

## Association of Inflammatory and Noninflammatory Breast Cancer with Socioeconomic Characteristics in the Surveillance, Epidemiology, and End Results Database, 2000–2007

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### Abstract

**Background:** Inflammatory breast cancer (IBC) is a rare and highly aggressive form of primary breast cancer. Little is known about the risk factors for IBC, specifically the association with socioeconomic position (SEP).

**Methods:** The association between breast cancer type (IBC vs. non-IBC) with county-level SEP in the Surveillance, Epidemiology, and End Results database for cases diagnosed from 2000 to 2007 was examined. County-level SEP characteristics included metropolitan versus non-metropolitan residence, percentage below the poverty level, percentage less than high-school graduate, and an index combining the poverty and high-school variables. IBC and non-IBC age-adjusted incidence rates were calculated, stratified on SEP and race/ethnicity. The odds of IBC versus non-IBC given a particular SEP characteristic, adjusting for age and race/ethnicity, was examined through fitting of hierarchical logistic regression models (HLM).

**Results:** Incidence rates for IBC generally increased as SEP decreased, whereas the opposite was found for non-IBC. HLM results showed that low SEP is associated with higher odds of IBC: highest ( $\geq 20\%$ ) versus lowest ( $< 10\%$ ) persons below the poverty level [OR (95% confidence interval, CI) = 1.25 (1.09–1.43)]; highest ( $> 28.76\%$ ) versus lowest ( $\leq 15.99\%$ ) persons less than high-school graduate [OR (95% CI) = 1.25 (1.10–1.42)]; and low SEP as measured by poverty-high school index versus high SEP [OR (95% CI) = 1.26 (1.11–1.44)].

**Conclusion:** Overall breast cancer has been found to be positively associated with SEP, whereas in this analysis, IBC was associated with decreasing SEP.

**Impact:** Studies focused on understanding the disparity in IBC incidence, as well as interventions to eliminate these differences are needed. *Cancer Epidemiol Biomarkers Prev*; 21(1): 155–65. ©2011 AACR.

### Introduction

Breast cancer is a heterogeneous disease, characterized by distinct tumor subtypes thought to correspond to different etiologies (1–5). Inflammatory breast cancer (IBC) is a rare and highly aggressive form of primary breast cancer (6–11). Although risk factors for IBC remain largely unknown, some studies have shown

different risk factor profiles for IBC as compared with non-IBC cases (12–15).

Breast cancer incidence in the United States is related to socioeconomic position (SEP; ref. 16), being greater among women with higher education and income (17, 18) and among women residing in communities with higher average levels of education and income (19–23). Although some studies have found much of this association can be explained by known breast cancer risk factors (17, 22), a study examining both individual- and community-level SEP revealed that after adjusting for individual SEP and breast cancer risk factors, women living in the highest SEP communities continued to have greater odds of having breast cancer than women living in the lowest SEP communities, suggesting community-level effects on breast cancer risk (16). Robert and colleagues hypothesized that these community effects could independently affect breast cancer risk through various pathways including more access to mammograms (leading to more breast cancer detection)

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and community norms such as exogenous hormone use, alcohol intake, and diet (16).

Higher incidence of overall breast cancer in urban areas, both in the United States and internationally, has been reported for many years (24–28). Residence is also related to SEP, with rural residents in the United States generally having lower income, less education, and lower health insurance coverage than their urban counterparts (29).

Given the lack of knowledge about factors associated with IBC incidence and the evidence that some overall breast cancer risk factors may not have the same effect on IBC risk, the aim of this study was to examine the association of county-level SEP measures to IBC and non-IBC incidence in the U.S. Surveillance, Epidemiology, and End Results (SEER) database linked to 2000 U.S. Census county-attribute data.

## Materials and Methods

### Data source

The SEER 17 Registries database linked to 2000 U.S. county attributes was used for this analysis (30). The population-linked data set includes all breast cancer cases from 2000 to 2007 for the following SEER registries: Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San-Francisco-Oakland, Seattle-Puget Sound, Utah, Los Angeles, San Jose-Monterey, rural Georgia, the Alaska Native Tumor Registry, Greater California, Kentucky, Louisiana, and New Jersey (31). The U.S. SEER database covers approximately 26% of the U.S. population, including 23% of African Americans, 40% of Hispanics, 42% of American Indians and Alaska Natives, 53% of Asians, and 70% of Hawaiian/Pacific Islanders (32).

### Individual-level measures

The outcome variable for this analysis was diagnosis of a first malignant primary breast cancer [International Classification of Diseases for Oncology (ICD-O-3) = C500–C509] as IBC or non-IBC. To be certain all IBC cases were captured, a comprehensive case definition was used where a breast cancer case having any one of the following codes assigned to the SEER variables below was classified as IBC (6, 15, 33–35):

- Site and morphology. Histologic type ICD-O-3 (2000–2007) = 8530 ("Inflammatory Carcinoma"; refs. 36, 37)
- Stage - TNM. Derived AJCC [American Joint Committee on Cancer] T, 6th ed (for cases 2004+) = T4d ("Inflammatory Carcinoma"; refs. 36, 38)
- Extent of disease [EOD] - CS.CS extension (for cases 2004+) = 71–73 (36, 39)
  - 71: "Diagnosis of inflammatory carcinoma without a clinical description of inflammation, erythema, edema, peau d'orange, etc., of more than 50% of the breast, with or without dermal

lymphatic infiltration. Inflammatory carcinoma, NOS."

