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Childhood Socioeconomic Status and Menarche: A Prospective Study

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Abstract

Purpose: The relationship between socioeconomic status (SES) and menarche has implications for understanding social level influences on early life development and adult disease, including breast cancer, but remains ill defined. We report here results from the Breast Cancer and the Environment Research Program, which permitted a longitudinal study of age at menarche in relationship to childhood SES in a diverse cohort of 1,069 girls across three urban areas of the United States.

Methods: We assessed the association of SES index quintiles with age at pubertal onset with breast budding and subsequent tempo to the age at menarche between 2004 and 2015 using multiple event Cox regression models to estimate hazard ratios and 95% confidence intervals.

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Results: In an unadjusted model, lower SES was predictive of both earlier pubertal onset and tempo and thus earlier age at menarche in trends across quintiles. After adjusting for the potentially mediating effects of BMI, SES trends remained significant for both outcomes. After adjusting for both BMI and race/ethnicity, the association with SES remained substantial for pubertal onset but was much diminished and nonsignificant for tempo and thus age at menarche.

Conclusions: These results suggest that a lower SES environment and social adversity affect the age at menarche primarily by hastening pubertal onset rather than by shortening tempo.

Earlier ages at menarche and pubertal onset have been well documented risk factors for breast cancer (1). It is also known that the age of menarche has decreased dramatically from the late 1800s to the mid-1900s, generally stabilizing since then, and that is has been generally associated with improvements in social conditions including nutritional status (2, 3). Also earlier age of menarche at a population level has historically been associated with higher socioeconomic status (SES) and improved social conditions (4). However, in our prior analysis of the age of pubertal onset we found that higher SES among young girls was related to later, not earlier, age of pubertal onset even after adjustment for the effects of race/ethnicity and BMI (5) which in previous studies by our group have had a strong influence on both pubertal onset (6) and menarche (7). Other recent U.S. studies have also found that earlier age of menarche was associated with lower SES in (8–10), although these earlier studies did not examine menarche in relation to pubertal onset and did not include diverse race/ethnic groups. In the current study we sought to extend our earlier findings by examining the relationship of childhood SES to the age of menarche in addition to the relationship to pubertal onset in a multiethnic cohort.

Our interest in childhood SES derives from the well documented effects of early life adversity on the hypothalamic-pituitary-adrenal (HPA) axis (11, 12), which may in turn influence the HPG axis to start puberty earlier (13). The reasons for earlier ages at puberal onset and menarche (4, 6, 14, 15) are unclear. Several studies have shown a relationship between BMI and the onset of puberty indicating that overweight and obese young girls tend to mature earlier than those who are not overweight (5, 6). However, studies that have examined the relationship between childhood SES and the onset of puberty have found inconsistent results. Recent studies from Sun et al. and Hiatt et al. found associations between lower SES and early pubertal development (5, 16). However, an earlier study from Windham et al. analyzing data from women in the Collaborative Perinatal Project from 1959–1966 found an association between girls with higher childhood SES and earlier menarche (17)—raising the question of whether, because of the obesity epidemic, the relationship between SES and menarche is changing.

Separately, both higher SES and early onset of menarche are established risk factors for breast cancer (1, 5). Women living in higher SES communities and women living in urban areas have greater risk of developing breast cancer than those living in lower SES communities or rural areas (18). Women who have higher levels of education and women with higher incomes also have a greater risk for breast cancer (2). These associations with SES related factors have been well established and associated with other predictors of breast

cancer, including differences in reproductive factors, higher alcohol intake, and greater use of hormone replacement therapy (2, 5).

Earlier onset of menarche is believed also to be associated with increased breast cancer risk due to increased estrogen exposure over the life course (2) and the hormonal milieu during puberty(19). For each year of earlier onset of menarche, a women's risk of breast cancer is increased by 5% (20). Known predictors of the onset of menarche include pre-pubertal BMI, exposure to endocrine disrupting chemicals (21), and psychosocial stressors that can disrupt the hypothalamic-pituitary-adrenal (HPA) axis (8, 11, 22). In turn, these exposures have been found to be associated with SES (9). What is not clear is whether there is an association between early childhood adversity as measured by SES and both the age of pubertal onset and menarche that can be demonstrated in longitudinal population-based ethnically-diverse studies. Suggested mechanisms have included the influence of early childhood obesity which triggers increased levels of leptin in adipocytes informing the body of increased energy stores and leading to earlier activation of the HPA axis (10, 22). As with pubertal onset most studies suggest that higher BMI is related to earlier onset of menarche (22–24).

