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Individual- and Neighborhood- Socioeconomic Status and Risk of Aggressive Breast Cancer Subtypes in a Pooled Cohort of Women From Kaiser Permanente Northern California

SES and Breast Cancer Subtypes

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Precis: Low nSES and individual-level education are independent predictors of more aggressive BC subtypes relative to LumA.

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Abstract

Background

Low socioeconomic status (SES) has been associated with higher risk of aggressive breast cancer (BC) subtypes but few studies have examined the independent effects of both neighborhood- and individual-level SES measures.

Methods

This study included 5,547 women from the Pathways and Life After Cancer Epidemiology (LACE) cohorts who were diagnosed with invasive BC. We used generalized estimating equation models to examine associations between neighborhood-level SES (composite score based on income, poverty, education, occupation, employment, rent, and house value) and individual-level SES (income, education) with BC subtype: Luminal B, Her2-enriched, and triple negative breast cancer relative to Luminal A. Models controlled for age, race, nativity, stage, days from diagnosis to survey, study cohort and simultaneously for neighborhood- and individual-level SES.

Results

In fully adjusted models, low neighborhood SES was significantly associated with the LumB (OR_{Q1vQ4}=1.31, 95% CI:1.11-1.54, p-trend=0.005) and TNBC subtypes (OR_{Q1vQ4}=1.32, 95% CI: 1.02-1.71, p-trend=0.037), relative to LumA. Conversely, individual education was significantly associated with only the Her2-e subtype (OR_{Q1vQ4}=1.68, 95% CI: 1.03-2.75, p-trend=0.030) relative to LumA. Individual income was not significantly associated with any BC subtype.

Conclusion

Neighborhood- and individual-level SES were independently associated with different BC subtypes; specifically, low nSES and individual-level education are independent predictors of more aggressive BC subtypes relative to LumA.

Introduction

Breast cancer (BC) is often classified into four intrinsic subtypes with unique gene expression profiles, often approximated by the expression of Her2 and the status of two hormone-receptors (HR), estrogen receptor (ER) and progesterone receptor (PR).[1–3] The use of IHC markers plus Ki-67 or a surrogate marker of cell proliferation such as tumor grade also improves the accuracy of approximating BC subtypes, reducing misclassification of the LumA and LumB subtypes.[3,4] The four BC subtypes from least to most aggressive are: Luminal A ($ER^+/PR^+/Her2^-$ and well/moderately differentiated), Luminal B ($ER^+/Her2^+$ or $ER^+/Her2^-$ and PR^- or poorly differentiated/undifferentiated), Her2-expressive ($ER^-/PR^-/Her2^+$), and TNBC ($ER^-/PR^-/Her2^-$).[5]

Women of lower socioeconomic status (SES) have a higher incidence of HR- subtypes compared with women of higher SES.[6–8] Most prior work has focused on the effects of neighborhood-level SES (nSES) on BC subtypes; women of higher nSES have had lower, whereas women of lower nSES have had higher, odds of HR- BC.[2,6–12] Commonly used nSES measures based on census data reflect both contextual (i.e. neighborhood-level) and compositional (i.e. individual-level) effects. Both nSES and individual-SES must be simultaneously examined to understand their independent effects, however few prior studies have taken this approach. Sineshaw created a composite SES variable using neighborhood-level income and individual-level insurance, and found that women with low SES had higher odds of HR- subtypes[13]; however, independent effects of neighborhood- and individual-level SES could not be ascertained from this study. Qin et al investigated the independent effect of nSES by adjusting for individual education, poverty level, and type of insurance, and found that Black women of lower SES had higher risk for TNBC relative to LumA.[14]

Despite the heterogeneity of SES measures, sample size, and data sources, the data suggest that women living in areas characterized as lower SES are more likely to be diagnosed with more aggressive BC subtypes.[2,7–13] To our knowledge, no studies have examined the independent effects of neighborhood- and individual-level SES on all major BC subtypes. Therefore, we investigated associations between multilevel SES and BC subtypes relative to LumA, combining data from two studies for a total of 5,547 racially diverse BC patients recruited from the Kaiser Permanente Northern California (KPNC) population.