- 72: "Diagnosis of inflammatory carcinoma with a clinical description of inflammation, erythema, edema, peau d'orange, etc., of less than or equal to 50% of the breast, with or without dermal lymphatic infiltration."
- 73: "Diagnosis of inflammatory carcinoma with a clinical description of inflammation, erythema, edema, peau d'orange, etc., of more than 50% of the breast, with or without dermal lymphatic infiltration."
- Extent of disease - Historic. EOD 10 - extent (for cases 2000–2003) = 70 (36, 40).
- 70: "Inflammatory carcinoma, including diffuse (beyond that directly overlying the tumor) dermal lymphatic permeation or infiltration."

All other histologic types were considered non-IBC. Breast cancers assigned to histologic codes 9590 and greater (lymphomas) were not included.

Age at diagnosis was analyzed as a continuous variable. A merged race and ethnicity variable with the following categories was also examined: Non-Hispanic White, Black, Hispanic White, Asian/Pacific Islander, and American Indian/Alaska Native.

### County-level measures

Four county-level measures of SEP derived from the 2000 U.S. census were used in this analysis (41). Counties were divided into metropolitan (metro) versus non-metro areas based on their 2003 U.S. Department of Agriculture Rural-Urban Continuum code (RUCC), as has been done in previous cancer studies (42–45). Codes 1–3 were defined as metro counties, whereas codes 4–9 defined non-metro counties (code definitions below).

Rural-Urban Continuum Code Definitions for 2003 (46, 47):

Metro counties:

- 1 (Counties in metro areas of  $\geq 1$  million population)
- 2 (Counties in metro areas of 250,000–1 million population)
- 3 (Counties in metro areas of  $< 250,000$  population)

Non-metro counties:

- 4 (Urban population of  $\geq 20,000$ , adjacent to a metro area)
- 5 (Urban population of  $\geq 20,000$ , not adjacent to a metro area)
- 6 (Urban population of 2,500–19,999, adjacent to a metro area)
- 7 (Urban population of 2,500–19,999, not adjacent to a metro area)
- 8 (Completely rural or  $< 2,500$  urban population, adjacent to a metro area)

- 9 (Completely rural or <2,500 urban population, not adjacent to a metro area)

Percentage of persons within a county living below the federal poverty level was divided into 3 categories: <10%, 10%–19.99%, and  $\geq$ 20%. This measure has been used in other SEER-based studies of SEP variation and disparities in cancer incidence and outcomes (48, 49). Percentage of the population below the poverty level has several advantages as a SEP measure. It is easily understood, being based on readily interpretable variables with *a priori* cutoff points, with areas having  $\geq$ 20% poverty generally considered "poverty areas" in census publications and studies using census data (48–51). Percentage below the poverty level also takes into account a family's size and age structure and is directly tied to the person's ability to buy a representative basket of goods and services, being updated annually by the U.S. Census Bureau to reflect changes in the Consumer Price Index (48, 52).

Education, specifically completion of high school measured at both the individual and aggregate level, has been previously shown to be positively associated with overall breast cancer incidence (19, 53). To examine the county-level effect of high-school education on IBC incidence, percentage of adults (older than 25 years) in a county who did not graduate from high school was divided into quartiles on the basis of the distribution of the variable across all counties in the United States using the SEER county attributes database (54). The quartiles were as follows:  $\leq$ 15.99%, 16%–20.80%, 20.81%–28.76%, and  $>$ 28.76%.

To examine the joint effect of poverty and education on the odds IBC versus non-IBC incidence, a composite measure of these two variables was also created. The percentage below high-school graduate quartiles were combined with the 3-category poverty variable to create high, middle, and low SEP categories as follows: high SEP, <10.00% poverty and <15.99% less than high-school graduate; low SEP, (i) 10%–19.99% poverty and  $>$ 28.76% less than high-school graduate or (ii)  $\geq$ 20% poverty and  $>$ 28.76% less than high school graduate or (iii)  $\geq$ 20% poverty and 20.81%–28.76% less than high-school graduate, with the middle SEP group being all remaining combinations. A similar index was used previously in a study examining overall breast cancer survival in the SEER database (43).

### Statistical analysis

Statistical software developed by the SEER program (SEER\*stat version 6.6.2, National Cancer Institute, Bethesda, MD) readily allows for the calculation of incidence rates using the incidence data set linked to county attribute and population data (55). Female adult (older than 18 years) IBC and non-IBC incidence rates (IR) for the period from 2000 to 2007 were calculated. IRs were directly age-adjusted to the 2000 U.S. standard population (56, 57) and further stratified on the following county-

level SEP measures: metro versus non-metro residence, percentage below poverty, and percentage less than high-school graduate, as well as race/ethnicity. Upper and lower 95% confidence intervals (CI) around the IR ratios were used to test for statistical significance. A 95% IR ratio (CI not including 1) was indicative of the rates being statistically significantly different at the 0.05 significance level (58). The 95% CIs for the IRs and IR ratios were calculated using the method described in the work of Tiwari and colleagues (59). While SEER\*stat allows for the calculation of incidence rates stratified by county attribute measures, it does not allow for the calculation of incidence rates by a variable created from the merging of two county attributes, such as the poverty-high school index.

