Impact of NCI Socioeconomic Index on the Outcomes of Nonmetastatic Breast Cancer Patients: Analysis of SEER Census Tract–Level Socioeconomic Database

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Abstract

The census tract–level socioeconomic status index is a composite score integrating 7 parameters. Lower socioeconomic status index is associated with worse breast cancer-specific survival. Further efforts need to be directed to improving breast cancer outcomes among women with socioeconomically vulnerable attributes.

Purpose: To assess the impact of National Cancer Institute socioeconomic status (SES) index on breast cancer–specific survival (BCSS) of nonmetastatic breast cancer patients registered within the Surveillance, Epidemiology and End Results (SEER) census tract–level SES database. **Patients and Methods:** The census tract–level SES index is a composite score integrating 7 parameters that assess different dimensions of SES. Women with a nonmetastatic breast cancer diagnosis (stage I-III) diagnosed during 2010-2015 and included in the SEER-SES specialized database were included in the current analysis. Multivariate Cox regression analysis was used to assess the impact of SES index on BCSS. **Results:** A total of 296,100 women with nonmetastatic breast cancer were included in the current study. The impact of SES index on BCSS was evaluated in the overall cohort of patients through multivariate Cox regression analysis (adjusted for age at diagnosis, race, stage, and breast cancer subtype). Lower SES was associated with worse BCSS (hazard ratio for group 1 [lowest SES group] vs. group 3 [highest SES group]: 1.428; 95% confidence interval, 1.359-1.499; $P < .001$). Using additional interaction testing within Cox regression models, the impact of SES on BCSS seems to be modified by breast cancer subtype (P for interaction $< .001$), race (P for interaction $= .001$), and stage (P for interaction $= .015$). **Conclusion:** Lower SES index is associated with worse BCSS. Further efforts need to be directed to improving breast cancer outcomes among women with socioeconomically vulnerable attributes (poverty, lower education, and unemployment).

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Introduction

Socioeconomic status (SES) is a comprehensive concept in health policy studies that encompasses diverse aspects.[1] These include, but are not limited to, income, employment status, educational status, and house value.[2] The impact of many of these aspects on health and disease statuses has been previously shown.[3] Indeed, numerous studies have previously highlighted the impact of different elements of SES on the outcomes of breast cancer patients. However, many of these studies were confounded by small sample size, suboptimal breast cancer treatment (by current standards), poor data quality, reliance on general county-level socioeconomic attributes, and/or nonstandardization of the models used to assess SES.[4-6]

More recently, the National Cancer Institute (NCI) developed a specialized database based on the Surveillance, Epidemiology, and End Results (SEER) registry with linkage to other publicly available social US data sets to explore the different dimensions of SES. Such a database should provide an excellent opportunity to evaluate the impact of SES on breast cancer outcomes in a population-based setting and in the context of currently accepted standard-of-care management approaches.

Establishing the value of this standardized measure of SES in the context of breast cancer treatment has important implications on the management of individual patients as well as universal health care policies in society.

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Table 1 Baseline Patient Characteristics