METHODS

Study Population

This study included BC survivors from the Pathways and Life After Cancer Epidemiology (LACE) cohorts. The Pathways cohort included 4,505 women recruited from KPNC between 2006-2013 who were at least 21 years old, diagnosed between 2005-2013 with invasive BC, had no history of cancer, spoke English, Spanish, Cantonese, or Mandarin, and lived within 65-miles of a field interviewer.[15] The LACE cohort included 2,263 women recruited primarily from KPNC (82%) between 2000-2002 who were ages 18-79 years at diagnosis, diagnosed between 1997-2000 with early-stage BC (stage I, II, or IIIA) within 39 months of enrollment, had no history of other cancer 5 years prior to enrollment, completed BC treatment, and had no evidence of recurrence at enrollment.[16] The Pathways survey was administered by an interviewer at an in-person interview. The LACE participants responded to a mailed, self-administered survey. In each cohort, women responded to questions on individual-level education and income. Additional details of the Pathways and LACE cohorts have been previously reported.[15,16]

For women from Pathways, current address at baseline was identified using census data which were already linked to 2010 geocodes. For women from LACE, address at baseline was obtained from the EHR, with missing addresses obtained from the following sources listed in order of preference: study database, paper survey, EHR within 2 years after baseline, cancer registry within 2 years after baseline, EHR within 2 years before baseline, and cancer registry within 2 years before baseline. The LACE addresses were geocoded in ArcGIS at the point address or street address levels, and the resulting coordinates were assigned to Census 2000 block groups and census tracts.

Women from the LACE study who were not recruited at KPNC were excluded due to lack of access to medical records (N=389). Women were excluded in a stepwise process if they had missing or incomplete immunohistochemistry (IHC) information (N=511), were missing data on individual education (N=12), neighborhood SES (N=155), zip code (N=117), or other covariates (N=37), were excluded from this analysis. The final study cohort included 4,079 women from the Pathways cohort and 1,468 women from the LACE cohort for a total of 5,547 women.

Study Variables

Breast cancer tissue markers and subtypes

Information on Her2 expression, hormone receptor status (ER and PR), and tumor grade was obtained from the KPNC Cancer Registry or through medical record review. We used the 2013 St. Gallen BC subtyping with grade in lieu of Ki-67 to categorize BC into four subtypes: Luminal A ($ER^+/PR^+/Her2^-$ and well/moderately differentiated), Luminal B ($ER^+/Her2^+$ or $ER^+/Her2^-$ and PR^- or poorly differentiated/undifferentiated), Her2-expressive ($ER^-/PR^-/Her2^+$), and TNBC ($ER^-/PR^-/Her2^-$).

Socioeconomic status

Individual-level SES

Individual-level education and income were used to measure individual-level SES.

In Pathways, women indicated their highest level of education from the following options: less than 8th grade, 8th to 11th grade, high school graduate or equivalent (GED), vocational or trade school, some college, college graduate, or post-graduate. In LACE, women indicated how many years of school they completed from the following options: 1-11 years, 12 years (high school graduate), 13-15 years (some college or technical school), 6 years (college graduate), and some graduate school or advanced degree. For our analyses, we generated a 4-level individual education variable with the following categories: high school degree or less, some college, college degree, and post-graduate. Women in the post-graduate category comprised the reference group.

In Pathways, women indicated total household income at the time of study enrollment using the following options: Less than $15,000, $15,000 to $19,999, $20,000 to $24,999, $25,000 to $34,999, $35,000 to $49,999, $50,000 to $69,999, $70,000 to $89,999, and $90,000 or more. In LACE, baseline income data were not available, however, income data were available from a follow-up questionnaire collected on average 5.2 years after baseline. Women indicated their household income in the last year, using the following options: less than $20,000, $20,000 to $39,999, $40,000 to $59,999, $60,000 to $79,000, $80,000 to $99,999, and $100,000 or more. Given differences in response options and in years of income ascertainment, we created cohort-specific income tertiles to enable harmonization of this variable. Women in the highest tertile (highest income) comprised the reference group.

Neighborhood-level SES

Neighborhood socioeconomic status (nSES) at the block group level was operationalized using a previously described and widely-used composite nSES score derived from principal components analysis, which utilized data from the 2000 Census (for cases enrolled prior to 2006) and 2006-2010 American Community Survey data (for cases enrolled in 2006 and onward).[17] The score was based on the following 7 components: income, poverty, education, occupation, employment, rent, and house value. Due to differences in census years in our dataset, a continuous measure of nSES could not be evaluated in this study. Therefore, study-specific score-based quartiles were created, then pooled in the final dataset ("pooled quartiles"). As a secondary measure, nSES quartiles by census year were created based on the statewide distribution of nSES scores in California ("state-based quartiles").

A heatmap of nSES in the KPNC service area was created based on the state-based quartiles of nSES (Figure 1). The map was created using KP Maps, an online geographic information system hosted by Kaiser Permanente.