To directly compare the association of IBC and non-IBC cases with SEP, hierarchical logistic regression models were fit using the SAS Glimmix procedure (version 9.1; SAS Institute Inc.; ref. 60). As women who reside in the same county may have similar, unmeasured characteristics, and therefore be more alike than individual women across different counties, it is important to take this intraclass correlation into account as ignoring it may lead to underestimation of the regression coefficient's SE (61, 62). A hierarchical modeling structure allows for the examination of both individual- and county-level fixed effects while accounting for the effect due to clustering within counties through the addition of a random intercept, leading to more accurate SE estimates (61–63).

Four separate HLMs were fit, with each model including one county-level SEP measure as well as age at diagnosis and merged race/ethnicity as independent variables. Age at diagnosis and race/ethnicity were included in all models due to their previously reported association with the incidence of different histopathologic types of breast cancer, specifically IBC (1, 6, 7, 15, 33, 64–66). All HLMs modeled the log ORs of IBC. The general model is outlined below where the county intercept becomes a linear combination of a grand mean ( $\alpha$ ), the county SEP fixed effect ( $\gamma$ ), and county random effects ( $\mu$ ), with  $\beta_1$  and  $\beta_2$  being individual fixed effects (63):

$$\text{logit}(\pi_{ij}) = \alpha + \gamma(\text{SEP})_j + \mu_j + \beta_1 \text{Age}_{ij} + \beta_2 \text{Race/Ethnicity}_{ij}$$

### Results

First primary breast cancer cases ( $n = 346,211$ ) in women older than 18 years diagnosed from 2000 to 2007 were available for this analysis; 39 cases missing county-level information and 2,545 cases missing race/ethnicity were excluded, leaving 343,627 cases. After these exclusions, there were 5,536 IBC and 338,091 non-IBC cases included in this analysis. In the model examining metro versus non-metro counties, a further 394 cases were excluded because of missing RUCC, leaving 5,525 IBC and 337,708 non-IBC cases for analysis.

**Table 1.** Socioeconomic and ethnic background characteristics of the SEER study population, 2000–2007

	IBC, n (%)	Non-IBC, n (%)
Mean age at diagnosis (SD)	58.0 (14.5)	60.7 (14.3)
Race/ethnicity		
Non-Hispanic White	3,707 (67.0)	253,442 (75.0)
Black	806 (14.6)	30,780 (9.1)
Hispanic White	704 (12.7)	29,111 (8.6)
Asian/Pacific Islander	280 (5.1)	23,252 (6.9)
American Indian/ Alaska Native	39 (0.7)	1,506 (0.4)
Residence at diagnosis <sup>a</sup>		
Metro county	4,966 (89.9)	304,346 (90.1)
Non-metro county	559 (10.1)	33,362 (9.9)
County-level, % below poverty		
<10.00	1,917 (34.6)	134,331 (39.7)
10.00–19.99	3,122 (56.4)	179,577 (53.1)
≥20.00	497 (9.0)	24,183 (7.2)
County-level, % less than high-school graduate		
≤15.99	1,669 (30.2)	118,092 (34.9)
16–20.80	1,699 (30.7)	107,849 (31.9)
20.81–28.76	855 (15.4)	45,123 (13.4)
>28.76	1,313 (23.7)	67,027 (19.8)
Poverty-high school index:		
High SEP	1,250 (22.6)	92,447 (27.3)
Middle SEP	2,845 (51.4)	171,883 (50.8)
Low SEP	1,441 (26.0)	73,761 (21.8)

NOTE: No other cases missing.

<sup>a</sup>A total of 394 cases were missing RUCC.

Table 1 describes the study population characteristics. The mean age at diagnosis for IBC was 58.0 versus 60.7 years for non-IBC. The majority of IBC cases were of Non-Hispanic White race/ethnicity (67.0%) followed by Black (14.6%), Hispanic White (12.7%), Asian/Pacific Islander (5.1%), and American Indian/Alaska Native (0.7%). The comparable percentages for non-IBC were 75.0%, 9.1%, 8.6%, 6.9%, and 0.4%; 22.6% of IBC cases were classified as high SEP using the poverty-high school index, whereas 51.4% were middle SEP and 26.0% low SEP. Using the same index, 27.3% of non-IBC cases were considered high SEP, 50.8% middle SEP, and 21.8% low SEP.

