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ORIGINAL PAPER

Disparities in breast cancer subtypes among women in the lower Mississippi Delta Region states

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Abstract

Purpose To describe and elucidate rates in breast cancer incidence by subtype in the federally designated Mississippi Delta Region, an impoverished region across eight Southern/Midwest states with a high proportion of Black residents and notable breast cancer mortality disparities.

Methods Cancer registry data from seven LMDR states (Missouri was not included because of permission issues) were used to explore breast cancer incidence differences by subtype between the LMDR's Delta and non-Delta Regions and between White and Black women within the Delta Region (2012–2014). Overall and subtype-specific age-adjusted incidence rates and rate ratios were calculated. Multilevel negative binomial regression models were used to evaluate how individual-level and area-level factors, like race/ethnicity and poverty level, respectively, affect rates of breast cancers by subtype.

Results Women in the Delta Region had higher rates of triple-negative breast cancer, the most aggressive subtype, than women in the non-Delta (17.0 vs. 14.4 per 100,000), but the elevated rate was attenuated to non-statistical significance in multivariable analysis. Urban Delta women also had higher rates of triple-negative breast cancer than non-Delta urban women, which remained in multivariable analysis. In the Delta Region, Black women had higher overall breast cancer rates than their White counterparts, which remained in multivariable analysis.

Conclusion Higher rates of triple-negative breast cancer in the Delta Region may help explain the Region's mortality disparity. Further, an important area of future research is to determine what unaccounted for individual-level or social area-level factors contribute to the elevated breast cancer incidence rate among Black women in the Delta Region.

Keywords Breast cancer · Triple-negative · Cancer disparities

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Introduction

The Delta Regional Authority (Delta Region, Supplemental Fig. 1) is a federally designated region that includes 252 counties in the eight Lower Mississippi Delta Region (LMDR) of Alabama, Arkansas, Illinois, Kentucky, Louisiana, Mississippi, Missouri, and Tennessee. More than a third of residents in the Delta Region are Black, and more than 20% of the population live in poverty [1]. Additionally, this region is largely rural and has limited access to healthcare services [2, 3]. These factors make the Region vulnerable to a myriad of health disparities, including breast cancer disparities. Women in the Delta Region have higher rates of breast cancer mortality than women in the rest of the country, including nine of the ten highest county-level breast cancer mortality rates [4, 5]. Further, Black women in the Delta Region have a higher breast cancer mortality rate than White women in the Region and a higher mortality rate than Black women in other parts of the country [4]. One recent study found that in six LMDR states, Black women had higher breast cancer incidence rates than White women [6]. There is limited research on what factors contribute to these mortality disparities and how breast cancer incidence is distributed within the Delta and non-Delta Regions of the LMDR states and by race within the Delta Region.

Breast cancer can be classified into four molecular subtypes based upon the presence or absence of two broad tumor characteristics—hormone (i.e., estrogen and progesterone) receptor (HR) and human epidermal growth factor 2 (HER2) status: (1) HR+/HER2−; (2) HR+/HER2+; (3) HR−/HER+; (4) HR−/HER2− ("triple-negative") [7]. Breast cancer subtypes play a role in cancer's aggressiveness and, in addition to stage at diagnosis and nodal status, inform the use of chemotherapy and targeted drug treatments [8]. HR+ cancers have a better prognosis and more comprehensive treatment options than HR− cancers [8–10]. Triple-negative breast cancer is the most aggressive and has limited treatment options [8]. While central cancer registries have been required to collect HR status since 1990, HER2 status has only been required since 2010 [7]. Therefore, population-based assessment of the distribution of breast cancer by subtype is burgeoning but still limited.

Risk of breast cancer by subtype varies by race/ethnicity, age, socioeconomic status, and geography. Multiple studies indicate that Black women have higher risk of HR- breast cancers compared to White women, even after controlling for other factors [11, 12]. Meanwhile, White women have higher rates of the HR+/HER2− cancers than other racial/ethnic groups [13]. Women under the age of 50 are at greater risk for HR− breast cancers [14, 15]. Although the relationship between HR− cancers and socioeconomic status is unclear in current studies, some have suggested that the poverty may be a social factor facilitating angiogenesis and other biological processes related to cancer growth, especially amongst Black women [16–20]. The incidence of each breast cancer subtype varies by geographic region: HR+/HER2− cancers cluster in the Northeast, and triple-negative cancers cluster in the South and Midwest [7, 16].

The Delta Region's sociodemographic composition suggests it may have higher incidence rates of triple-negative cancers that may contribute to the breast cancer mortality disparity. Therefore, our objective was threefold. First, we described the subtype-specific incidence rates of breast cancer in the Delta Region compared to those in the non-Delta Region of the LMDR states. Second, we determined how subtype-specific incidence rates differ between White and Black women within the Delta Region. Thirdly, we determined how the differences in these subtype rates may be explained by individual-level and area-level factors, like age and county-level poverty rates, respectively.

Methods

Cancer incidence data

We used data from the North American Association of Central Cancer Registries (NAACCR) Cancer in North America Deluxe File [21]. This file provided individual-level data on all breast cancer cases diagnosed between 2012 and 2014 in seven LMDR States (Alabama, Arkansas, Illinois, Kentucky, Louisiana, Mississippi, and Tennessee). Missouri's registry did not provide the necessary consent for their data to be used.