The answer to these questions are relevant to the complex etiology of breast cancer, which is characterized by multiple interacting factors, including those that act early in life (25). Breast cancer is the most common cancer among women in the United States and in both developed and developing countries (1, 14, 26). The factors most "upstream" from the biologic mechanisms leading to breast cancer are those in the social and physical environment reflected by SES (25). It is clear from studies of the international variation in mortality rates (27), the changing patterns with immigration to high incidence countries (28), and studies of external factors along the life course (3) that physical and social factors have strong and persistent influence on breast carcinogenesis. We were interested in exploring childhood SES as a reflection of these upstream factors related to the age of menarche.

We report here on a longitudinal study of the relationship of childhood SES to menarche in a diverse cohort across three urban areas of the United States between 2004 and 2015. The measurement of SES included several well accepted variables, and the outcome of age at menarche was documented by multiple maternal and child self-reports as were race/ethnicity with body mass index (BMI) measured at least annually in clinic. Our analysis is unique in including the effect of SES on both pubertal onset and tempo to menarche in the same girls.

METHODS

Study population

The Breast Cancer and the Environment Research Program (BCERP) was a consortium of three longitudinal studies to examine the effects of environmental exposures on pubertal onset because of its relationship to breast cancer risk. The details of the study design have been previously described and several analyses of the influence of developmental and chemical environmental factors have been published (5, 6, 29–31). Between 2004–2007, 1239 girls aged 6–8 years old were enrolled from the Greater San Francisco Bay Area, the

Greater Cincinnati Area, and East Harlem in New York City (hereafter referred to as San Francisco Area, Cincinnati, and New York City). Institutional Review Boards at each institution approved study procedures.

Questionnaires were completed annually during in-person interviews in California and New York sites, and semi-annually by self-administration for the first five years and then by interview in Cincinnati. Anthropometry measuring height and weight was performed annually in San Francisco and New York City and semi-annually in Cincinnati at the time of pubertal assessment (7). We report on an analysis that included 1,069 girls for which assessment of breast development, menarche, anthropometric measures, and questionnaire responses were obtained.

Socioeconomic status

SES factors were self-reported on the questionnaire by a parent, legal guardian, or primary caregiver with baseline data used for this analysis. SES measures included education of the mother (or the primary female guardian), household income, occupation of the primary financial provider, home ownership, and whether the household was led by a single female. Household income was measured as the total income of all wage earners in a household and was recorded as *<$25,000, $25-$50,000, $50-$100,000, or >$100,000 per year*, occupation of the primary financial provider was coded as *professional, non-manual, and manual;* and mother's education was recorded as ≤ *high school, some college, bachelor's degree, or* ≥ *master's degree* (7). Home ownership was recorded as *rent* or *other* and female head of household was a binary variable recorded as *yes* or *no*. An SES index that included measures of household income, mother's education, and home ownership was constructed constructed by standardizing each variable to mean zero and standard deviation one (i.e., subtracting the mean of the variable from the value of the variable for each girl and dividing by the standard deviation) and then summing the standardized values of the 3 variables (5). Occupation was excluded from the index because of a large number of missing values and because this variable did not change the predictive value of the index.

Breast development

Pubertal onset was measured via breast development using Tanner staging (3, 32) In an in-person clinic visit the standard Tanner five-stage classification scheme was used (7) for describing the onset and progression of breast changes by inspection (33) and palpation of the breast (15). Breast stage 2 (B2) or higher (B2+) was used for assignment of pubertal onset .

Menarche

Menarche was reported by a parent, legal guardian, or primary caregiver and confirmed participant self-reports (7). The parent was asked about the month and year, or age, that their daughter experienced her first menstrual period. Girls also provided a date of menarche during the annual questionnaire. Age at menarche was derived from an algorithm that gave primacy to the parental/guardian reported information which was available for most girls. Detailed methodology for assessing the age of menarche has been previously reported (7).

Covariates

Height and weight measurements were obtained at each clinic visit using calibrated scales and stadiometers by research staff that were trained and certified uniformly across all sites. BMI was calculated as weight in kilograms divided by squared height in meters. BMI percentiles were obtained for each participant from age and sex-specific growth charts from the Centers for Disease Control and Prevention for 2000 and were categorized as *<50, 50 to 85, and >=85* (34). Race/ethnicity was categorized as *black, Hispanic or Latina, Asian American, and white* following a hierarchical algorithm that made each race/ethnicity category mutually exclusive. Mother's self-reported age at menarche was categorized as follows: <12 years, 12–13 years, and ≥14 years (30).