Characteristic	All Patients (N = 296,100)	Group 1 (N = 71,670)	Group 2 (N = 98,849)	Group 3 (N = 125,581)	*P*
Age					<.001
<40 y	13,666 (4.6)	3539 (5)	4628 (4.7)	5443 (4.3)	
40-69 y	197,755 (66.8)	47,312 (66)	64,979 (65.7)	85,464 (68.1)	
≥70 y	84,679 (28.6)	20,763 (29)	29,242 (29.6)	34,674 (27.6)	
Race					<.001
White (non-Hispanic)	205,841 (69.5)	39,737 (55.4)	69,780 (70.6)	96,324 (76.7)	
Black (non-Hispanic)	28,181 (9.5)	14,803 (20.7)	8591 (8.7)	4787 (3.8)	
Hispanic	33,201 (11.2)	12,979 (18.1)	11,498 (11.6)	8724 (6.9)	
Asian/Pacific Islander	26,150 (8.8)	3364 (4.7)	8074 (8.2)	14,712 (11.2)	
American Indian	1335 (0.5)	531 (0.7)	484 (0.5)	320 (0.3)	
Unknown	1392 (0.5)	256 (0.4)	422 (0.4)	714 (0.6)	
Stage					<.001
I	159,524 (53.9)	35,024 (48.9)	52,921 (53.5)	71,579 (57)	
II	102,443 (34.6)	26,637 (37.1)	34,334 (34.7)	41,472 (33)	
III	34,133 (11.5)	10,009 (14)	11,594 (11.7)	12,530 (10)	
Subtype					<.001
Hormone receptor positive/HER2 negative	220,690 (74.5)	50,787 (70.9)	73,438 (74.3)	96,465 (76.8)	
HER2 positive	42,612 (14.4)	11,086 (15.5)	14,348 (14.5)	17,178 (13.7)	
Triple negative	32,798 (11.1)	9797 (13.7)	11,063 (11.2)	11,938 (9.5)	
Surgery					<.001
No	13,323 (4.5)	3889 (5.4)	4243 (4.3)	5191 (4.1)	
Breast-conserving surgery	159,444 (53.8)	35,774 (49.9)	53,327 (53.9)	70,343 (56)	
Mastectomy	122,944 (41.5)	31,892 (44.5)	41,131 (41.6)	49,921 (39.8)	
Unknown	389 (0.1)	115 (0.2)	148 (0.1)	126 (0.1)	
Chemotherapy					<.001
Yes	115,653 (39.1)	30,306 (42.6)	38,606 (39.1)	46,741 (37.2)	
No/unknown	180,447 (60.9)	41,364 (57.7)	60,243 (60.9)	78,840 (62.8)	
Radiotherapy					<.001
Yes	145,734 (49.2)	33,374 (46.6)	49,226 (49.8)	63,134 (50.3)	
No/unknown	150,366 (50.8)	38,296 (53.4)	49,623 (50.2)	62,447 (49.7)	

Data are presented as n (%).

We sought to assess the impact of NCI SES index on the outcomes of nonmetastatic breast cancer patients registered within the SEER census tract–level SES database.

Patients and Methods

About the NCI-SEER Census Tract–Level SES Database

The census tract–level SES index is a composite score endorsed by the NCI. It is based on previously published work that integrates 7 parameters that assess different dimensions of census tracts' SES.[7,8] These parameters include median household income and median house value/rent. They include also the percent of unemployment, the percent of working-class people, and the percent below 150% of the poverty line. They also include education index.[9] Details about geographic definitions and data linkage procedures for this specialized database are provided elsewhere.[10] After generating SES index, SES tertiles for census tracts were produced, with equal populations in each tertile (group 1, group 2, and group 3).

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Because this study was based on a publicly available database without identifying patient information, informed consent was not needed.

Case Selection Criteria

The following selection criteria were used to select women for inclusion into the current analysis: diagnosis of stage I, II, or III breast carcinoma (according to the anatomic staging system of the American Joint Committee on Cancer); complete information about SES index tertile at the time of diagnosis; complete information about hormone receptor (HR) and HER2 status (in order to determine breast cancer subtype); and diagnosis year between 2010 and 2015 (to make sure that the staging and management of included patients followed currently accepted standards).

Table 2 Multivariate Cox Regression Analysis for Factors Affecting Breast Cancer–Specific Survival

Parameter	Hazard Ratio (95% Confidence Interval)	*P*
Age		
40-69 y	Reference	
<40 y	1.075 (0.994-1.163)	.072
≥70 y	2.286 (2.196-2.380)	<.001
Tertile		
Group 3	Reference	
Group 1	1.428 (1.359-1.499)	<.001
Group 2	1.192 (1.137-1.249)	<.001
Race		
White	Reference	
Black	1.296 (1.227-1.370)	<.001
Hispanic	1.053 (0.992-1.119)	.091
Asian	0.817 (0.753-0.886)	<.001
Subtype		
Triple negative	Reference	
Luminal	0.292 (0.279-0.305)	<.001
HER2 overexpressed	0.395 (0.373-0.418)	<.001
Stage		
III	Reference	
I	0.079 (0.075-0.084)	<.001
II	0.284 (0.272-0.296)	<.001

The following definitions were used for different breast cancer subtypes: luminal ($HR^+/HER2^-$), triple negative (HR^-, $HER2^-$), and HER2 overexpressed ($HR^{any}/HER2^+$).

Data Collection

The following data were collected from each included patient (where available): age at diagnosis, race, SES index tertile, breast cancer stage (American Joint Committee on Cancer, 7th edition, staging system), breast cancer subtype, and treatment with surgery, chemotherapy, or radiotherapy. The primary end point of the current study was breast cancer–specific survival (BCSS; defined as the time from breast cancer diagnosis until death from breast cancer). Survival follow-up was done up to December 2015.