Inclusion/exclusion criteria aimed to optimize the accuracy of rate calculations and data quality for breast cancer subtype analyses as guided by previous study [13]. Cases included all invasive female breast cancers, but excluded histology codes indicative of mesothelioma, Kaposi's sarcoma, or leukemia/lymphoma and cases missing on race/ethnicity and county of residence, cases 85+ years of age, and/or cases reported by death certificate, autopsy report, nursing home, or hospice. Using collaborative staging site-specific factors and guidance from previous registry-based studies, molecular subtypes of breast cancer cases were categorized: (1) HR+/HER2−; (2) HR+/HER2+; (3) HR−/HER2+; (4) HR−/HER2− (triple-negative); (5) unknown [11]. Following the precedent of previous cancer registry analyses, estrogen receptor (ER) and progesterone receptor (PR) were considered jointly as a cancer case's HR status [9, 11, 12, 17]. ER+ and/or PR+ or borderline status were considered HR+; cases that were ER− and PR− were considered HR−. HER2 cases that were borderline were considered unknown. Cases

for which status was otherwise unknown or had no testing documented or performed were considered of unknown subtype.

Area-level data

County-level variables were extracted from the American Community Survey (ACS), National Cancer Institute (NCI), United States Department of Agriculture (USDA), and the Area Health Resource File (AHRF) [22–25]. 2010–2014 ACS county-level estimates of % living in poverty, median household income, % with at least a high school education, and % of the population that identify as Black were extracted [22]. USDA's Rural–Urban Continuum Codes characterized rural and urban counties by a county's population size and adjacency to a metropolitan area (urban = 1–3; rural = 4–9) [23]. NCI's State Cancer Profile provided county-level modeled estimates of the percentage of women aged 40+ who had a mammogram in the past 2 years [24]. County-level number of primary care physicians per 100,000 (i.e., provider density) were extracted from the AHRF [25].

Age-adjusted incidence rates and rate ratio calculations

We calculated age-adjusted incidence rates (IR) and rate ratios (RR) with 95% confidence intervals for all invasive breast cancers combined, individual subtypes, and unknown subtype by Delta and non-Delta Region status. Stratified analyses were performed by race/ethnicity, rural–urban status, and % in poverty. We also calculated age-specific rates for all invasive breast cancers combined and across subtype groups by Delta Region status. Additional IR and RR calculations were performed to evaluate racial, rural–urban, and poverty level differences within the Delta Region specifically. These analyses were performed using SEER*Stat 8.4.3.

Multilevel regression models

Proc GLIMMIX in SAS 9.4 was used to construct multilevel regression models to calculate RRs for all breast cancers, each subtype individually, and breast cancers of unknown subtype as a means of comparing the Delta Region to the non-Delta Region overall and stratified by race/ethnicity, rural–urban status, and poverty level. Parallel analyses were performed examining solely Delta Region cases to assess race/ethnic, rural–urban, and poverty level differences within the Region.

Because counts were overdispersed for all breast cancers combined, each individual subtype, and for cancers of unknown subtype, we constructed multilevel negative binomial regression models. For these models, analyses cells were constructed containing the number of cases in each county within each analysis cell, which were divided by age (< 50 years of age and 50+ years of age) and race/ethnicity (Non-Hispanic White, Non-Hispanic Black, and Hispanic/Non-Hispanic/Other). Analysis groups were divided at age 50 because it is the age at which estrogen receptor-negative cancer rates peak; it can be used as a proxy age for menopause; and it is the recommended initiation age for mammography for women of average risk [26–28]. County was included in all models as both a random and a fixed effect and analysis cells were considered in all models as fixed effects. Age and race/ethnicity-specific rates were calculated for the entire geographic area of our study to estimate the expected counts for each analysis cell. The natural log of these expected counts was included in each model as an offset variable.

We used sociodemographic factors identified in previous research as area-level variables to be considered in the multivariable regression model building process [29]. These factors may explain incidence rate differences between the Delta and non-Delta Regions within the seven LMDR states. Because sociodemographic variables are often collinear, correlations among these variables were assessed and were indeed found to be strong. Therefore, only one sociodemographic variable was included in the model—poverty level—as poverty has been considered the most robust socioeconomic variable for measuring inequalities in cancer incidence [30]. Other area-level variables included in the analysis were rural–urban status, provider density, and mammography utilization. Provider density proved to be non-significant in all models and caused poorer goodness of fit as measured by the Akaike Information Criterion, and therefore was excluded in final models. Exponentials of resultant coefficients were used to estimate RRs.

Results

A total of 82,223 invasive breast cancer cases were diagnosed in these seven LMDR states between 2012 and 2014. Among these cases, 19,334 (23.5%) occurred in the Delta Region, and 62,889 (76.5%) occurred in the non-Delta Region. Supplementary Table 1 summarizes the distribution of subtypes by sociodemographic characteristics.