Table 2 provides the age-adjusted IRs (per 100,000) and IR ratios for IBC according to SEP characteristics and race/ethnicity and Table 3 provides the corresponding results for non-IBC. There was no difference in the overall IBC IRs for metro versus non-metro residence. When these rates were stratified by race/ethnicity, the only significant difference found was for Blacks (metro IR = 3.4, non-metro IR = 4.8). The IBC IRs for counties where >10% of the residents were below the poverty level were generally

significantly higher for all races combined, Non-Hispanic Whites, and Blacks. No significant difference was seen in IBC poverty stratified rates for Hispanic Whites, Asians/Pacific Islanders, or American Indians/Alaska Natives. The IBC IRs for counties where a higher percentage of the population had not graduated from high school followed a similar pattern as the poverty variable.

Non-IBC IRs for those living in non-metro counties were significantly lower for all races combined and Non-Hispanic Whites but significantly higher for Asians/Pacific Islanders and American Indians/Alaska Natives race/ethnicity groups. There was no significant difference in the metro and non-metro IRs for Blacks and Hispanic Whites. Non-IBC IRs for those living in counties where >10% of the residents were below the poverty level were significantly lower for all races combined, Non-Hispanic Whites, Hispanic Whites, Asians/Pacific Islanders, and American Indians/Alaska Natives, with no significant difference in rates observed for Blacks. The non-IBC IRs for counties where a higher percentage of the population had not graduated from high school followed a similar pattern as the poverty variable.

Table 4 gives the ORs and 95% CIs for the 4 HLMs. In these models, which account for the clustering of cases within counties, after adjustment for age at diagnosis and race/ethnicity, residing in a high poverty county (≥20%), a county in the highest quartile of persons with less than a high school degree, and a low SEP county based on the poverty-high school index was significantly associated with higher odds of IBC [OR (95% CI) = 1.25 (1.09–1.43), 1.25 (1.10–1.42), and 1.26 (1.11–1.44), respectively]. Younger age and Black, Hispanic White, and American Indian/Alaska Native race/ethnicity were also significantly associated with higher odds of IBC in all models, whereas Asian/Pacific Islander race/ethnicity was significantly associated with lower odds of IBC.

## Discussion

Contrary to the previously reported positive association between urban residence, SEP, and overall breast cancer occurrence (16–28), this study found that living in a high poverty county (≥20%), a county with a high percentage of less than high-school graduates, and residing in a low SEP county as defined by the poverty-high school index were significantly associated with IBC, even after adjustment for age at diagnosis and race/ethnicity.

Prior studies examining overall breast cancer occurrence have found it to be associated with urban residence and higher SEP (16–28). However, the majority of breast cancers are non-IBC and thus determining IBC's association with SEP based on studies of all breast cancer types is difficult. This study used an inclusive definition to separately characterize IBC from all other breast cancer types and then directly compared IBC with non-IBC through use of HLMs adjusting for age and race/ethnicity, to specifically examine SEP and its association with IBC as a distinct breast cancer entity.

**Table 2.** Age-adjusted IBC incidence rates per 100,000 and rate ratios (95% CI) stratified by county-level SEP and race/ethnicity, 2000–2007

Variable	All races combined		Non-Hispanic White		Black	
	IR	Rate ratio (95% CI)	IR	Rate ratio (95% CI)	IR	Rate ratio (95% CI)
Metro	2.3 (2.3–2.4)		2.3 (2.2–2.4)		3.4 (3.2–3.7)	
Non-metro	2.3 (2.1–2.5)	0.99 (0.90–1.08)	2.2 (2.0–2.4)	0.95 (0.85–1.05)	4.8 <sup>a</sup> (3.7–6.1)	1.40 (1.06–1.81)
County-level, % below poverty						
<10.00 <sup>d</sup>	2.2 (2.1–2.3)	1.00	2.2 (2.1–2.3)	1.00	2.8 (2.3–3.3)	1.00
10.00–19.99	2.4 <sup>b</sup> (2.3–2.5)	1.12 (1.06–1.19)	2.4 <sup>b</sup> (2.3–2.5)	1.07 (1.00–1.15)	3.7 <sup>b</sup> (3.4–4.0)	1.31 (1.08–1.60)
≥20.00	2.7 <sup>b</sup> (2.4–2.9)	1.24 (1.12–1.37)	2.5 (2.2–2.8)	1.12 (0.99–1.27)	3.7 <sup>b</sup> (3.0–4.5)	1.32 (1.01–1.72)
County-level, % less than high-school graduate						
≤15.99 <sup>d</sup>	2.1 (2.0–2.2)	1.00	2.1 (2.0–2.2)	1.00	3.2 (2.8–3.8)	1.00
16–20.80	2.3 <sup>c</sup> (2.2–2.4)	1.09 (1.02–1.17)	2.4 <sup>c</sup> (2.2–2.5)	1.11 (1.03–1.21)	3.4 (2.9–3.9)	1.04 (0.84–1.28)
20.81–28.76	2.6 <sup>c</sup> (2.4–2.8)	1.23 (1.13–1.33)	2.5 <sup>c</sup> (2.3–2.7)	1.18 (1.06–1.31)	3.3 (2.9–3.8)	1.03 (0.84–1.27)
>28.76	2.6 <sup>c</sup> (2.4–2.7)	1.20 (1.12–1.30)	2.5 <sup>c</sup> (2.4–2.7)	1.20 (1.09–1.32)	4.1 <sup>c</sup> (3.6–4.8)	1.28 (1.04–1.58)
Variable	Hispanic White		Asian/Pacific Islander		American Indian/Alaska Native	
	IR	Rate ratio (95% CI)	IR	Rate ratio (95% CI)	IR	Rate ratio (95% CI)
Metro	2.4 (2.2–2.6)		1.3 (1.1–1.4)		1.2 (0.7–1.9)	
Non-metro	2.6 (1.7–3.7)	1.05 (0.69–1.55)	1.4 (0.7–2.4)	1.08 (0.55–1.92)	1.6 (0.6–3.5)	1.35 (0.43–3.47)
County-level, % below poverty						
<10.00 <sup>d</sup>	2.3 (1.9–2.8)	1.00	1.2 (1.0–1.5)	1.00	2.5 (1.4–4.0)	1.00
10.00–19.99	2.4 (2.2–2.6)	1.05 (0.85–1.30)	1.3 (1.1–1.5)	1.08 (0.84–1.39)	1.2 (0.6–2.1)	0.49 (0.22–1.08)
≥20.00	2.7 (2.1–3.4)	1.18 (0.87–1.60)	0.8 (0.2–2.0)	0.62 (0.16–1.68)	1.3 (0.5–2.8)	0.55 (0.19–1.41)
County-level, % less than high-school graduate						
≤15.99 <sup>d</sup>	2.0 (1.6–2.5)	1.00	1.2 (1.0–1.5)	1.00	2.3 (1.4–3.7)	1.00
16–20.80	2.5 (2.2–2.9)	1.25 (0.96–1.64)	1.2 (1.0–1.4)	0.95 (0.70–1.28)	1.3 (0.4–2.9)	0.55 (0.16–1.46)
20.81–28.76	2.4 (1.9–2.9)	1.17 (0.86–1.59)	1.6 (0.9–2.6)	1.29 (0.71–2.22)	0.9 (0.2–2.4)	0.40 (0.10–1.23)
>28.76	2.5 (2.2–2.8)	1.24 (0.97–1.60)	1.4 (1.1–1.8)	1.13 (0.82–1.56)	1.3 (0.6–2.6)	0.57 (0.22–1.35)