Statistical analyses

Analyses were performed with SAS® (version 9.3 and 9.4, SAS Institute, Incorporated, Cary, North Carolina) using de-identified participant information. Participant characteristics were compared across sites using chi-square tests (Table 1). To evaluate the association of SES categories and covariates with age at menarche in comparison with age at onset of breast development, we created multiple event Cox regression models to estimate adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs); the models included strata for the two types of events, with risk of menarche beginning at age of onset of breast development (B2), and interactions between each predictor and event type. Each girl contributed 2 observations, one for each event, with risk of menarche beginning at age of onset of breast development (B2); a robust sandwich variance estimator was used to account for within-person correlation of observations. Because age at onset of breast development was interval censored (by exam visits), we interpolated within the observed interval during which B2+ was observed for each girl by taking the age corresponding to the midpoint of the cumulative probability of onset at the beginning and end of the interval according to a Weibull distribution estimated for each study site. Linear interpolation was used to estimate BMI % at the interpolated age using BMI% at endpoints of the observed B2 age interval (median length 1.0 year); for girls whose age at B2 before interpolation was left- or right-censored, BMI% at B2 was set to BMI% at the right or left end of the age interval, respectively. BMI% was included as a time-varying covariate in adjusted models, with childhood BMI% predicting age of pubertal onset as in our previous work (5), and BMI% at B2 predicting subsequent age at menarche. We first created unadjusted models to estimate the association of each predictor (SES variable or covariate) with age at menarche and onset of breast development (Table 2). We then created adjusted models including quintiles of the SES index along with (1) BMI% only and (2) BMI% and race/ethnicity to assess the mediating effect of BMI% on both outcomes (Table 3); we also performed a sensitivity analysis that adjusted for mother's age at menarche as well. Finally, we estimated race/ethnic-specific effects (Table 4) and site-specific effects (Table 5) by including interactions of each predictor with race/ethnicity or study site, respectively. Analogous models were created to estimate linear trends in SES quintiles (coded 1–5) treated as a numeric variable. Statistical significance was assessed at the 0.05 level (2-sided).

RESULTS

A total of 1,069 girls were in the analytic sample, 1,037 (97%) of whom contributed follow-up time between age at onset of breast development and age at menarche. Exclusions resulted for 32 girls because age of menarche (n=6) or censoring (n=26) occurred before the interpolated age of B2. At baseline the mean age was 7.3 years (standard deviation 0.7). The sample had a high degree of geographic, race/ethnic and socioeconomic diversity with some marked contrasts between sites. Girls from New York tended to come from lower income families; 56% of girls lived in households with an annual income of <$25,000 (Table 1). Fully 61.2% had mothers with less than or equal to a high school degree. In contrast, 71.6% of girls in the Cincinnati Area and 78.5% of girls in the San Francisco Area lived in a household with an annual income of over $50,000. Out of the three sites, the New York City site had the largest proportion of girls in the lowest quintile of SES—approximately 53% of this sample. The Cincinnati and San Francisco Area sites had similar distributions with regard to the SES index and had a larger number of girls in the 4^{th} and 5^{th} quintiles than New York. All girls from the New York City site were black (38.8%) or Hispanic (61.2%), by study design, while 38.3% of girls from the Cincinnati Area site and 45.5% of girls from the San Francisco Area site were either black or Hispanic. Lastly, the New York City site had the highest percentage of girls with a BMI greater than or equal to the 85^{th} percentile at baseline (38.8%) while Cincinnati and San Francisco sites had 29.1% and 29.5% of girls greater than or equal to the 85^{th} percentile respectively.

In unadjusted models, the SES index was predictive of earlier age at menarche in a low to high gradient across all quintiles (Table 2). This trend was significant ($p < .0001$) and similar to that of the SES index and age at breast stage B2 in the same girls ($p < .0001$). Girls with a BMI greater than or equal to the 85^{th} percentile and the 50^{th} to 85^{th} percentile at B2 had a significantly higher probability of experiencing an earlier onset of menarche than girls below the 50^{th} percentile (HR=2.31; 95% CI: 1.97–2.71 vs. HR=1.77; 95% CI: 1.52–2.05, respectively). An earlier onset of menarche was observed among Hispanic and, to a lesser extent, for Black girls compared to their white counterparts, HR=1.93 (95% CI: 1.66–2.24) and HR=1.57 (95% CI: 1.34–1.83), respectively. This association differed from pubertal onset, which was earlier in Black girls than Hispanic girls compared to White girls, HR=1.68 (95% CI: 1.43–1.96) and HR=1.24 (95% CI: 1.07–1.44), respectively. For each of the individual components of the SES index, earlier menarche was more prevalent among girls with the low SES values including lower annual household income, mothers with less than a high school degree, and living in rented homes. Lastly, girls whose mothers had earlier ages at menarche (<12 years) were also strongly likely to have earlier ages at menarche than girls whose mother's age at menarche was later (Table 2).