For all breast cancer cases, the IR was lower in the Delta Region (IR = 116.2 per 100,000) compared to the non-Delta Region (IR = 120.8; RR = 0.96; 95% CI 0.95–0.98) (Table 1). The rates of all breast cancers combined and stratified by age (< 50 or 50+ years of age) were higher in the non-Delta Region for both stratifications. When rates were stratified by race/ethnicity, non-Hispanic White women in the Delta Region had a statistically significantly lower rate of breast cancer than non-Delta White women (RR = 0.92;

Table 1 Age-adjusted incidence rates of invasive breast cancer and hormone receptor positive breast cancers by Delta Region status and stratified by age, race/ethnicity, rural–urban status, and poverty level

	All cases			HR+/HER2+			HR+/HER2−		
	Cases	IR[a]	RR (95% CI)	Cases	IR[a]	RR (95% CI)	Cases	IR[a]	RR (95% CI)
All									
Delta	19,334	116.2	**0.96 (0.95–0.98)**	1,911	11.8	**0.93 (0.88–0.98)**	11,684	69.4	**0.88 (0.86–0.90)**
Non-Delta	62,889	120.8	Ref	6,419	12.7	Ref	41,311	78.7	Ref
< 50 years old									
Delta	3,664	42.1	0.98 (0.94–1.02)	469	5.4	**0.88 (0.79–0.98)**	1,918	22.0	**0.88 (0.84–0.93)**
Non-Delta	12,198	43.0	Ref	1,728	6.1	Ref	7,126	25.0	Ref
50+ years old									
Delta	15,670	321.9	**0.96 (0.94–0.97)**	1,442	29.4	0.95 (0.90–1.01)	9,766	200.7	**0.88 (0.86–0.90)**
Non-Delta	50,691	336.6	Ref	4,691	30.8	Ref	34,185	227.6	Ref
Non-Hispanic Whites									
Delta	12,795	114.5	**0.92 (0.91–0.94)**	1,273	11.9	**0.92 (0.86–0.98)**	8,285	72.9	**0.88 (0.86–0.90)**
Non-Delta	50,586	123.9	Ref	5,052	13.0	Ref	34,281	82.9	Ref
Non-Hispanic Blacks									
Delta	6,089	122.9	0.99 (0.96–1.03)	591	11.9	0.94 (0.84–1.04)	3,118	63.3	**0.93 (0.88–0.97)**
Non-Delta	8,728	123.8	Ref	911	12.7	Ref	4,772	68.4	Ref
Hispanics									
Delta	282	89.1	1.05 (0.92–1.19)	31	8.8	0.84 (0.55–1.23)	184	59.4	1.09 (0.92–1.27)
Non-Delta	2,213	84.8	Ref	289	10.4	Ref	1,383	54.8	Ref
Urban									
Delta	12,222	119.7	**0.97 (0.95–0.99)**	1,200	11.9	**0.93 (0.87–0.99)**	7,529	73.2	**0.90 (0.87–0.92)**
Non-Delta	49,817	123.2	Ref	5,082	12.8	Ref	33,182	81.6	Ref
Rural									
Delta	7,112	110.8	0.98 (0.96–1.01)	711	11.4	0.95 (0.87–1.05)	4,155	63.4	**0.92 (0.88–0.96)**
Non-Delta	13,072	112.6	Ref	1,337	12.0	Ref	8,129	69.0	Ref
< 20% below poverty									
Delta	8,824	119.0	**0.97 (0.95–0.99)**	891	12.2	0.96 (0.89–1.03)	5,425	72.3	**0.89 (0.86–0.92)**
Non-Delta	52,265	122.9	Ref	5,288	12.7	Ref	34,816	81.3	Ref
20+% below poverty									
Delta	10,510	114.0	1.02 (1.00–1.05)	1,020	11.4	0.93 (0.85–1.02)	6,259	67.0	1.00 (0.96–1.03)
Non-Delta	10,624	111.3	Ref	1,131	12.2	Ref	6,495	67.2	Ref

IR incidence rate, *RR* rate ratio, *Ref* reference group

Statistically significant RRs ($p < 0.05$) are in bold

[a]Rates are expressed per 100,000 population

95% CI 0.91–0.94). The Delta Region had statistically significantly lower rates of both HR+/HER2+ (RR = 0.93; 95% CI 0.88–0.98) and HR+/HER2− (RR = 0.88; 95% CI 0.86–0.90) breast cancers than the non-Delta Region. Non-Hispanic Black Delta women (RR = 0.93; 95% CI 0.88–0.97) had statistically significantly lower rates of HR+/HER2− cancers than those in the non-Delta Region, as did non-Hispanic White women (RR = 0.88; 95% CI 0.86–0.90).

Women in the Delta Region (IR = 17.0) had statistically significantly higher rates of triple-negative breast cancer than non-Delta Region women (IR = 14.4) (RR = 1.18; 95% CI 1.13–1.24) (Table 2). In stratified analyses, the greatest rate difference was among Delta women under 50 years of age who had statistically significantly higher rates of triple-negative breast cancer than their non-Delta counterparts (RR = 1.29; 95% CI 1.18–1.40). Non-Hispanic Black women in the Delta Region (IR = 26.8) had statistically significantly higher rates of triple-negative breast cancer than their non-Delta counterparts (IR = 24.6) (RR = 1.09; 95% CI 1.01–1.17). Urban women in the Delta Region had statistically significantly higher triple-negative breast cancer IRs than non-Delta urban women (RR = 1.26; 95% CI 1.19–1.33). Rates of unknown subtype were higher in the Delta Region than the non-Delta Region (RR = 1.30; 95% CI 1.23–1.37). Age-specific rates overall and by subtype are displayed in Supplemental Fig. 2.