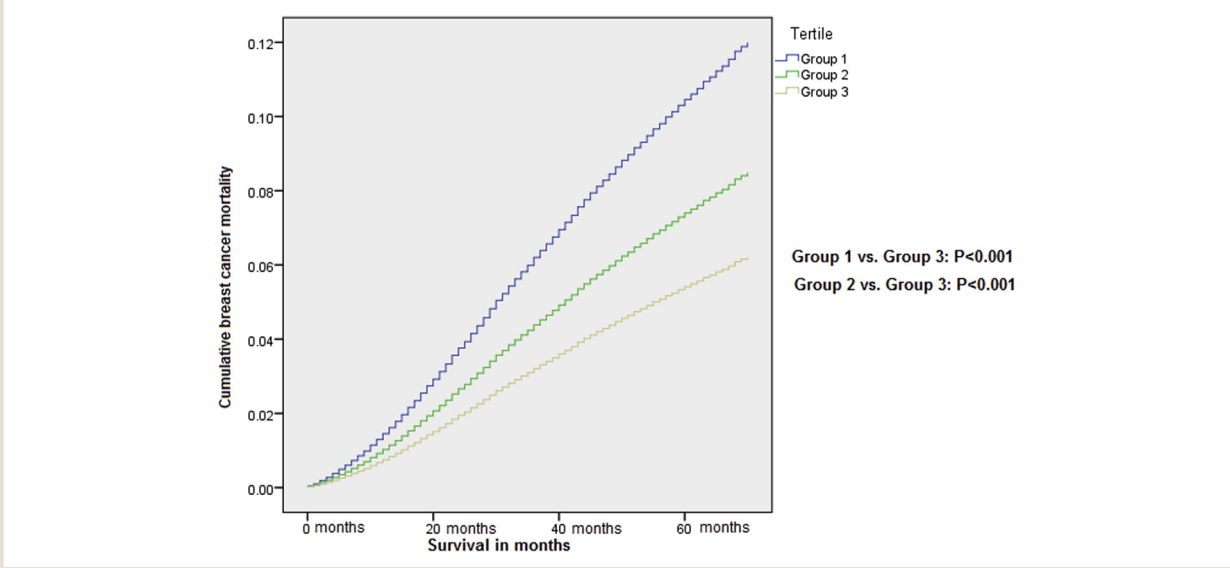
Statistical Analyses

The chi-square test was initially used to compare differences in clinicopathologic and treatment characteristics according to the SES group. Multivariate Cox regression analysis was then used to assess the factors predicting BCSS. It included the following factors: age at diagnosis, race, stage, breast cancer subtype, and SES group. Because there were not enough details regarding chemotherapy and radiotherapy doses and regimens, it was not possible to include them within the multivariate Cox regression model.

Additional multivariate analyses were then conducted to assess the impact of SES index on breast cancer survival in clinically defined subgroups of patients (according to race, breast cancer subtype, or stage). SPSS 20 (IBM, Armonk, NY) was used to perform all statistical analyses.

In order to provide a more robust assessment of the impact of SES within each racial group, propensity score matching was conducted for patients with each of the 4 principal racial groups (white, black, Hispanic, and Asian/Pacific Islander). Within each group, patients with low SES (ie, group 1) were matched with patients with higher SES (ie, groups 2 and 3). Covariates within the propensity score matching included age at diagnosis, stage, and subtype. The matching procedure was nearest neighbor matching (1:1). This part

Figure 1 Unadjusted Cox Hazard for BCSS According to SES



Abbreviations: BCSS = breast cancer–specific survival; SES = socioeconomic status.

Table 3 Impact of Socioeconomic Index on Breast Cancer–Specific Survival According to Breast Cancer Subtype

Breast Cancer Subtype	Index	Hazard Ratio (95% Confidence Interval)	*P*
Luminal subtype	**Tertile**		
	Group 3	Reference	
	Group 1	1.447 (1.351-1.549)	<.001
	Group 2	1.247 (1.170-1.329)	<.001
HER2 overexpressed	**Tertile**		
	Group 3	Reference	
	Group 1	1.626 (1.444-1.830)	<.001
	Group 2	1.164 (1.036-1.308)	.011
Triple negative	**Tertile**		
	Group 3	Reference	
	Group 1	1.284 (1.177-1.402)	<.001
	Group 2	1.109 (1.019-1.207)	.017

Multivariate Cox regression analysis was adjusted for age, stage, and race.

of the analysis was conducted by R software (R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org/). The impact of SES on BCSS was then evaluated (in the post-matching cohort of each racial subgroup) through multivariate Cox regression analysis adjusted for age, stage, and subtype.