After adjustment for BMI% alone, lower SES remained a significant predictor of earlier pubertal onset and menarche. However, in the model adjusting for BMI% and race/ethnicity, the relationship between SES index and early onset of menarche was diminished and no longer statistically significant, although the trend in age at menarche was quite similar to the trend observed for onset of breast development (trend difference p= 0.087) (Table 3). Earlier menarche and age at B2 remained strongly related to higher BMI and both Black and Hispanic race/ethnicity. BMI% greater than or equal to the 85^{th} percentile was actually

associated with the highest risk for all race/ethnic groups. The most notable difference between the B2 and menarche results was that Hispanic girls were now significantly more likely to have earlier menarche after B2 (i.e., shorter tempo), even more so than Black girls. Results were similar with adjustment for mother's age at menarche (data not shown).

In the model with race/ethnic-specific effects (Table 4) SES was a significant predictor for the early onset of menarche among Hispanic girls (p for trend =0.011) but not for other race/ethnic groups. The SES index was a significant predictor for pubertal onset for both Hispanic and White girls (p <.0001 and .009, respectively), and again the general trend was similar for menarche compared to B2 in each ethnic group.

For models with site-specific effects (Table 5), there were no significant trends for the SES index and an earlier age of menarche at any site and for pubertal onset a significant trend only in San Francisco (p =.013). However, numbers of girls in each category in each site were small and HRs were therefore unstable.

DISCUSSION

Using an SES index consisting of household income, mother's education, and home ownership and adjusting for race/ethnicity and BMI% at two time points in development, we found a weak trend for a relationship between lower SES and earlier age of menarche, but one not significantly different from the previously observed stronger relationship between the SES index and onset of B2 in the same girls [4]. BMI% and race/ethnicity were each stronger predictors for the onset of menarche than the SES index when mutually adjusted.

Our results are consistent with but not as strong as other studies that have found associations between lower SES and earlier onset of menarche, which may be due at least in part to inconsistencies in the variables used to create an SES index. Similar to the present study, James-Todd et al. used an SES index consisting of household income, parental education, and parental occupation, while Braithwaite et al. created an SES index with only household income and parental education (9, 35). Deardorff et al. assessed separate measures of SES including grandfather's and grandmother's highest level of education and maternal prenatal healthcare (24). A standardized SES index may help mitigate these inconsistencies.

The relationship between race/ethnicity and onset of menarche is fairly consistent in the literature with Black and Hispanic girls experiencing an earlier onset of menarche than white girls (24, 35, 36), and our result that Hispanic and Black girls reached menarche earlier than white girls is consistent with existing literature.

BMI% was a stronger predictor of both pubertal onset and the age of menarche than the SES index used in the study. Specifically, girls with a BMI greater than or equal to the 85th percentile had the highest risk of both early pubertal onset and earlier age of menarche among Black, Hispanic, and white girls. Extensive literature has documented the relationship between an increased prevalence of obese adolescent girls and a decrease in the age of pubertal onset. Our data are consistent with lower childhood SES being a driver of both higher BMI and earlier pubertal onset. This relationship should be further explored as

interventions to improve diets and prevent obesity in children may reduce the risk of earlier onset of menarche and adverse outcomes in adulthood including breast cancer.

This study has several strengths, including the prospective design and routine follow-up using annual surveys and physical examinations. Additionally, the cohort was racially and socioeconomically diverse and, in contrast to earlier studies, included both Hispanic and Asian American girls. Uniquely, we were able to compare the relationship of SES to pubertal onset as measured by Tanner Stage B2 as well as to menarche in the same girls. One limitation, however, was that that the SES quintiles across the three sites were unbalanced, with New York City containing more girls in the lowest quintiles and no girls of white race and San Francisco and Cincinnati containing more girls in the highest quintiles. This could not be remedied since the original designs were established at the three sites separately and significant modifications in sampling frames were not feasible after the study commenced. In addition, changes in girls' SES over time were not measured. Onset of menarche was self-reported, but we noted little difference between reporting from mothers/guardians and girls about girls' first experience of menses, as previously described in a study by Biro et al (7).