Table 2 Age-adjusted incidence rates of hormone receptor-negative breast cancers and unknown subtype by Delta Region status by age, race/ethnicity, rural–urban status, and poverty level

	HR−/HER2+			Triple negative			Unknown		
	Cases	IR[a]	RR (95% CI)	Cases	IR[a]	RR (95% CI)	Cases	IR[a]	RR (95% CI)
All									
Delta	872	5.3	1.03 (0.95–1.11)	2,735	17.0	**1.18 (1.13–1.24)**	2,132	12.7	**1.30 (1.23–1.37)**
Non-Delta	2,677	5.2	Ref	7,334	14.4	Ref	5,150	9.8	Ref
< 50 years old									
Delta	190	2.2	0.98 (0.83–1.15)	735	8.4	**1.29 (1.18–1.40)**	352	4.0	**1.34 (1.18–1.52)**
Non-Delta	631	2.2	Ref	1,858	6.6	Ref	855	3.0	Ref
50+ years old									
Delta	682	14.0	1.05 (0.96–1.14)	2,000	40.9	**1.13 (1.08–1.19)**	1,780	36.9	**1.28 (1.21–1.36)**
Non-Delta	2,044	13.4	Ref	5,476	36.1	Ref	4,295	28.7	Ref
Non-Hispanic Whites									
Delta	502	4.6	0.91 (0.82–1.01)	1,341	12.8	0.97 (0.91–1.03)	1,394	12.3	**1.26 (1.18–1.34)**
Non-Delta	2,011	5.1	Ref	5,176	13.2	Ref	4,066	9.8	Ref
Non-Hispanic Blacks									
Delta	348	6.9	1.09 (0.94–1.26)	1,340	26.8	**1.09 (1.01–1.17)**	692	14.1	**1.20 (1.08–1.33)**
Non-Delta	461	6.3	Ref	1,760	24.6	Ref	824	11.8	Ref
Hispanics									
Delta	***	***	***	31	10.1	1.03 (0.68–1.50)	28	8.5	1.41 (0.90–2.13)
Non-Delta	114	3.8	Ref	269	9.8	Ref	158	6.0	Ref
Urban									
Delta	585	5.8	**1.13 (1.02–1.24)**	1,803	18.0	**1.26 (1.19–1.33)**	1,105	10.7	**1.16 (1.08–1.24)**
Non-Delta	2,069	5.2	Ref	5,705	14.3	Ref	3,779	9.3	Ref
Rural									
Delta	287	4.5	0.84 (0.72–0.98)	932	15.6	1.06 (0.97–1.16)	1,027	15.9	**1.37 (1.26–1.49)**
Non-Delta	606	5.4	Ref	1,629	14.7	Ref	1,371	11.6	Ref
< 20% below poverty									
Delta	389	5.3	1.03 (0.92–1.15)	1,151	16.2	**1.13 (1.06–1.20)**	968	13.0	**1.39 (1.29–1.49)**
Non-Delta	2,175	5.1	Ref	5,983	14.3	Ref	4,003	9.4	Ref
20+% in poverty									
Delta	483	5.3	1.00 (0.88–1.14)	1,584	17.8	1.21 (1.12–1.31)	1,164	12.5	1.06 (0.97–1.15)
Non-Delta	500	5.3	Ref	1,351	14.7	Ref	1,147	11.9	Ref

IR incidence rate, *RR* rate ratio, *Ref* reference group

Statistically significant RRs ($p < 0.05$) are in bold

[a]Rates are expressed per 100,000 population

In the Delta Region specifically, non-Hispanic Black women had statistically significantly higher breast cancer rates than non-Hispanic White women (RR = 1.07; 95% CI 1.04–1.11) (Table 3). For HR+/HER2− breast cancers, Hispanic and non-Hispanic Black women had statistically significantly lower rates than non-Hispanic White Delta Region women. Both overall rates of breast cancer and HR+/HER2− breast cancers were lower in the rural and more impoverished Delta Region compared to the urban and less impoverished areas of the Region. Rates of HR−/HER2+ were higher in Delta Region non-Hispanic Black women than non-Hispanic White women (RR = 1.49; 95% CI 1.28–1.71) (Table 4). Triple-negative breast cancer rates were more than twice as high among non-Hispanic Black women (IR = 26.8) compared to non-Hispanic White women in the Delta Region (IR = 12.8) (RR = 2.10; 95% CI 1.94–2.27). Unknown subtype IRs were higher in non-Hispanic Black women compared to non-Hispanic White women and rural compared to urban women in the Delta Region.