Other covariates

Information on age, race, and nativity were self-reported at baseline. Consistent with prior studies, covariates included age at diagnosis, race (NLW, Black, Latina, Asian, or other race), nativity (foreign-born or U.S.-born), study (Pathways or LACE), days from diagnosis to study enrollment, and stage at diagnosis (stages I through IV). Age, race, nativity, and stage were selected a priori as potential confounding variables; we adjusted for study and days from diagnosis to study enrollment to address potential sampling differences between cohorts.

Statistical Analysis

We used generalized estimating equation (GEE) models to compute adjusted odds ratios (ORs) for each BC subtype (relative to LumA), while accounting for clustering by zip code using

an exchangeable correlation structure for the working covariance. We considered alternative clustering models (generalized linear mixed models with logit link) with clustering at the census block group or tract level, however 85% of block groups and 52% of tracts in this study contained only 1-2 women. We chose zip codes to account for clustering as 25% of zip codes in our study contained 1-2 women, with 75% of zip codes containing >2 women. GEE models were used because parameter estimates are robust to any underlying neighborhood correlation structure that may be present.[18] In age-adjusted models, we separately examined bivariate associations between neighborhood- and individual-level SES variables and BC subtype, adjusting for age at diagnosis. In Model 1, we additionally adjusted for race, nativity, study, days from diagnosis to study enrollment, and stage at diagnosis. Model 2 additionally included either nSES or individual education and income. Model 3 is included only in Table 4 (associations for individual education), which additionally adjusted for individual income. Pair-wise correlations for neighborhood- and individual- SES predictors revealed weak correlations ($r<0.25$), allowing for simultaneous inclusion in final models.

To assess heterogeneity by study cohort, we computed the Q-statistic comparing the study-specific effects for the fully adjusted models. When the Q-statistic indicated statistically significant heterogeneity, we reported study-specific findings.

To determine if reproductive factors might help to explain associations of nSES (pooled quartiles) with BC subtype, we additionally evaluated models adjusted for parity (continuous) and breastfeeding (ever/never) which were available for 99.8% of the women in our dataset. Models included covariates from 'Model 2' plus parity and breastfeeding.

Results

In pooled data, neighborhood SES differed by age, race/ethnicity, stage, state-based nSES quartile, individual education, and individual income (Table 1). The highest nSES quartile included higher proportions of NLW (76%) and Asian women (13%), and lower proportions of Black (2%) and Latina women (7%), relative to the lowest nSES quartile (NLW-58%, Asian-9%, Black-15%, and Latina-15%). Women from higher nSES areas had higher levels of individual education and income, consistent with the notion that nSES is in part determined by the composition of its inhabitants.

Study cohorts differed by days from diagnosis to baseline, race/ethnicity, nativity, BC subtype, state-based nSES quartile, individual education, and individual income (Supplementary Table 1). The LACE study enrolled a higher proportion of NLW women (78.2% vs 64.0% in Pathways), and women residing in the highest state-based nSES quartile (46.9% vs. 40.4%). The Pathways study enrolled a higher proportion of foreign-born women (20.9% vs. 14.2% in LACE), women with higher educational attainment (college degree or higher 49.3% vs. 34.1% in LACE), and women in the highest individual income tertile (31.3% vs 20.6% in LACE).

In the map of state-based nSES quartiles in the KPNC region (Figure 1), areas of higher nSES (lighter shade) tended to occur in more urbanized areas (San Francisco, Oakland, San Jose) and areas located on the coast. Areas of lower nSES (darker shade) were typically more inland and in relatively rural areas (Fresno, Modesto, Stockton).

Lower nSES as defined by the pooled quartile was associated with higher odds of all three BC subtypes relative to LumA in age-adjusted models (Table 2). Adjustment for potential confounders (Model 1) attenuated effects for all three subtypes, and the association for Her2-e was no longer statistically significant. Adjustment for individual-SES (Model 2) further attenuated effect estimates for Her2-e and slightly attenuated them for TNBC. In the fully

adjusted model, associations remained significant for LumB (OR_{Q1vQ4}=1.31, 95% CI: 1.11-1.54, p-trend=0.005) and TNBC (OR_{Q1vQ4}=1.32, 95% CI: 1.02-1.71, p-trend=0.037). In analyses adjusted additionally for history of breastfeeding and parity, neither parity nor breastfeeding was associated with LumB, but parity was associated with Her2e (OR=1.19, 95% CI: 1.09, 1.30 p-continuous<0.001), and both parity (OR=1.10, 95% CI: 1.03, 1.18 p-continuous=0.006) and never breastfeeding (OR=1.32, 95% CI: 1.08, 1.62 p=0.007) were associated with TNBC. Nevertheless, adjusting additionally for breastfeeding and parity did not qualitatively alter the ORs for the associations of nSES with BC subtype (data not shown). We found no evidence for heterogeneity by study cohort in these analyses.