<sup>a</sup>Non-metro rate significantly different from metro rate ( $P < 0.05$ ).

<sup>b</sup>Rate significantly different from <10.00% rate ( $P < 0.05$ ).

<sup>c</sup>Rate significantly different from ≤15.99% rate ( $P < 0.05$ ).

<sup>d</sup>Referent category for rate ratios.

Residing in a county with a large percentage of persons below the poverty level, less than high-school graduates, and in the low SEP group of the poverty-high school index were all associated with IBC in this analysis, suggesting that poverty and education are capturing similar aspects of SEP that affect IBC incidence. As SEP measures, poverty and education both act as a summary measure of a county's SEP and can be compared over time and across U.S. geographic areas (50). While poverty and education are correlated, as each has been shown to be related to overall breast cancer incidence, they were included as separate SEP measures as well as in a combined index in this analysis (16–23, 67). Metro versus non-metro area of residence at diagnosis captures various characteristics that can be directly and/or indirectly related to an individual's health, such as population density, geographic isolation, exposure to agriculture, industrial or commer-

cial complexes, and proximity and access to health care services (68, 69). Furthermore, there are many ways to classify counties based on characteristics such as administrative units, land use, and economic concepts (68). It is possible the definition of metro versus non-metro used in this analysis does not capture specific factors that may be related to IBC and thus explain the lack of association seen.

Although risk factors for IBC remain largely unknown, some studies have shown different risk factor profiles for patients with IBC as compared with patients with non-IBC. Chang and colleagues found that high BMI was significantly associated with increased risk of IBC, regardless of menopausal status (12). This is in contrast to overall breast cancer, where higher premenopausal weight has been shown to reduce risk (70). Chang and colleagues also found patients with IBC were more likely

**Table 3.** Age-adjusted non-IBC IRs per 100,000 and rate ratios (95% CI) stratified by county-level SEP and merged race/ethnicity, 2000–2007