In multivariable analysis, the Delta Region had higher rates of unknown subtype (RR = 1.19; 95% CI 1.05–1.35) compared to the non-Delta Region, but there were no other statistically significant differences between the regions after accounting for age and race/ethnicity groupings and area-level factors (Table 5). There were no significant Delta/

Table 3 Age-adjusted incidence rates of all breast cancer cases and hormone receptor positive breast cancers by race/ethnicity, rural–urban status, and poverty level in the Delta Region

	All cases			HR+/HER2+			HR+/HER2−		
	Cases	IR[a]	RR (95% CI)	Cases	IR[a]	RR (95% CI)	Cases	IR[a]	RR (95% CI)
Race/ethnicity									
Hispanic	282	89.1	0.78 (0.69–0.88)	31	8.8	0.74 (0.49–1.06)	184	59.4	**0.82 (0.70–0.95)**
Non-Hispanic Black	6,089	122.9	**1.07 (1.04–1.11)**	591	11.9	1.00 (0.90–1.11)	3,118	63.3	**0.87 (0.83–0.91)**
Non-Hispanic White	12,795	114.5	Ref	1,273	11.9	Ref	8,285	72.9	Ref
Rural–urban status									
Rural	7,112	110.8	**0.93 (0.90–0.95)**	711	11.4	0.96 (0.87–1.06)	4,155	63.4	**0.87 (0.83–0.90)**
Urban	12,222	119.7	Ref	1,200	11.9	Ref	7,529	73.2	Ref
Poverty level									
20+% poverty	10,510	114.0	**0.96 (0.93–0.99)**	1,020	11.4	0.93 (0.85–1.02)	6,259	67.0	**0.93 (0.89–0.96)**
< 20% poverty	8,824	119.0	Ref	891	12.2	Ref	5,425	72.3	Ref

IR incidence rate, *RR* rate ratio, *Ref* reference group

Statistically significant RRs ($p < 0.05$) are in bold

[a]Rates are expressed per 100,000 population

Table 4 Age-adjusted incidence rates of hormone receptor-negative breast cancers and unknown subtype in the Delta Region by race/ethnicity, rural–urban status, and poverty level in the Delta Region

	HR−/HER2+			Triple negative			Unknown		
	Cases	IR[a]	RR (95% CI)	Cases	IR[a]	RR (95% CI)	Cases	IR[a]	RR (95% CI)
Race/ethnicity									
Hispanic	***	***	***	31	10.1	0.79 (0.53–1.13)	28	8.5	0.69 (0.45–1.00)
Non-Hispanic Black	348	6.9	**1.49 (1.28–1.71)**	1,340	26.8	**2.10 (1.94–2.27)**	692	14.1	**1.15 (1.04–1.26)**
Non-Hispanic White	502	4.6	Ref	1,341	12.8	Ref	1,394	12.3	Ref
Rural–urban status									
Rural	287	4.5	0.79 (0.68–0.91)	932	15.6	**0.86 (0.80–0.94)**	1,027	15.9	**1.48 (1.35–1.61)**
Urban	585	5.8	Ref	1,803	18.0	Ref	1,105	10.7	Ref
Poverty level									
20+% poverty	483	5.3	1.00 (0.87–1.15)	1,584	17.8	**1.10 (1.01–1.19)**	1,164	12.5	0.97 (0.88–1.05)
< 20% poverty	389	5.3	Ref	1,151	16.2	Ref	968	13.0	Ref

IR incidence rate, *RR* rate ratio, *Ref* reference group

***Rate ratio suppressed as it is based on fewer than 16 cases; statistically significant RRs ($p < 0.05$) are in bold

[a]Rates are expressed per 100,000 population

non-Delta differences in rates of any kind after controlling for relevant factors for either age stratification, except for unknown subtype in women aged 50+ in the Delta Region (RR = 1.17; 95% CI 1.03–1.34). Among rural populations, the Delta Region had lower rates of HR−/HER2+ (RR = 0.80; 95% CI 0.69–0.93) and higher rates of unknown status (RR = 1.26; 95% CI 1.08–1.47) compared to the non-Delta Region after accounting for confounders. Among urban populations, the Delta Region had statistically significantly higher rates of triple-negative breast cancer (RR = 1.10; 95% CI 1.01–1.20) after controlling for relevant factors.

In the Delta Region alone, non-Hispanic Black women had higher rate of breast cancers (RR = 1.06; 95% CI 1.02–1.10) after accounting for age and area-level factors (Table 6). Hispanics had lower rates of HR+/HER2− cancers (RR = 0.82; 95% CI 0.69–0.97) compared to non-Hispanic White women after accounting for age and area-level variables. Compared to urban populations, rural populations had higher rates of breast cancers of unknown subtypes (RR = 1.42; 95% CI 1.14–1.76) after controlling for confounders.

Table 5 Multilevel negative binomial regression modeling of invasive breast cancers by Delta Region status and stratified by age, race/ethnicity, rural–urban status, and poverty level