Similarly, lower nSES as defined by the state-based quartile was associated with higher odds of all three BC subtypes relative to LumA in age-adjusted models (Table 3). Adjustment for potential confounders (Model 1) and individual-SES (Model 2) attenuated effect estimates for the Her2-e and TNBC subtypes. In Model 2, though effects were highest in Q2, we noted a statistically significant association between nSES and LumB (p-trend=0.031). Again, we found no evidence for heterogeneity by study cohort.

Lower individual education was associated with higher odds of the Her2-e and TNBC subtypes relative to LumA, in age- and multivariate-adjusted models (Table 4). Adjustment for nSES (Model 2) slightly attenuated the association with the Her2-e and TNBC subtypes. Additional adjustment for individual income (Model 3) did not further attenuate associations, however, the association remained significant for only Her2-e (OR_{Q1vQ4}=1.68, 95% CI: 1.03-2.75, p-trend=0.030). The Q-statistics for associations with LumB and Her2-e suggested study heterogeneity, therefore study specific associations are presented.

Lower individual income was not significantly associated with any BC subtype in covariate-adjusted analyses (data not shown).

Discussion

In a large cohort of breast cancer survivors in Northern California, we evaluated the associations between neighborhood- and individual-level socioeconomic status and BC subtypes. In models simultaneously adjusted for individual- and neighborhood-level SES, pooled SES was associated with LumB and TNBC, state-based nSES was only associated with LumB, and individual education was only associated with Her2-e. Individual income was not associated with BC subtype in any fully adjusted model. Our findings suggest that both lower nSES and individual education are important predictors of aggressive BC subtypes relative to the least aggressive LumA subtype, reflecting either a relatively lower incidence of LumA or higher incidence of HR- BC. To our knowledge, our study is the first study of multilevel SES and all BC subtypes.

Previous studies evaluating the relationship between SES and BC subtypes indicate a positive association between low nSES and more aggressive BC subtypes. Most prior studies utilized cancer registry data and were not able to account for individual-SES. In studies utilizing California Cancer Registry data, women who lived in areas of higher median household income had lower odds of TNBC[6], whereas women of lower nSES (measured as a composite index score) were overrepresented in Her2-e and TNBC[7,9], and Hispanic women of lower nSES had increased risk of TNBC and Her2-e.[10] In studies utilizing SEER data, women diagnosed with BC subtypes other than HR+/Her2- were more likely to live in impoverished counties[2], whereas women living in high poverty areas had higher odds of TNBC[12], women living in a medium- or high-poverty county had higher risk of HR- BC[8], and women of higher nSES had higher risk of

HR+ BC subtypes[11]. Despite the heterogeneity in methods including SES measures, sample size, and data sources, most studies show that women living in areas characterized by lower SES are more likely to be diagnosed with more aggressive BC subtypes relative to LumA.[2,7–13] Our findings are consistent with prior work but provide further evidence of contextual influences independent of the individual influences of income and education.

Mechanisms purported to explain the association between SES and BC subtypes include reproductive and environmental factors, and chronic stress. Reproductive factors like parity, breast feeding, time from menarche to first pregnancy, age at first birth, and oral contraceptive use have each been shown to be differentially associated with BC subtypes.[19–22] Over the past several decades, the availability of hormonal contraceptives and an increasing number of women entering the workforce have delayed age at first birth, particularly among women with greater educational attainment.[23–25] A 2014 literature review found moderate to strong evidence that nulliparity or low parity, a long interval between menarche to first pregnancy, and higher age at first birth were all associated with higher risk of HR+ BC.[19] Other studies found that parous women who never breast fed had elevated risk of HR- BC[20,21] and breast feeding was associated with lower risk of TNBC[22]. As women with higher levels of education tend to delay childbearing and have lower parity, their risk increases for HR+ BC.[19] Conversely, women of lower SES and with less education are less likely to use contraception, more likely to be younger at first birth, and have higher parity with lower rates of breastfeeding, all of which increase risk of HR- BC.[19,23] Consistent with individual SES trends, low nSES is also predictive of increased adolescent pregnancy and birthrate, decreased contraceptive use,[26] and lower rates of breast feeding[27]. Low nSES can affect reproductive behaviors, especially in adolescent women, through implicit social norms shaping attitudes around reproductive behavior, and the perception of few

opportunities for upward social mobility resulting in lower perception of costs associated with unplanned pregnancy.[28] Nonetheless, in multivariable models additionally adjusted for history of breastfeeding (ever/never) and parity, ORs for the associations of nSES with BC subtype were unchanged (data not shown).