Results

Patient Characteristics

A total of 296,100 women with nonmetastatic breast cancer were included in the current study. Of these, 71,670 patients were in SES group 1 at time of diagnosis, 98,849 in group 2, and 125,581 in group 3. Comparing the 3 groups together, patients with lower SES were more likely to be older at presentation ($P < .001$), to be black ($P < .001$), to have triple-negative breast cancer subtype ($P < .001$), and to have more advanced disease stage at presentation ($P < .001$). They were also less likely to receive breast-conserving surgery ($P < .001$) and less likely to receive radiotherapy ($P < .001$), but more likely to receive systemic chemotherapy ($P < .001$) (Table 1). The mean ± standard deviation follow-up was 31.47 ± 20.41 months. The number of breast cancer deaths in SES group 1 was 3623 deaths (5.1%); group 2, 3674 (3.7%); and group 3, 3477 (2.8%).

Table 4 Impact of Socioeconomic Index on Breast Cancer–Specific Survival According to Race

Race	Index	Hazard Ratio (95% Confidence Interval)	*P*
White non-Hispanic	**Tertile**		
	Group 3	Reference	
	Group 1	1.478 (1.392-1.569)	<.001
	Group 2	1.212 (1.147-1.280)	<.001
Black non-Hispanic	**Tertile**		
	Group 3	Reference	
	Group 1	1.240 (1.079-1.425)	.002
	Group 2	1.116 (0.959-1.300)	.157
Hispanic	**Tertile**		
	Group 3	Reference	
	Group 1	1.473 (1.275-1.703)	<.001
	Group 2	1.137 (0.974-1.327)	.104
Asian/Pacific Islander	**Tertile**		
	Group 3	Reference	
	Group 1	1.260 (1.017-1.563)	.035
	Group 2	1.059 (0.889-1.262)	.518

Multivariate Cox regression analysis was adjusted for age, stage, and race.

Table 5 Impact of Socioeconomic Index on Breast Cancer–Specific Survival According to Breast Cancer Stage

Breast Cancer Stage	Index	Hazard Ratio (95% Confidence Interval)	*P*
Stage I	**Tertile**		
	Group 3	Reference	
	Group 1	1.518(1.344-1.715)	<.001
	Group 2	1.299 (1.162-1.452)	<.001
Stage II	**Tertile**		
	Group 3	Reference	
	Group 1	1.489 (1.378-1.608)	<.001
	Group 2	1.175 (1.091-1.265)	<.001
Stage III	**Tertile**		
	Group 3	Reference	
	Group 1	1.341 (1.245-1.444)	<.001
	Group 2	1.163 (1.083-1.249)	<.001

Multivariate Cox regression analysis adjusted for age, breast cancer subtype, and race.

Impact of SES Index on BCSS in Overall Cohort

The impact of the SES index on BCSS was evaluated in the overall cohort of patients by multivariate Cox regression analysis. Lower SES was associated with worse BCSS (hazard ratio for group 1 vs. group 3, 1.428; 95% confidence interval, 1.359-1.499; $P < .001$) (Table 2).

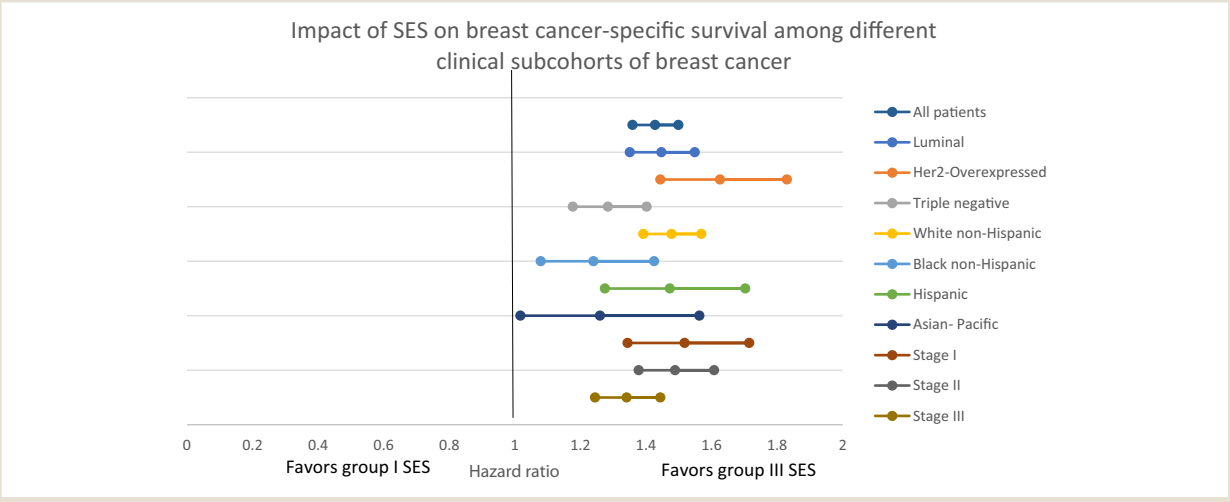
Using additional interaction testing within Cox regression models, the impact of SES on BCSS seems to be modified by breast cancer subtype (P for interaction < .001), race (P for interaction = .001), and stage (P for interaction = .015). Figure 1 shows unadjusted Cox hazard for BCSS according to SES.