	All breast cancers RR (95% CI)	HR+/HER2+ RR (95% CI)	HR+/HER2− RR (95% CI)	HR−/HER2+ RR (95% CI)	Triple negative RR (95% CI)	Unknown RR (95% CI)
All cases[a]	1.00 (0.97–1.02)	0.95 (0.89–1.01)	0.98 (0.94–1.02)	0.96 (0.87–1.05)	1.01 (0.95–1.08)	**1.19 (1.05–1.35)**
Age[b]						
50+ years old	0.99 (0.97–1.02)	0.94 (0.87–1.02)	0.98 (0.94–1.02)	0.96 (0.87–1.07)	0.99 (0.93–1.06)	**1.17 (1.03–1.34)**
< 50 years old	1.01 (0.96–1.06)	0.96 (0.85–1.08)	0.98 (0.91–1.05)	0.93 (0.77–1.11)	1.09 (0.98–1.22)	1.22 (0.98–1.51)
Race/ethnicity[c]						
Non-Hispanic White	0.98 (0.95–1.01)	0.95 (0.89–1.03)	0.96 (0.92–1.00)	0.92 (0.82–1.02)	1.00 (0.93–1.07)	**1.18 (1.04–1.35)**
Non-Hispanic Black	1.04 (0.98–1.09)	0.80 (0.70–0.90)	1.01 (0.94–1.09)	0.86 (0.69–1.06)	1.07 (0.96–1.18)	1.14 (0.90–1.44)
Hispanic	1.02 (0.85–1.21)	0.92 (0.62–1.36)	1.08 (0.88–1.32)	***	1.02 (0.75–1.38)	1.02 (0.66–1.58)
Rural–urban status[d]						
Rural	1.00 (0.97–1.03)	0.94 (0.85–1.03)	0.99 (0.94–1.04)	**0.80 (0.69–0.93)**	0.93 (0.85–1.02)	**1.26 (1.08–1.47)**
Urban	0.99 (0.95–1.03)	0.95 (0.87–1.04)	0.95 (0.90–1.02)	1.07 (0.95–1.20)	**1.10 (1.01–1.20)**	1.06 (0.85–1.31)
Poverty level[e]						
< 20% below poverty	0.98 (0.94–1.01)	0.97 (0.89–1.06)	0.91 (0.86–0.96)	1.01 (0.89–1.15)	1.07 (0.98–1.17)	**1.29 (1.07–1.55)**
20+ % below poverty	1.00 (0.97–1.04)	0.93 (0.85–1.01)	1.02 (0.97–1.08)	0.90 (0.78–1.04)	0.93 (0.84–1.01)	1.15 (0.97–1.37)

Non-Delta Region is reference group, *RR* rate ratio

[a]Adjusting for age, race/ethnicity, rural–urban status, poverty level, area mammography utilization, and race/rural–urban status interaction (if statistically significant)

[b]Adjusting for race/ethnicity, rural–urban status, area mammography utilization, and race/rural–urban status interaction

[c]Adjusting for age, area mammography utilization, and poverty level

[d]Adjusting for age, race/ethnicity, area mammography utilization, and poverty level

[e]Adjusting for age, race/ethnicity, area mammography utilization, rural–urban status, and race/rural–urban status interaction

***Rate ratio suppressed as it is based on fewer than 16 cases: statistically significant RRs ($p < 0.05$) are in bold

Table 6 Multilevel negative binomial regression modeling of invasive breast cancer by subtype in the Delta Region

	All breast cancers RR (95% CI)	HR+/HER2+ RR (95% CI)	HR+/HER2− RR (95% CI)	HR−/HER2+ RR (95% CI)	Triple negative RR (95% CI)	Unknown RR (95% CI)
Race/ethnicity						
Non-Hispanic White	Ref	Ref	Ref	Ref	Ref	Ref
Non-Hispanic Black	**1.06 (1.02–1.10)**	1.02 (0.89–1.16)	0.98 (0.92–1.04)	1.10 (0.93–1.29)	1.05(0.96– 1.15)	0.99 (0.89–1.11)
Hispanic	0.93 (0.84–1.03)	0.96 (0.67–1.36)	**0.82 (0.69–0.97)**	***	0.97 (0.74–1.29)	1.10 (0.81–1.49)
Rural–urban status						
Urban	Ref	Ref	Ref	Ref	Ref	Ref
Rural	0.99 (0.95–1.04)	0.97 (0.86–1.09)	0.98 (0.92–1.04)	0.86 (0.73–1.01)	0.97 (0.88–1.06)	**1.42 (1.14–1.76)**
Poverty level						
< 20% below poverty	Ref	Ref	Ref	Ref	Ref	Ref
20+% below poverty	0.96 (0.92–1.00)	0.94 (0.85–1.05)	0.99 (0.93–1.06)	0.98 (0.84–1.15)	**0.89 (0.81–0.99)**	0.97 (0.78–1.20)

RR rate ratio; all models also adjusted for age group, mammography utilization, and race rural–urban status interaction (if significant)

***Rate ratio suppressed as it is based on fewer than 16 cases; statistically significant RRs ($p < 0.05$) are in bold

Discussion

We examined breast cancer IR differences between the Delta and non-Delta regions of seven LMDR states for all cancers and stratified by subtype. Overall breast cancer IRs were higher in the non-Delta Region. However, women in the Delta Region had higher IRs of triple-negative breast cancer compared to non-Delta Region women. This difference was restricted to Black in particular, but not White women. Regardless of stratifications, Delta women had higher rates of unknown subtype. After accounting for

confounding characteristics, the elevated rate of triple-negative breast cancer in the Delta Region was attenuated. However, among women living in urban counties, the elevated rate of triple-negative breast cancer in the Delta Region remained after adjustment. Analyses of data from the Delta Region only indicated that Black women in the region had higher rates of breast cancer overall than White women, but rates of HR+/HER2- were higher in the White women. The elevated overall breast cancer incidence rate in Black Delta women remained in multivariable analysis. Black women in the Delta Region also had higher rates of both HR−/HER2+ and triple-negative breast cancers in descriptive analysis.