Environmental exposures may also contribute to findings. Areas of lower SES and higher concentration of ethnic minorities tend to have higher exposure to air pollutants, hazardous jobs, and deteriorating housing.[29] Previous studies have linked environmental exposures to BC[30], and a recent study has shown that heavy metal air pollutants can increase the risk of some BC subtypes.[31]

The psychological environment may also differentially influence BC subtypes.[32] Women of low SES tend to be exposed to chronic stress related to financial insecurity, discrimination, and lack of safety. Chronic stress may suppress production of estrogen, which may increase the risk of aggressive BC types.[32] Chronic stress may also lead to unhealthy behavioral coping through poorer diet and reduction in physical activity leading to obesity, which is a risk factor of HR- BC in pre-menopausal women.[32,33]

Strengths of this study include the ability to adjust simultaneously for neighborhood- and individual-level SES variables, large study size, and data on receptor variables and grade that allowed for the careful development of BC subtypes. Unlike registry based studies, our study cohort affords a unique opportunity to adjust simultaneously for neighborhood- and individual-level SES. Most previous work evaluated BC subtypes using only IHC markers, however, the use of IHC markers plus Ki-67 or a surrogate marker of cell proliferation such as tumor grade improves the accuracy of approximating BC subtypes, reducing misclassification of the LumA and LumB subtypes.[3,4]

Inferences about the associations between neighborhood-SES and BC subtypes should be made cautiously. Women in this study were geocoded based on their residence at the time of study enrollment, and we could not take into account how long women were living in their current residence or any early-life neighborhood exposures. Nonetheless, people tend to move to socioeconomically similar neighborhoods so this may not be a major concern.[34] The women in our cohort tended to live in areas of higher nSES, resulting in a skewed distribution and limited power in some analyses when using state-based quartiles. To address this imbalance, we pooled study-specific nSES quartiles to ensure an even distribution of women. As a result, the pooled 'High nSES' reference group represents areas of higher nSES relative to the state-based 'High nSES' reference group. Results for both categorizations of nSES have been presented for comparison. As Her2-e BC is less common, our cohort included relatively few women with the Her2-e subtype resulting in limited power to examine associations. Lastly, our study population included only women diagnosed with breast cancer in Northern California raising concerns about generalizability. Nevertheless, our results are consistent with previous studies conducted in data from national samples (SEER 17[8] and SEER 18[2] data), and in data from a different locale (Atlanta-based population[12]), allaying concerns.

In summary, we found that neighborhood- and individual-level SES were independently associated with different BC subtypes relative to LumA. Our results show that low nSES and individual-level education are independent predictors of more aggressive BC subtypes relative to LumA, even after adjustment for covariates and simultaneous adjustment for neighborhood- and individual- level SES. Further study is needed to determine the exact mechanisms of how neighborhood- and individual- level SES affects risk of BC subtypes.

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Table 1: Baseline Characteristics by Pooled Quartile of Neighborhood SES (N=5,547)

	Neighborhood SES, Pooled Quartile*				
	Q4 High nSES	Q3 Mid-high nSES	Q2 Mid-low nSES	Q1 Low nSES	p-value†
N	1387	1387	1387	1386	
Cohort Variables					
Study (%)					
LACE	26.5	26.5	26.5	26.5	
Pathways	73.5	73.5	73.5	73.5	
Days from diagnosis to baseline (%)					
<52 days	24.7	27.2	28.1	27.0	0.598
52-75 days	28.3	29.5	27.3	27.1	
76-519 days	27.7	26.0	26.2	27.3	
520+ days	19.3	17.4	18.5	18.6	
Demographic variables					
Age at diagnosis (%)					
<50	20.0	25.7	21.7	22.3	0.009
50-64	47.4	41.9	46.9	44.6	
65+	32.6	32.4	31.4	33.1	
Race/ethnicity (%)					
Non-Latina White	76.1	69.4	67.9	57.7	<0.001
Black	2.3	4.8	8.1	14.9	
Latina	6.5	9.0	11.3	15.4	
Asian	12.9	13.8	9.5	9.4	
Other	2.2	3.0	3.2	2.6	
Foreign born (%)	19.7	20.6	18.2	18.3	0.310
Tumor Characteristics					
AJCC Stage (%)					
I	54.0	52.6	50.5	48.9	0.049
II	38.1	37.6	40.5	42.1	
III	6.9	8.4	8.4	7.6	
IV	1.0	1.4	0.7	1.4	
BC Subtype (%)					
LumA	54.2	49.6	48.4	44.2	<0.001
LumB	31.2	34.0	33.5	35.1	
Her2-e	4.1	4.9	5.2	5.1	
TNBC	10.6	11.5	12.9	15.6	
Neighborhood SES					
State-based quartiles (%)					
Quartile 1 (Low nSES)	0.0	0.0	0.0	27.9	<0.001
Quartile 2 (Mid-low nSES)	0.0	0.0	6.9	69.5	
Quartile 3 (Mid-high nSES)	0.0	31.7	93.2	2.7	
Quartile 4 (High nSES)	100.0	68.4	0.0	0.0	