In conclusion, we found a relationship of a lower SES index to an earlier age of menarche that was much diminished and not statistically significant after adjusting for BMI% and race/ethnicity. However, as documented in the earlier study (5) SES was more clearly related to pubertal onset, as measured by breast development, in the same girls even after adjustment for BMI% and race/ethnicity. In a sense then, the additional time added by tempo added little to the relationship between SES and pubertal onset in these girls. We thus speculate that SES is related to factors that have a stronger influence on pubertal onset at a neuroendocrine level than on menarche as described in the Introduction. Also, interestingly, but unexplained, the age of menarche seems more sensitive to SES-related factors at the time of puberty in Hispanic girls than to those in other race/ethnic groups, including black girls. Future studies should distinguish between pubertal onset and the age of menarche to further clarify this relationship and to determine mechanisms through which SES influences menarche. It is plausible that SES works through exposure to environmental toxins (particularly endocrine disrupting chemicals), the lack of material resources or stress related factors associated with social disadvantage. Finally, these data as well as those from other recent studies suggest that the well-established relationship between higher SES and breast cancer onset (3, 28) may be changing with time in developed countries. Insofar as it is related to an earlier age at pubertal onset and menarche it will be contributing to a longer period of time during which women are exposed to circulating estrogens(2). This possible trend should be monitored and studied further.

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Abbreviations

B2	breast stage 2
BMI	body mass index
CIs	confidence intervals
HR	hazard ratio
SES	socioeconomic status

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Implications:

Girls from families of lower SES are likely to experience earlier onset of puberty, not menarche, independent of the effect of prepubertal obesity and race/ethnicity. A better understanding is needed of the effects on early pubertal development of environmental, material and stress related factors associated with social disadvantage.

Table 1:

Characteristics of a sample of 1069 girls aged 6–8 years at baseline by study site for household socioeconomic status (SES) variables, girl's race/ethnicity, girl's body mass index percentile (BMI%) at baseline, BMI% at onset of breast development (B2), and mother's age at menarche in the Breast Cancer and the Environment Research Program (BCERP), 2004–2015.

Variable	New York City (East Harlem) (n=348), n (%)	Cincinnati Area (n=290), n (%)	San Francisco Area (n=431), n (%)	All (n=1069), n (%)	Chi-Square Value
SES Index					445.0127
Quintile 1 (Lowest)	160 (53.0)	14 (6.3)	18 (4.3)	192 (20.4)	
Quintile 2	96 (31.8)	25 (11.2)	60 (14.5)	181 (19.3)	
Quintile 3	40 (13.2)	54 (24.1)	89 (21.5)	183 (19.5)	
Quintile 4	5 (1.7)	70 (31.3)	114 (27.5)	189 (20.1)	
Quintile 5	1 (0.3)	61 (27.2)	133 (32.1)	195 (20.7)	
Total	302	224	414	940	
Missing	46	66	17	129	
Household Income					419.5782
<$25,000	181 (56.0)	26 (10.9)	22 (5.2)	229 (23.2)	
$25–50,000	100 (31.0)	42 (17.6)	69 (16.3)	211 (21.4)	
$50–100,000	38 (11.8)	96 (40.2)	149 (35.1)	283 (28.7)	
≥100,000	4 (1.2)	75 (31.4)	184 (43.4)	263 (26.7)	
Total	323	239	424	986	
Missing	25	51	7	83	
Education of Mother					268.2164
≤ High School	200 (61.2)	25 (9.5)	76 (18.0)	301 (29.7)	
Some College or Vocational	90 (27.5)	101 (38.5)	124 (29.3)	315 (31.1)	
Bachelor's Degree	26 (8.0)	89 (34.0)	133 (31.4)	248 (24.5)	
Master's Degree or Higher	11 (3.4)	47 (17.9)	90 (21.3)	148 (14.6)	
Total	327	262	423	1012	
Missing	21	28	8	57	
Occupation of Primary Financial Provider					
Manual	136 (47.7)	40 (15.9)	50 (11.7)	226 (23.5)	155.6269
Non-Manual	111 (38.9)	102 (40.5)	199 (46.7)	412 (42.8)	
Professional	38 (13.3)	110 (43.7)	177 (41.5)	325 (33.7)	