Descriptive analysis found that women in the Delta Region had lower breast cancer IRs overall and for the HR+/HER2− subtype than women in the Delta Region across most stratifications, although this was explained by factors like age, race, and area-level variables. Previous studies have shown that—generally speaking at a state level—mammography utilization is associated with higher rates of breast cancer overall and HR+/HER2− specifically [13]. Similarly, a pooled analysis by Akinyemiju et al. found higher rates of breast cancer in urban populations [31]. Indeed, over the last 20 years, the Delta Region has consistently had lower rates of mammography utilization compared to the non-Delta part of the LMDR and the rest of the country [3, 32]. Further, the Delta Region is more rural than the rest of the LMDR [3, 33]. The lower overall rates of breast cancer and HR+/HER2− breast cancers in the Delta Region corroborate previous studies and may be explained by utilization of mammography and rurality of the Delta Region [3, 13, 31, 32, 34].

Triple-negative breast cancer IRs were higher in the Delta Region compared to the non-Delta Region overall and among non-Hispanic Blacks and urban populations, specifically, which may help explain the Region's higher breast cancer mortality rate, as triple-negative breast cancers have worse survival than other subtypes [4]. Multiple studies have shown higher rates of triple-negative breast cancer in the South and Midwest than other parts of the country. These findings indicate that elevated rates may be particularly high within specific sub-areas notably the Delta Region [13, 16].

Urban women in the Delta Region had higher rates of triple-negative breast cancer, even after accounting for important risk factors like age and race. However, other risk factors like greater parity and lack of breastfeeding/short duration of breastfeeding among parous women can increase one's risk for triple-negative breast cancer [35], but we were unable to account for them in our study. Among metropolitan areas with greater than half a million residents, the Memphis metropolitan area—the largest city in the Delta Region—has the highest birth rates in the country [36]. Caution must be exercised not to fall prey to ecological fallacy, but the high birth rate among urban women in the Delta Region may play a role in the high rate of triple-negative breast cancer. Additionally, multiple studies have shown that parous women who do not breastfeed or who had short breastfeeding duration are at greater risk for triple-negative breast cancer, and similarly, breastfeeding has been shown to reduce the risk of triple-negative breast cancers in parous women [35, 37, 38]. However, the effect of individual-level parity, breastfeeding initiation, and breastfeeding duration in the urban Delta is unknown. Future research should aim to further explore the factors that contribute to these higher rates of triple-negative breast cancer in the urban Delta.

In the Delta Region, non-Hispanic Black women had higher rates of breast cancer compared to non-Hispanic White women in both descriptive and multivariable analyses. This finding corroborates a study by DeSantis et al. which found that breast cancer IRs in five Delta Region states were higher in Black women than in White women [6]. Previous studies have suggested that the convergence of breast cancer IRs in Black and White populations is driven by increased mammography utilization and increased rates of HR+/HER2− or ER+ breast cancers among Black women [6, 39]. In the Delta Region, however, the elevated rates of breast cancer among Black women are driven by HR− cancers, as both HR−/HER2+ and triple-negative breast cancer rates are higher among Black women. The elevated incidence of breast cancer in Black women, even after accounting for age and area-level factors, suggests that there may be other area-level factors or individual factors specific to Black women in the region that may contribute to higher rates. Perceived experience of racial discrimination has been associated with increased risk of breast cancer, especially in young Black women, among whom HR− cancers are more common [40]. Similarly, Geronimus et al. posit a "weathering hypothesis," where Black women disproportionately experience a myriad of life stressors that contribute to biological indicators of stress (i.e., shorter telomere length and increased allostatic load) subsequently putting them at greater risk for chronic diseases, potentially including HR− breast cancers [41–43]. Hébert et al. also note that racial and ethnic minorities may experience particular social stressors and biological sequelae that increase risk for cancer [44]. A study by Krieger found that Black women born in or living in states that once had discriminatory Jim Crow laws (which includes six of the seven states in the present study) had higher rates of estrogen receptor-negative cancers than those born in states that did not have Jim Crow laws [45]. While the relationship between racial discrimination and increased cumulative stressors and their impacts on breast cancer is a burgeoning field of study, the history and lasting effects of slavery, segregation, and marginalization, which may be more concentrated in the Delta Region, may indeed play a role in the elevated risk of breast cancer among Black women in the Region [46]. There

is a great opportunity for social epidemiologists and other researchers to further explicate the relationship between the historical and current social context of the Delta Region and its effect on breast cancer.

Higher rates of unknown subtype in the Delta Region were found in both descriptive and multivariable analyses across many stratifications. The study inclusion/exclusion criteria aimed to maximize completeness of subtype data. However, missing information on cancer cases is more common among Black women and in areas of low socioeconomic status [47–49]. Race- and county-level poverty were included in multivariable analysis and rates of unknown subtype, yet higher rates of unknown status remained, especially in the rural Delta. In addition to socioeconomic factors, the location of case ascertainment may play a role in data completeness [7, 46]. Breast cancer cases diagnosed among rural Delta Region women may be more likely to be diagnosed in smaller hospitals in impoverished areas where data reporting may be incomplete. Further, there is a nationwide cancer registrar shortage which could be at an even greater shortage in the Delta Region [50]. This may affect the abstraction of cancer information in the Region's rural hospitals in particular. Additionally, the rate of unknown subtype subsequently has an effect on the other rates. For example, HER2+ is the more common HER2 status, but in order for a case to be defined by that status, a definitive HER2 status of positive must be reported. Thus, HER2+ cancers, in particular, may be underrepresented. Future research should explore the multilevel factors that may affect data completeness to help ensure accurate population statistics and cancer control efforts.