Table 1, Continued: Baseline Characteristics by nSES

Individual SES					
Education (%)					
HS or less	10.7	16.7	21.1	27.3	<0.001
Some college	28.2	34.8	37.9	42.4	
College degree	28.3	26.5	23.4	17.8	
Post-graduate	32.8	22.1	17.7	12.4	
Income‡ (%)					
Tertile 1 (<$49,000)	16.8	24.2	29.0	39.5	<0.001
Tertile 2 ($40,000-$89,000)	25.6	28.3	30.5	27.9	
Tertile 3 ($80,000+)	42.5	32.5	23.9	14.7	
Missing	15.1	14.9	16.6	17.9	

*Study-specific nSES quartiles were created then pooled

†p-value for ordinal variables generated from Mantel-Haenszel $\chi 2$ test; p-value for non-ordinal variables generated from Pearson's $\chi 2$ test.

‡Individual income tertiles were created for each study separately then pooled, resulting in overlapping ranges.

Supplementary Table 1: Baseline Characteristics by Study Cohort (N=5,547)

	LACE	Pathways	p-value*
N	1,468	4,079	
Cohort Variables			
Days from diagnosis to baseline (%)			
<52 days	0.0	36.4	<0.001
52-75 days	0.0	38.2	
76-519 days	30.3	25.5	
520+ days	69.7	0.0	
Demographic variables			
Age at diagnosis (%)			
<50	23.1	22.2	0.098
50-64	46.6	44.7	
65+	30.3	33.1	
Race/ethnicity (%)			
Non-Latina White	78.2	64.0	<0.001
Black	5.9	8.1	
Latina	6.2	12.1	
Asian	6.7	13.1	
Other	3.1	2.6	
Foreign born (%)	14.2	20.9	<0.001
Tumor Characteristics			
AJCC Stage (%)			
I	46.7	53.2	0.071
II	50.7	35.5	
III	2.6	9.7	
IV	0.0	1.5	
BC Subtype (%)			
LumA	47.3	49.7	<0.001
LumB	35.2	32.8	
Her2-e	4.4	5.0	
TNBC	13.0	12.5	
Neighborhood SES			
Pooled quartiles† (%)			
Quartile 1 (Low nSES)	25.0	25.0	0.991
Quartile 2 (Mid-low nSES)	25.0	25.0	
Quartile 3 (Mid-high nSES)	25.0	25.0	
Quartile 4 (High nSES)	25.0	25.0	
State-based quartiles (%)			
Quartile 1 (Low nSES)	5.3	7.6	<0.001
Quartile 2 (Mid-low nSES)	17.2	19.7	
Quartile 3 (Mid-high nSES)	30.6	32.3	
Quartile 4 (High nSES)	46.9	40.4	
Individual SES			
Education (%)			
HS or less	27.6	15.8	<0.001

Supplementary Table 1, Continued: Baseline Characteristics by Study Cohort

Some college	38.3	34.9	
College degree	14.3	27.5	
Post-graduate	19.8	21.8	
Income‡ (%)			
Tertile 1 (<$49,000)	23.7	28.7	<0.001
Tertile 2 ($40,000-$89,000)	26.2	28.8	
Tertile 3 ($80,000+)	20.6	31.3	
Missing	29.5	11.3	

* p-value for ordinal variables generated from Mantel-Haenszel $\chi 2$ test; p-value for non-ordinal variables generated from Pearson's $\chi 2$ test.

† Study-specific nSES quartiles were created then pooled

‡ Individual income tertiles were created for each study separately then pooled, resulting in overlapping tertile ranges.

Table 2: Odds ratios of pooled nSES quartiles and BC subtypes (relative to LumA) (N=5,547)