Variable		New York City (East Harlem) (n=348), n (%)	Cincinnati Area (n=290), n (%)	San Francisco Area (n=431), n (%)	All (n=1069), n (%)	Chi-Square Value
	Total	285	252	426	963	
	Missing	63	38	5	106	
Home Ownership						
	Rent	329 (94.8)	54 (21.7)	120 (28.0)	503 (49.1)	441.6435
	Other	18 (5.2)	195 (78.3)	309 (72.0)	522 (50.9)	
	Total	347	249	429	1025	
	Missing	1	41	2	44	
Female Head of Household						34.1569
	Yes	100 (28.7)	48 (17.6)	53 (12.3)	201 (19.1)	
	No	248 (71.3)	224 (82.4)	378 (87.7)	850 (80.9)	
	Total	348	272	431	1051	
	Missing	0	18	0	18	
Girl's Race/Ethnicity						454.2298
	White	0 (0.0)	175 (60.3)	184 (42.7)	359 (33.6)	
	Black	135 (38.8)	100 (34.5)	93 (21.6)	328 (30.7)	
	Hispanic	213 (61.2)	11 (3.8)	103 (23.9)	327 (30.6)	
	Asian	0 (0.0)	4 (1.4)	51 (11.8)	55 (5.1)	
	Total	348	290	431	1069	
	Missing	0	0	0	0	
Girl's BMI (at Baseline) BMI%						12.6203
	BMI >85th Percentile	135 (38.8)	84 (29.1)	127 (29.5)	346 (32.4)	
	BMI 50–84th Percentile	114 (32.8)	94 (32.5)	159 (36.9)	367 (34.4)	
	BMI <50th Percentile	99 (28.4)	111 (38.4)	145 (33.6)	355 (33.2)	
	Total	348	289	431	1068	
	Missing	0	1	0	1	
Girl's BMI (at B2) BMI%						14.2263
	BMI >85th Percentile	144 (41.7)	89 (30.9)	130 (30.2)	363 (34.1)	
	BMI 50–84th Percentile	102 (29.6)	91 (31.6)	146 (33.9)	339 (31.9)	
	BMI <50th Percentile	99 (28.7)	108 (37.5)	155 (36.0)	362 (34.0)	
	Total	345	288	431	1064	
	Missing	3	2	0	5	

Variable	New York City (East Harlem) (n=348), n (%)	Cincinnati Area (n=290), n (%)	San Francisco Area (n=431), n (%)	All (n=1069), n (%)	Chi-Square Value
Mother's Age at Menarche					5.2366
<12 Years Old	97 (29.3)	63 (23.3)	101 (23.7)	261 (25.4)	
12 to 13 Years Old	159 (48.0)	151 (55.9)	227 (53.3)	537 (52.3)	
>=14 Years Old	75 (22.7)	56 (20.7)	98 (23.0)	229 (22.3)	
Total	331	270	426	1027	
Missing	17	20	5	42	

Note: p<.0001 for cross-site comparison of all variables tabulated except BMI % (baseline: p=0.0133; B2: p=0.0066). and mother's age at menarche (p=0.26)

Table 2:

Unadjusted associations (hazard ratios and 95% CIs) of SES index, BMI%, race/ethnicity, site, household income, education of mother, household ownership and mother's age at menarche with age of onset of breast development and age at menarche in the BCERP, 2004–2015.

Variable	Age at Breast Stage B2			Age at Menarche		
	HR	95% CI	p-value	HR	95% CI	p-value
SES Index (n_{B2}=940, n=912)						
Quintile 1 (Lowest)	1.60	1.33–1.94	<.0001	1.84	1.49–2.27	<.0001
Quintile 2	1.68	1.37–2.05	<.0001	1.73	1.41–2.12	<.0001
Quintile 3	1.39	1.16–1.68	.0004	1.52	1.25–1.85	<.0001
Quintile 4	1.19	0.99–1.42	.067	1.23	1.03–1.47	.025
Quintile 5 (ref)	1			1		
BMI% (n_{B2}=1068, n=1033)						
≥85th	2.15	1.83–2.53	<.0001	2.31	1.97–2.71	<.0001
50th to <85th	1.37	1.19–1.57	<.0001	1.77	1.52–2.05	<.0001
<50th (ref)	1			1		
Race/Ethnicity (n_{B2}=1069, n=1037)						
Black	1.68	1.43–1.96	<.0001	1.57	1.34–1.83	<.0001
Hispanic	1.24	1.07–1.44	.004	1.93	1.66–2.24	<.0001
Asian	0.80	0.62–1.03	.077	1.13	0.89–1.43	.307
White (ref)	1			1		
Site (n_{B2}=1069, n=1037)						
New York City	1.62	1.41–1.86	<.0001	1.45	1.24–1.68	<.0001
Cincinnati Area	1.72	1.45–2.02	<.0001	0.97	0.84–1.11	.650
San Francisco Area	1			1		
Household Income (n_{B2}=986, n=958)						
<$25,000	1.53	1.29–1.80	<.0001	1.61	1.34–1.93	<.0001
$25–50,000	1.71	1.42–2.07	<.0001	1.72	1.42–2.07	<.0001
$50–100,000	1.30	1.11–1.52	.001	1.24	1.06–1.45	.006
≥100,000 (ref)	1			1		
Education of Mother (n_{B2}=1012, n=980)						
≤ High School	1.32	1.09–1.60	.005	1.57	1.30–1.91	<.0001