Variable	All races combined			Non-Hispanic White			Black		
	IR	Rate ratio (95% CI)	IR	Rate ratio (95% CI)	IR	Rate ratio (95% CI)	IR	Rate ratio (95% CI)	
Metro	144.4 (143.9–144.9)		158.7 (158.0–159.3)		136.3 (134.7–137.9)		136.3 (134.7–137.9)		
Non-metro	135.5 <sup>a</sup> (134.0–137.0)	0.94 (0.93–0.95)	139.1 <sup>a</sup> (137.5–140.7)	0.88 (0.87–0.89)	131.6 (125.4–138.0)	0.97 (0.92–1.01)	131.6 (125.4–138.0)	0.97 (0.92–1.01)	
County-level, % below poverty									
<10.00 <sup>d</sup>	151.9 (151.0–152.7)	1.00	159.5 (158.6–160.5)	1.00	135.1 (131.8–138.5)	1.00	135.1 (131.8–138.5)	1.00	
10.00–19.99	139.8 <sup>b</sup> (139.2–140.5)	0.92 (0.91–0.93)	155.7 <sup>b</sup> (154.8–156.6)	0.98 (0.97–0.98)	136.0 (134.1–137.9)	1.01 (0.98–1.04)	136.0 (134.1–137.9)	1.01 (0.98–1.04)	
≥20.00	129.9 <sup>b</sup> (128.2–131.5)	0.86 (0.84–0.87)	139.3 <sup>b</sup> (137.2–141.5)	0.87 (0.86–0.89)	137.4 (133.1–141.9)	1.02 (0.98–1.06)	137.4 (133.1–141.9)	1.02 (0.98–1.06)	
County-level, % less than high-school graduate									
≤15.99 <sup>d</sup>	151.2 (150.4–152.1)	1.00	158.6 (157.6–159.6)	1.00	135.9 (132.7–139.2)	1.00	135.9 (132.7–139.2)	1.00	
16–20.80	146.7 <sup>c</sup> (145.8–147.6)	0.97 (0.96–0.98)	158.8 (157.7–159.9)	1.00 (0.99–1.01)	137.6 (134.5–140.8)	1.01 (0.98–1.05)	137.6 (134.5–140.8)	1.01 (0.98–1.05)	
20.81–28.76	136.7 <sup>c</sup> (135.5–138.0)	0.90 (0.89–0.91)	147.1 <sup>c</sup> (145.4–148.7)	0.93 (0.92–0.94)	134.8 (132.0–137.7)	0.99 (0.96–1.02)	134.8 (132.0–137.7)	0.99 (0.96–1.02)	
>28.76	131.6 <sup>c</sup> (130.6–132.6)	0.87 (0.86–0.88)	152.7 <sup>c</sup> (151.2–154.2)	0.96 (0.95–0.97)	135.8 (132.5–139.1)	1.00 (0.97–1.03)	135.8 (132.5–139.1)	1.00 (0.97–1.03)	
Variable	Hispanic White			Asian/Pacific Islander			American Indian/Alaska Native		
IR	Rate ratio (95% CI)	IR	Rate ratio (95% CI)	IR	Rate ratio (95% CI)	IR	Rate ratio (95% CI)	IR	Rate ratio (95% CI)
Metro	105.0 (103.7–106.3)		108.1 (106.6–109.5)		50.3 (46.8–53.9)		50.3 (46.8–53.9)		1.40 (1.21–1.61)
Non-metro	103.6 (97.5–110.0)	0.99 (0.93–1.05)	117.3 <sup>a</sup> (110.3–124.7)	1.09 (1.02–1.16)	70.3 <sup>a</sup> (62.2–79.3)		70.3 <sup>a</sup> (62.2–79.3)		
County-level, % below poverty									
<10.00 <sup>d</sup>	122.6 (119.4–125.8)	1.00	115.1 (112.8–117.4)	1.00	106.4 (98.2–115.0)	1.00	106.4 (98.2–115.0)	1.00	
10.00–19.99	101.5 <sup>b</sup> (100.1–103.0)	0.83 (0.80–0.85)	105.4 <sup>b</sup> (103.6–107.2)	0.92 (0.89–0.94)	47.3 <sup>b</sup> (43.3–51.6)	0.44 (0.40–0.50)	47.3 <sup>b</sup> (43.3–51.6)	0.44 (0.40–0.50)	
≥20.00	98.2 <sup>b</sup> (94.5–102.0)	0.80 (0.77–0.84)	79.0 <sup>b</sup> (71.0–87.6)	0.69 (0.62–0.76)	52.8 <sup>b</sup> (46.4–59.8)	0.50 (0.43–0.58)	52.8 <sup>b</sup> (46.4–59.8)	0.50 (0.43–0.58)	
County-level, % less than high-school graduate									
≤15.99 <sup>d</sup>	121.2 (117.7–124.7)	1.00	116.9 (114.3–119.5)	1.00	115.3 (107.4–123.7)	1.00	115.3 (107.4–123.7)	1.00	
16–20.80	113.2 <sup>c</sup> (110.7–115.8)	0.93 (0.90–0.97)	104.5 <sup>c</sup> (102.2–106.8)	0.89 (0.87–0.92)	46.7 <sup>c</sup> (40.7–53.2)	0.40 (0.35–0.47)	46.7 <sup>c</sup> (40.7–53.2)	0.40 (0.35–0.47)	
20.81–28.76	101.2 <sup>c</sup> (98.0–104.5)	0.84 (0.80–0.87)	89.3 <sup>c</sup> (83.5–95.3)	0.76 (0.71–0.82)	45.3 <sup>c</sup> (38.9–52.5)	0.39 (0.33–0.46)	45.3 <sup>c</sup> (38.9–52.5)	0.39 (0.33–0.46)	
>28.76	96.0 <sup>c</sup> (94.2–97.8)	0.79 (0.77–0.82)	107.4 <sup>c</sup> (104.7–110.2)	0.92 (0.89–0.95)	32.6 <sup>c</sup> (28.2–37.6)	0.28 (0.24–0.33)	32.6 <sup>c</sup> (28.2–37.6)	0.28 (0.24–0.33)	