	Pooled, study-based nSES quartile#				
	Q4 (ref)	Q3	Q2	Q1	P-trend
LumA (N=2,723)	751	688	671	613	
LumB (N=1,856)	432	472	465	487	
OR, Age-adjusted†	1.00	1.18	1.20	1.38	<0.001
95% CI		(1.01, 1.38)	(1.02, 1.42)	(1.19, 1.60)	
OR, Model 1‡	1.00	1.15	1.15	1.29	0.004
95% CI		(0.98, 1.34)	(0.97, 1.37)	(1.11, 1.50)	
OR, Model 2§	1.00	1.16	1.16	1.31	0.005
95% CI		(0.99, 1.36)	(0.97, 1.39)	(1.11, 1.54)	
Q-statistic¶	0.61				
p-value	0.431				
Her2-e (N=267)	57	68	72	70	
OR, Age-adjusted†	1.00	1.27	1.40	1.52	0.016
95% CI		(0.91, 1.77)	(1.00, 1.96)	(1.08, 2.15)	
OR, Model 1‡	1.00	1.26	1.36	1.41	0.069
95% CI		(0.89, 1.77)	(0.96, 1.92)	(0.97, 2.05)	
OR, Model 2§	1.00	1.18	1.27	1.28	0.230
95% CI		(0.84, 1.68)	(0.89, 1.82)	(0.85, 1.92)	
Q-statistic¶	0.14				
p-value	0.705				
TNBC (N=701)	147	159	179	216	
OR, Age-adjusted†	1.00	1.15	1.34	1.77	<0.001
95% CI		(0.91, 1.44)	(1.06, 1.70)	(1.40, 2.25)	
OR, Model 1‡	1.00	1.05	1.15	1.39	0.007
95% CI		(0.84, 1.33)	(0.90, 1.48)	(1.09, 1.78)	
OR, Model 2§	1.00	1.04	1.13	1.32	0.037
95% CI		(0.83, 1.31)	(0.87, 1.46)	(1.02, 1.71)	
Q-statistic¶	0.58				
p-value	0.446				

†Adjusted for age at diagnosis.

‡Model 1 adjusted for possible confounders including age at diagnosis (continuous), race (NLW, Black, Latina, Asian, Other), nativity (US born, foreign born), AJCC stage (I,II,III,IV), days from diagnosis to baseline measures (<52, 52-75, 76-519, 520+), and study (LACE, Pathways).

§Model 2 adjusted for variables in Model 1 plus individual education and individual income.

¶Q-statistic calculated for Model 2 using continuous variable for days from diagnosis to study enrollment, and recategorized stage variable where stage II, III, and IV are collapsed into one level (given differences in study recruitment).

Study-specific nSES quartiles were created then pooled

Table 3: Odds ratios for associations of state-based nSES quartiles with BC subtypes (relative to LumA) (N=5,547)

	State-based nSES quartile#				
	Q4 (ref)	Q3	Q2	Q1	P-trend
LumA (2,723)	1229	849	464	181	
LumB (N=1,856)	743	610	384	119	
OR, Age-adjusted†	1.00	1.19	1.37	1.09	0.002
95% CI		(1.03, 1.38)	(1.17, 1.61)	(0.83, 1.43)	
OR, Model 1‡	1.00	1.17	1.30	1.02	0.024
95% CI		(1.01, 1.36)	(1.11, 1.53)	(0.78, 1.35)	
OR, Model 2§	1.00	1.17	1.31	1.03	0.031
95% CI		(1.01, 1.37)	(1.11, 1.55)	(0.77, 1.37)	
Q-statistic¶	0.28				
p-value	0.597				
Her2-e (N=267)	102	95	47	23	
OR, Age-adjusted†	1.00	1.35	1.24	1.59	0.032
95% CI		(1.02, 1.78)	(0.87, 1.77)	(0.99, 2.54)	
OR, Model 1‡	1.00	1.33	1.16	1.39	0.168
95% CI		(1, 1.77)	(0.8, 1.68)	(0.82, 2.38)	
OR, Model 2§	1.00	1.27	1.08	1.27	0.405
95% CI		(0.95, 1.71)	(0.73, 1.61)	(0.74, 2.21)	
Q-statistic¶	1.06				
p-value	0.303				
TNBC (N=701)	261	214	163	63	
OR, Age-adjusted†	1.00	1.17	1.65	1.63	<0.001
95% CI		(0.96, 1.42)	(1.32, 2.05)	(1.13, 2.34)	
OR, Model 1‡	1.00	1.07	1.41	1.18	0.017
95% CI		(0.88, 1.31)	(1.13, 1.76)	(0.83, 1.68)	
OR, Model 2§	1.00	1.05	1.35	1.09	0.087
95% CI		(0.86, 1.29)	(1.06, 1.71)	(0.76, 1.56)	
Q-statistic¶	0.16				
p-value	0.684				

†Adjusted for age at diagnosis.

‡Model 1 adjusted for possible confounders including age at diagnosis (continuous), race (NLW, Black, Latina, Asian, Other), nativity (US born, foreign born), AJCC stage (I,II,III,IV), days from diagnosis to baseline measures (<52, 52-75, 76-519, 520+), and study (LACE, Pathways).

§Model 2 adjusted for variables in Model 1 plus individual education and individual income.