Variable	Age at Breast Stage B2			Age at Menarche		
	HR	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Some College or Vocational	1.32	1.10–1.59	.003	1.39	1.16–1.67	.0004
Bachelor's Degree	1.06	0.88–1.28	.526	1.04	0.87–1.24	.687
Master's Degree or Higher (ref)	1			1		
Home Ownership (n_{B2}=1025, n=994)						
Rent	1.33	1.18–1.51	<.0001	1.44	1.27–1.63	<.0001
Other (ref)	1			1		
Mother's Age at Menarche (n_{B2}=1027,n=996)						
<12 Years Old	1			1		
12 to 13 Years Old	0.84	0.72–0.98	.029	0.74	0.64–0.85	<.0001
>=14 Years Old	0.70	0.58–0.85	.0002	0.58	0.49–0.69	<.0001

Note: The SES Index trend was significant at p<.0001 for both age at pubertal onset and age at menarche and there was no difference in the trends (p=0.24)

Table 3:

Associations (hazard ratios and 95% confidence intervals) of the SES index, adjusted for (1) BMI% only and (2) BMI% and race/ethnicity, with age of onset of breast development and age at menarche in the BCERP, 2004–2015.

	Model 1						Model 2					
Variable	***Age at Breast Stage B2 (n=939)***			***Age at Menarche (n=908)***			***Age at Breast Stage B2 (n=939)***			***Age at Menarche (n=908)***		
	HR	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
SES Index												
Quintile 1 (Lowest)	1.56	1.29–1.90	<.0001	1.62	1.31–2.01	<.0001	1.48	1.15–1.89	.002	1.17	0.91–1.51	.230
Quintile 2	1.63	1.34–1.98	<.0001	1.46	1.19–1.80	0.0002	1.40	1.10–1.78	.007	1.13	0.90–1.42	.307
Quintile 3	1.34	1.10–1.64	.004	1.31	1.06–1.61	0.011	1.28	1.04–1.58	.020	1.09	0.88–1.35	.456
Quintile 4	1.14	0.93–1.39	.209	1.12	0.94–1.34	0.212	1.11	0.91–1.35	.318	1.07	0.89–1.28	.481
Quintile 5 (ref)	1			1			1			1		
BMI%												
>=85	2.15	1.82–2.54	<.0001	2.21	1.86–2.64	<.0001	2.23	1.89–2.64	<.0001	2.12	1.77–2.52	<.0001
50 to <85	1.42	1.21–1.66	<.0001	1.76	1.50–2.07	<.0001	1.45	1.24–1.69	<.0001	1.77	1.51–2.08	<.0001
<50 (ref)	1			1			1			1		
Race/Ethnicity												
Black	--	--	--	--	--	--	1.39	1.13–1.69	.001	1.41	1.16–1.71	.0006
Hispanic	--	--	--	--	--	--	0.92	0.74–1.13	.425	1.59	1.28–1.98	<.0001
Asian	--	--	--	--	--	--	0.85	0.63–1.15	.292	1.22	0.93–1.59	.156
White (ref)	--	--	--	--	--	--	1			1		

Table 4:

Association (HR + 95% CI's) of SES Index with onset of breast development and age at menarche by race/ethnicity, BCERP 2004–2015.

