status and environmental toxicant concentrations in adults in the USA: NHANES 2001-2010. Environ Int 2013;59:328–35.
54. de Kok IM, van Lenthe FJ, Avendano M, Louwman M, Coebergh JW, Mackenbach JP. Childhood social class and cancer incidence: results of the globe study. Soc Sci Med 2008;66:1131–9.
55. Pudrovska T, Anikputa B. The role of early-life socioeconomic status in breast cancer incidence and mortality: unraveling life course mechanisms. J Aging Health 2012;24:323–44.
56. Wang Y, Lobstein T. Worldwide trends in childhood overweight and obesity. Int J Pediatr Obes 2006;1:11–25.
57. Ruder EH, Dorgan JF, Kranz S, Kris-Etherton PM, Hartman TJ. Examining breast cancer growth and lifestyle risk factors: early life, childhood, and adolescence. Clin Breast Cancer 2008;8:334–42.
58. Baer HJ, Tworoger SS, Hankinson SE, Willett WC. Body fatness at young ages and risk of breast cancer throughout life. Am J Epidemiol 2010; 171:1183–94.