¶Q-statistic calculated for Model 2 using continuous variable for days from diagnosis to study enrollment, and recategorized stage variable where stage II, III, and IV are collapsed into one level (given differences in study recruitment).

#For each censal year, quartiles were created based on the state distribution of nSES at the census block group level, then were applied to addresses of the women in the cohort

Table 4: Odds Ratios for Associations of Individual Education with BC Subtypes (Relative to LumA) (N=5,554)

	Individual-level education				
	Post-Graduate	College degree	Some college	HS degree or less	P-trend*
LumA (N=2,723)	583	662	994	484	
LumB (N=1,856)	423	361	624	448	
OR, Age-adjusted†	1.00	0.91	0.88	1.08	0.754
95% CI		(0.77, 1.09)	(0.76, 1.03)	(0.9, 1.3)	
OR, Model 1‡	1.00	0.93	0.87	1.02	0.699
95% CI		(0.78, 1.11)	(0.74, 1.02)	(0.84, 1.23)	
OR, Model 2§	1.00	0.91	0.83	0.96	0.303
95% CI		(0.76, 1.09)	(0.71, 0.98)	(0.78, 1.16)	
OR, Model 3¶	1.00	0.90	0.82	0.93	0.211
95% CI		(0.75, 1.08)	(0.69, 0.96)	(0.77, 1.14)	
Q statistic**	4.64				
p-value	0.031				
LACE (N=517) Model 3¶,#	1.00	0.91	1.10	1.15	0.301
95%CI		(0.61, 1.36)	(0.81, 1.49)	(0.82, 1.63)	
PATHWAYS (N=1,339)					
Model 3¶,#	1.00	0.89	0.73	0.85	0.022
95%CI		(0.72, 1.09)	(0.6, 0.87)	(0.66, 1.09)	
Her2-e (N=267)	36	51	104	76	
OR, Age-adjusted†	1.00	1.69	1.74	1.83	0.006
95% CI		(1.11, 2.56)	(1.16, 2.62)	(1.18, 2.84)	
OR, Model 1‡	1.00	1.59	1.77	1.80	0.007
95% CI		(1.03, 2.46)	(1.16, 2.7)	(1.13, 2.86)	
OR, Model 2§	1.00	1.56	1.70	1.71	0.023
95% CI		(1, 2.43)	(1.1, 2.63)	(1.05, 2.77)	
OR, Model 3¶	1.00	1.55	1.70	1.68	0.030
95% CI		(0.99, 2.43)	(1.09, 2.63)	(1.03, 2.75)	
Q statistic**	3.78				
p-value	0.052				
LACE (N=65) Model 3¶,#	1.00	1.27	1.41	3.07	0.009
95%CI		(0.47, 3.48)	(0.59, 3.35)	(1.32, 7.13)	
PATHWAYS (N=203)					
Model 3¶,#	1.00	1.52	1.72	1.10	0.452
95%CI		(0.95, 2.45)	(1.05, 2.81)	(0.59, 2.05)	
TNBC (N=701)	137	154	264	146	
OR, Age-adjusted†	1.00	0.88	1.13	1.42	0.002
95% CI		(0.68, 1.14)	(0.91, 1.41)	(1.1, 1.84)	
OR, Model 1‡	1.00	0.91	1.04	1.34	0.036
95% CI		(0.7, 1.18)	(0.83, 1.31)	(1.01, 1.76)	

Table 4, Continued: Individual Education and BC subtypes

OR, Model 2§	1.00	0.89	1.00	1.25	0.125
95% CI		(0.68, 1.16)	(0.79, 1.26)	(0.94, 1.67)	
OR, Model 3¶	1.00	0.89	0.99	1.22	0.171
95% CI		(0.68, 1.16)	(0.78, 1.26)	(0.92, 1.63)	
Q statistic**	0.29				
p-value	0.586				

†Adjusted for age at diagnosis

‡Model 1 adjusted for possible confounders including age at diagnosis (continuous), race (NLW, Black, Latina, Asian, Other), nativity (US vs. foreign born), AJCC stage (I,II,III,IV), days from diagnosis to baseline measures (continuous), and study (LACE, Pathways)

§Model 2 adjusted for variables in Model 1 plus pooled nSES

¶Model 3 adjusted for variables in Model 2 plus individual income

** Q-statistic calculated for Model 2 using continuous variable for days from diagnosis to study enrollment, and recategorized stage variable where stage II, III, and IV are collapsed into one level (given differences in study recruitment).

#Study-specific associations shown for Model 3 due to evidence of study heterogeneity

Figure 1: State-based nSES quartiles using 2010 US Census data in the Kaiser Permanente Northern California service area