Impact of SES Index on BCSS in Specific Subgroups

According to Breast Cancer Subtype. Table 3 details the impact of SES index on BCSS among the 3 breast cancer subtypes (luminal, HER2 overexpressed, and triple negative). This was done through multivariate Cox regression modeling for each of the 3 subtypes adjusted for age at diagnosis, race, and stage. Although lower SES index seems to be associated with worse survival in the 3 subtypes ($P < .05$), the effect seems to be pronounced among luminal and HER2-overexpressed subtypes compared to the triple-negative subtype.

According to Race. Through multivariate Cox regression modeling adjusted for age at diagnosis, stage, and breast cancer subtype, the impact of SES index was further evaluated in each of the 4 principal race groups (white non-Hispanic, black non-Hispanic, Asian, and Hispanic). Although lower SES index seems to be associated with worse survival in the 4 racial groups ($P < .05$), the impact seemed to

Figure 2 Forest Plot Summarizing Impact of SES (Group 1 Versus Group III) on BCSS



Abbreviations: BCSS = breast cancer–specific survival; SES = socioeconomic status.

be more pronounced among the white non-Hispanic group compared to the black non-Hispanic group (Table 4).

According to Disease Stage. Through multivariate Cox regression modeling, the impact of SES index on BCSS was assessed in the 3 anatomic stages (I, II, and III). This was adjusted for age at diagnosis, race, and breast cancer subtype. The negative impact of lower SES index seemed to be more pronounced among stage I and II disease compared to stage III disease (Table 5).

Table 6 Multivariate Cox Regression Analysis for Impact of Socioeconomic Index on Breast Cancer–Specific Survival According to Race in Postmatching Cohort

Race	Index	Hazard Ratio (95% Confidence Interval)	*P*
White non-Hispanic	**Tertile**		
	Group 3	Reference	
	Group 1	6.979 (5.590-6.715)	<.001
	Group 2	1.421 (1.052-1.920)	.022
Black non-Hispanic	**Tertile**		
	Group 3	Reference	
	Group 1	1.246 (1.081-1.436)	.002
	Group 2	1.149 (0.986-1.338)	.075
Hispanic	**Tertile**		
	Group 3	Reference	
	Group 1	3.190 (2.541- 4.005)	<.001
	Group 2	1.104 (0.836-1.458)	.484
Asian/Pacific Islander	**Tertile**		
	Group 3	Reference	
	Group 1	4.633 (2.318-9.262)	<.001
	Group 2	1.540 (0.586-4.047)	.381

Multivariate Cox regression analysis adjusted for age, stage and subtype.

Figure 2 shows a summary of the impact of SES on BCSS among different breast cancer clinical subgroups.

Impact of SES Index on BCSS in Different Racial Subgroups in Postmatching Cohort

After propensity score matching, a total of 39,737 white patients in SES group 1 were matched with 39,737 white patients in groups 2 and 3. A total of 13,378 black patients in group 1 were matched with 13,378 black patients in groups 2 and 3. A total of 12,979 Hispanic patients in group 1 were matched with 12,979 Hispanic patients in groups 2 and 3. A total of 3364 Asian/Pacific Islander patients in group 1 were matched with 3364 Asian/Pacific Islander patients in groups 2 and 3.

Multivariate Cox regression analysis for the impact of SES on BCSS was then conducted for each of the racial subgroups, and the findings were similar to the prematching results (Table 6).

Discussion

The current study provided an assessment of the prognostic utility of NCI's SES index in the context of a nonmetastatic breast cancer diagnosis. It showed that lower SES index is associated with worse BCSS.