<sup>a</sup>Non-metro rate significantly different from metro rate ( $P < 0.05$ ).<sup>b</sup>Rate significantly different from <10.00% rate ( $P < 0.05$ ).<sup>c</sup>Rate significantly different from ≤15.99% rate ( $P < 0.05$ ).<sup>d</sup>Referent category for rate ratios

**Table 4.** ORs (95% CI) from 4 HLMs examining the relationship between county-level sociodemographic factors and IBC, SEER Program, 2000–2007<sup>a</sup>

Variable	OR (95% CI)
<i>Model 1</i>	
Non-metro <sup>b</sup>	1.00
Metro	0.90 (0.81–1.00)
Age at diagnosis	0.99 (0.99–0.99)
Race/ethnicity	
Non-Hispanic White <sup>b</sup>	1.00
Black	1.73 (1.59–1.87)
Hispanic White	1.46 (1.34–1.59)
Asian/Pacific Islander	0.79 (0.69–0.89)
American Indian/Alaska Native	1.55 (1.06–2.26)
<i>Model 2</i>	
County-level, % below poverty	
<10.00 <sup>b</sup>	1.00
10.00–19.99	1.06 (0.96–1.18)
≥20.00	1.25 (1.09–1.43)
Age at diagnosis	0.99 (0.99–0.99)
Race/ethnicity	
Non-Hispanic White <sup>b</sup>	1.00
Black	1.70 (1.56–1.84)
Hispanic White	1.44 (1.32–1.57)
Asian/Pacific Islander	0.78 (0.69–0.89)
American Indian/Alaska Native	1.59 (1.14–2.22)
<i>Model 3</i>	
County-level, % less than high-school graduate	
≤15.99 <sup>b</sup>	1.00
16–20.80	1.04 (0.93–1.17)
20.81–28.76	1.11 (0.97–1.28)
>28.76	1.25 (1.10–1.42)
Age at diagnosis	0.99 (0.99–0.99)
Race/ethnicity	
Non-Hispanic White <sup>b</sup>	1.00
Black	1.70 (1.57–1.85)
Hispanic White	1.44 (1.32–1.57)
Asian/Pacific Islander	0.78 (0.69–0.89)
American Indian/Alaska Native	1.62 (1.16–2.26)
<i>Model 4</i>	
Poverty-high school index	
High SEP <sup>b</sup>	1.00
Middle SEP	1.10 (0.98–1.22)
Low SEP	1.26 (1.11–1.44)
Age at diagnosis	0.99 (0.99–0.99)
Race/ethnicity	
Non-Hispanic White <sup>b</sup>	1.00
Black	1.70 (1.56–1.84)
Hispanic White	1.44 (1.32–1.57)
Asian/Pacific Islander	0.78 (0.69–0.89)
American Indian/Alaska Native	1.61 (1.15–2.25)

<sup>a</sup>All variables in each column are mutually adjusted for each other.

<sup>b</sup>Referent category.

to be premenopausal and have younger age at menarche and first birth than patients with non-IBC and non-breast cancer (12).

A study conducted in France by Le and colleagues found that patients with IBC had a lower educational level, a higher BMI, a longer cumulative duration of breastfeeding, and included a greater proportion of non-European women than patients with non-IBC (13). A recent study of Egyptian breast cancer cases found that patients with IBC had significantly lower parity than patients with non-IBC (14). Furthermore, a 2010 study based in Tunisia reported a rural predominance of IBC among the cases studied and hypothesized that the reduction in IBC seen in that country was due, in part, to increasing SEP (71).

In this analysis, IBC was associated with younger age and Black race/ethnicity, whereas Asian/Pacific Islander race/ethnicity was associated with lower odds of IBC, as found in previous studies (1, 6, 7, 15, 33, 64–66). White Hispanic and American Indian/Alaska Native race/ethnicity were also found to be significantly associated with IBC. A previous study showed no difference in the age-adjusted IBC IR between Hispanic and non-Hispanic women for cases diagnosed from 1994 to 1998 reported to the North American Association of Central Cancer Registries (64). However, this study did not classify Hispanic origin as mutually exclusive from other race/ethnicities and used the more restrictive ICD-O-3 8530 code to define IBC (64). Younger age at IBC diagnosis has been reported for American Indian/Alaska Native women as compared with White women (6, 64), although no studies which directly compared the IRs or proportion of IBC between American Indian/Alaska Native women and other race/ethnicities were located.

The strengths of this study include the use of the U.S. SEER database, 5 mutually exclusive race/ethnicity categories, a comprehensive definition of IBC, and a hierarchical modeling structure. The SEER program is considered the standard for cancer registry data quality worldwide (72). Quality control studies, including case-finding, recoding, and reliability studies, are continually conducted by the SEER program to ensure data included in the registries are accurate and collected and recorded in a uniform and timely manner across all registries (72). As IBC is a relatively rare diagnosis, the U.S. SEER database, which covers 26% of the U.S. population residing in varying regions and geographic areas with overrepresentation of minority groups, allows for the stratification of IBC incidence by SEP and race/ethnicity categories (32).