	Age at Breast Stage B2 (n=939)				Age at Menarche (n=908)			
	Black	***Hispanic***	***Asian***	***White***	***Black***	***Hispani***	***Asianc***	***White***
	HR (95% CI)	***HR (95% CI)***	***HR (95% CI)***	***HR (95% CI)***	***HR (95% CI)***	***HR (95% CI)***	***HR (95% CI)***	***HR (95% CI)***
SES Index								
Quintile 1 (Lowest)	1.32 (0.68–2.58)	1.79 (1.15–2.80)			0.95 (0.61–1.48)	1.23 (0.80–1.89)		
Quintile 2	1.28 (0.66–2.49)	1.96 (1.22–3.13)		1.82 (1.11–2.99)	1.19 (0.81–1.74)	1.10 (0.69–1.77)		1.01 (0.62–1.65)
Quintile 3	1.73 (0.86–3.47)	1.05 (0.63–1.74)	1.35 (0.69–2.63)	1.25 (0.95–1.64)	1.50 (0.97–2.31)	0.72 (0.43–1.20)	1.09 (0.61–1.96)	1.20 (0.86–1.66)
Quintile 4	1.72 (0.86–3.45)	0.70 (0.36–1.37)	0.69 (0.36–1.34)	1.18 (0.94–1.49)	1.38 (0.92–2.08)	0.82 (0.47–1.45)	0.69 (0.39–1.21)	1.11 (0.88–1.39)
Quintile 5 (ref)	1	1	1	1	1	1	1	1
p-value for trends	0.448	<.0001	0.477	0.009	0.118	0.011	0.864	0.342
BMI%								
>=85th	3.33 (2.39–4.64)	2.23 (1.68–2.97)	1.82 (0.61–5.46)	1.61 (1.22–2.12)	2.47 (1.76–3.47)	2.11 (1.56–2.84)	1.65 (0.65–4.19)	2.12 (1.61–2.79)
50 to <85th	1.77 (1.31–2.41)	1.28 (0.91–1.79)	0.87 (0.52–1.45)	1.52 (1.23–1.90)	2.25 (1.64–3.09)	1.80 (1.27–2.56)	1.45 (0.84–2.48)	1.69 (1.33–2.14)
<50% (ref)	1	1	1	1	1	1	1	1

Table 5:

Association (HR + 95% CI's) of SES Index by Study Site location adjusted for BMI% and race/ethnicity for onset of breast development and age at menarche, BCERP 2004–2015.

	Age at Breast Stage B2						*Age at Menarche*					
	New York City		**Cincinnati Area***		**San Francisco Area**		**New York City**		**Cincinnati Area***		**San Francisco Area**	
	HR	***95% CI***	***HR***	***95% CI***	***HR***	***95% CI***	***HR***	***95% CI***	***HR***	***95% CI***	***HR***	***95% CI***
SES Index												
Quintile 1 (Lowest)	0.89	0.65–1.22	0.85	0.43–1.70	1.68	1.09–2.61	0.89	0.59–1.33	1.42	0.82–2.46	1.31	0.76–2.26
Quintile 2	1.13	0.81–1.57	0.58	0.29–1.15	1.38	0.97–1.97	1.07	0.71–1.64	0.84	0.50–1.42	1.12	0.79–1.59
Quintile 3	-		1.45	0.88–2.37	1.12	0.87–1.45	-		1.31	0.90–1.89	1.01	0.74–1.38
Quintile 4	-		1.41	0.94–2.13	0.99	0.79–1.25	-		1.14	0.81–1.59	1.02	0.81–1.30
Quintile 5 (ref)	1		1		1		1		1		1	
p-value for trend	0.998		0.297		0.013		0.371		0.731		0.397	
BMI%												
>=85	3.74	2.77–5.04	5.12	3.36–7.80	1.47	1.17–1.85	2.13	1.56–2.92	2.42	1.74–3.36	2.09	1.61–2.72
50 to <85	1.72	1.26–2.36	2.70	1.86–3.92	1.19	0.97–1.47	2.31	1.63–3.27	2.41	1.77–3.28	1.43	1.15–1.78
<50 (ref)	1		1		1		1		1		1	
Race/Ethnicity												
Black	1.06	0.82–1.36	2.37	1.57–3.56	1.73	1.32–2.27	0.55	0.41–0.74	1.95	1.41–2.69	1.57	1.19–2.07
Hispanic	1'		-		0.89	0.69–1.16	1		-		1.20	0.88–1.63
Asian	-		-		1.06	0.77–1.45	-		-		1.12	0.82–1.52
White	-		1		1		-		1		1	

• Asians and Hispanics were not included for Cincinnati Area due to small numbers