In the current cohort of patients, those with lower SES index were more likely to be black and to have a triple-negative phenotype. This is consistent with previous population-based studies in the United States.[11,12] Such patients were also more likely to have an advanced disease stage at presentation, which might be linked to lack of access to proper screening and early diagnostic services among people with lower SES. This higher probability of advanced disease stage at presentation was probably the reason behind the higher use of chemotherapy in this group, as well as less use of breast-conserving surgery/radiotherapy in this group.

The current study is in line with numerous previously published population-based studies that have confirmed the negative prognostic impact of lower SES on the outcomes of breast cancer patients.[4-6]

However, the current study is unique in its reliance on a national database that was specifically developed and maintained to answer this question. This should increase the credibility of the results of the current study. Moreover, many of the previous SEER analyses evaluating this research question were based on county-level socioeconomic data (as opposed to the current study, which relies on census tract–level data). This further boosts the reliability of the current analysis.

Despite the clear strengths of the current study (including a large number of patients, the well-known rigorous quality assurance policies of the SEER database, and a reliance on a dedicated database for SES), the current study has a few limitations that need to be recognized. First, the current cohort of patients had several missing important baseline patient-related variables like performance status and comorbidities, which might have affected the veracity of survival analyses. In order to mitigate the confounding impact of these missing variables on noncancer mortality, the current study relied on BCSS (and not overall survival) as the primary end point. Second, there was a lack of detailed technical information about approaches and doses of systemic chemotherapy and radiotherapy. Third, the current study was based on a cohort of patients from the United States. Because of the differences in health care coverage patterns between the United States and other Western countries as well as the rest of the world, caution needs to be exercised before extrapolating the results of the current analysis into other countries/health care systems. Fourth, although the NCI-SES index represents a good step in terms of standardizing ways of reporting SES, we have to remember that it is still an area-based attribute (rather than an individualized assessment of SES). Moreover, it is a relatively new parameter with limited validation studies outside of North America. These considerations should make us approach the current results with caution. An optimal assessment of the impact of SES on breast cancer outcomes would preferably include an individualized assessment of socioeconomic parameters at the time of cancer diagnosis (which is unfortunately not available currently for the SEER database).

The current study highlights the impact of several social determinants (like income, education, and occupational status) on the outcomes of cancer patients in general, and breast cancer patients in particular. These parameters are frequently ignored by the health care professionals dealing with cancer patients. There is a need to increase the awareness of this dimension of care among all health care workers dealing with cancer patients, and this should be incorporated as a fundamental part of their training. There is a need to convey the same message to the public to highlight the potential impact of minimizing social disparities on the outcomes of cancer patients.

The current study also highlights the complexities surrounding the analysis of racial/ethnic variations in breast cancer outcomes. While biology might partially explain the differences between the outcomes of non-Hispanic white and non-Hispanic black patients (eg, the triple-negative phenotype is more prevalent in patients with African ancestry[11,12]), SES differences and consequent disparities in access to timely cancer care are important variables to help explain the racial differences in breast cancer outcomes. Whereas health care systems have limited potential to modify genetic risk factors in an individual patient, health care systems can improve the access of all patients (regardless of their SES) to the best available cancer care. Thus, reducing access disparities to proper cancer treatment should be considered a public health imperative.

In conclusion, lower SES index is associated with worse BCSS. Further research is needed to assess the mechanisms of interactions between SES and cancer outcomes.

Clinical Practice Points

- The census tract–level SES index is a composite score integrating 7 parameters that assess different dimensions of SES.
- Women with a nonmetastatic breast cancer diagnosis (stage I-III) diagnosed during 2010 to 2015 and included in the SEER-SES specialized database were included in the current analysis.
- Multivariate Cox regression analysis was used to assess the impact of SES index on BCSS.
- A total of 296,100 women with nonmetastatic breast cancer were included in the current study.
- The impact of SES index on BCSS was evaluated in the overall cohort of patients through multivariate Cox regression analysis (adjusted for age at diagnosis, race, stage, and breast cancer subtype).
- Lower SES was associated with worse BCSS (hazard ratio for group 1 [lowest SES group] vs. group 3 [highest SES group], 1.428; 95% confidence interval, 1.359-1.499; $P < .001$).
- Using additional interaction testing within Cox regression models, the impact of SES on BCSS seems to be modified by breast cancer subtype (P for interaction $< .001$), race (P for interaction $= .001$), and stage (P for interaction $= .015$).

Disclosure

The authors have stated that they have no conflict of interest.

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