Previous studies have been limited to reporting IBC rates and proportions for a limited number of race/ethnicity categories, usually for White, Black, and Other, due to small numbers of cases as well as the manner in which these data were recorded by SEER (1, 7, 15, 33, 73). Beginning with the November 2005 SEER data submission, the algorithms for creating the race recode variables within the SEER database were revised, allowing for the examination of incidence for 4 race categories: White, Black, American Indian/Alaska Native, and Asian/Pacific

Islander, as well as Hispanic ethnicity (73). The race and Hispanic ethnicity data can also now be merged to create mutually exclusive race/ethnicity categories (73). This allowed for the current analysis to report results for 5 mutually exclusive race/ethnicity categories, as opposed to the more limited race/ethnicity analyses in previous IBC studies.

IBC studies have been hampered by lack of a standard case definition (6, 11, 74). Previous studies have used the ICD-O code 8530 designation to define IBC (7, 64, 65, 75, 76). ICD-O code 8530 is a pathologic designation requiring plugging of the dermal lymphatics with tumor emboli and does not consider clinical skin changes (6). However, this conservative IBC definition is not consistent with the current AJCC staging manual guidelines and may underestimate the true incidence of IBC (6, 7, 64, 77). SEER EOD codes are based on a combined clinical and operative/pathologic assessment abstracted from the pathology report and allow for identification of IBC cases that do not have ICD-O code 8530 as the pathologic diagnosis for years prior to 2004 (7). From 2004 forward, SEER includes a variable with derived AJCC staging, which allows for the identification of IBC cases defined as the primary tumor designation of "T4d" (35, 36). The comprehensive IBC definition used in this article is similar to that used in recent IBC studies (6, 15, 33–35). Use of this definition should help ensure less misclassification of IBC cases to the non-IBC group. Finally, use of a hierarchical modeling structure allows for the calculation of more accurate SEs, thus adding confidence to any significant results found (61–63).

A few limitations should be noted when interpreting the results of this analysis. Though SEER data are broadly representative of the U.S. population, cases recorded in the SEER database are more likely to be foreign born and urban than the U.S. population as measured in the 2000 census (78). There are also a relatively small number of American Indian/Alaska Native IBC cases available for this analysis ( $n = 39$ ), which is reflected in the wide 95% CIs around the IR and OR estimates for this race/ethnicity category. However, because of the U.S. SEER's large size and more than 30 years of follow-up, it is generally considered to accurately represent the overall U.S. cancer population (78).

Another limitation is the lack of individual-level SEP information in the U.S. SEER database and the inherent ecologic bias in interpreting the results of this analysis at the individual level. Any associations seen between county-level SEP and IBC occurrence in this analysis may not necessarily be observed were individual-level SEP available and used in the analysis (79). Therefore, the results of this analysis are better interpreted at the contextual level, that is, the effect being measured is that of residing in a county with a particular SEP characteristic, not that of the breast cancer cases' individual SEP. However, a study comparing census-level SEP measures with individual-level measures found they were similarly associated with individual-level health outcomes (52).

Furthermore, the U.S. SEER database linked to U.S. census data provides a unique opportunity to conduct analyses stratified by race/ethnicity and county-level SEP measures on a relatively large number of IBC and non-IBC cases.

Overall breast cancer has been found to be positively associated with SEP, whereas in this analysis, IBC was associated with decreasing SEP. One explanation for these results is that women of lower SEP have less access to health care that would lead to early detection and the resultant neglected breast cancer develops into IBC. Some earlier IBC work suggested that it may be a subtype of locally advanced breast cancer rather than a distinct entity (80). However, the majority of recent studies on the epidemiology, clinical and prognostic characteristics, biology, and molecular genetics of IBC suggest it is likely a distinct biologic entity from other breast cancer (10, 12–15, 35, 81–84). Another explanation is that breast cancers occurring in women of lower SEP presenting with skin involvement are misdiagnosed as IBC (85, 86). However, there is little literature, especially in the United States, suggesting women of lower SEP are at higher risk for IBC, so it is unlikely that clinicians would be more likely to look for and diagnose (or misdiagnose) IBC disproportionately in women of lower SEP.

These results are in keeping with a growing amount of evidence showing IBC likely has a different risk factor profile than other breast cancers and is a distinct biologic entity (10, 12–15, 35, 81–84). Few studies have examined the epidemiology of rarer forms of breast cancer such as IBC, though studies that have suggested the general breast cancer risk profile may not hold for rarer breast cancer subtypes (1, 65, 87). Further investigation into the etiology of IBC is needed to elucidate risk factors for the disease that would help guide prevention and screening programs, especially studies which examine individual- and community-level associations between multiple SEP measures and IBC incidence. However, these results also indicate studies designed to investigate why the disparity of higher incidence of IBC in lower SEP groups and racial/ethnic minorities is observed, as well as potential interventions to eliminate these differences, are called for. Furthermore, because treatment is especially urgent in IBC, design and implementation of strategies that would promote earlier IBC diagnosis among lower SEP groups and racial/ethnic minorities, which traditionally experience less access to early detection programs, would likely have a direct and favorable impact on their prognosis.

#### Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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