Our study was not without limitations. First, Missouri did not provide active consent for their data to be included in this study. Its exclusion may affect the study findings. For example, Delta Region disparities were identified for triple-negative breast cancers in urban populations especially. The absence of data from non-Delta urban areas with a high proportion of Black residents like St. Louis and Kansas City may affect subtype-specific findings. Also, data on individual-level factors that affect the risk of different breast cancer subtypes are not available, including breastfeeding, oral contraceptive use, parity, age a first live birth, obesity, breastfeeding, diet, and physical activity. Additionally, we were not able to account for other important factors like individual-level income.

Our study also had several strengths. First, it was one of the first to explore cancer incidence across the multi-state Delta Region, as well as one of the first to explore differences in breast cancer subtype at a sub-state level. Second, we utilized population-based data inclusive of all cancer cases diagnosed in the LMDR states. Third, we employed multilevel modeling to explore place-based effects on cancer, which is underutilized in rural cancer research in particular [51].

Conclusions

The high rate of triple-negative breast cancer in the Delta Region may help explain the breast cancer mortality disparity that exists in the Region. Both the elevated rates of triple-negative breast cancer in the urban Delta region and the overall elevated rate of breast cancer among Black women in the Delta may be explained by individual-level factors like parity and breastfeeding initiation or duration. Additionally, these elevated rates may be explained by more upstream, area-level factors like discrimination that affect the biology of cancer etiology in Black, urban women. Future research should explore the effect of unmeasured individual and area-level factors that may contribute to the disparities experienced by women in the Delta Region.

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References

1. Delta Regional Authority (2017) Today's Delta: a research tool for the region: 3rd edition. http://dra.gov/images/uploads/content_files/DRA_Todays_Delta_2016.pdf Accessed 9 Aug 2017
2. Delta Regional Authority (2016) Promoting a healthy Delta. http://dra.gov/initiatives/promoting-a-healthy-delta/. Accessed 5 Nov 2016
3. Gennuso KP, Jovaag A, Catlin BB, Rodock M, Park H (2016) Assessment of factors contributing to health outcomes in the eight states of the Mississippi Delta Region. Prev Chronic Dis 13:E33. https://doi.org/10.5888/pcd13.150440
4. Zahnd WE, Jenkins WD, Mueller-Luckey GS (2017) Cancer mortality in the Mississippi Delta Region: descriptive epidemiology and needed future research and interventions. J Health Care Poor Underserved 28(1):315–328. https://doi.org/10.1353/hpu.2017.0025
5. Mokdad AH, Dwyer-Lindgren L, Fitzmaurice C, Stubbs RW, Bertozzi-Villa A, Morozoff C et al (2017) Trends and patterns of disparities in cancer mortality among US counties, 1980-2014. JAMA 317(4):388–406. https://doi.org/10.1001/jama.2016.20324
6. DeSantis CE, Fedewa SA, Goding Sauer A, Kramer JL, Smith RA, Jemal A (2016) Breast cancer statistics, 2015: convergence of incidence rates between black and white women. CA Cancer J Clin 66(1):31–42. https://doi.org/10.3322/caac.21320
7. Anderson WF, Rosenberg PS, Katki HA (2014) Tracking and evaluating molecular tumor markers with cancer registry data: HER2 and breast cancer. J Natl Cancer Inst. https://doi.org/10.1093/jnci/dju093

8. Phipps A, Li CI (2010) Breast cancer biology and clinical characteristics. In: Li CI (ed) Breast cancer epidemiology. Springer, New York
9. Grann VR, Troxel AB, Zojwalla NJ, Jacobson JS, Hershman D, Neugut AI (2005) Hormone receptor status and survival in a population-based cohort of patients with breast carcinoma. Cancer 103(11):2241–2251. https://doi.org/10.1002/cncr.21030
10. Akinyemiju T, Moore JX, Ojesina AI, Waterbor JW, Altekruse SF (2016) Racial disparities in individual breast cancer outcomes by hormone-receptor subtype, area-level socio-economic status and healthcare resources. Breast Cancer Res Treat 157(3):575–586. https://doi.org/10.1007/s10549-016-3840-x
11. Howlader N, Altekruse SF, Li CI, Chen VW, Clarke CA, Ries LA et al (2014) US incidence of breast cancer subtypes defined by joint hormone receptor and HER2 status. J Natl Cancer Inst. https://doi.org/10.1093/jnci/dju055
12. Llanos AA, Chandwani S, Bandera EV, Hirshfield KM, Lin Y, Ambrosone CB et al (2015) Associations between sociodemographic and clinicopathological factors and breast cancer subtypes in a population-based study. Cancer Causes Control 26(12):1737–1750. https://doi.org/10.1007/s10552-015-0667-4
13. Kohler BA, Sherman RL, Howlader N, Jemal A, Ryerson AB, Henry KA et al (2015) Annual report to the nation on the status of cancer, 1975-2011, featuring incidence of breast cancer subtypes by race/ethnicity, poverty, and state. J Natl Cancer Inst 107(6):djv048. https://doi.org/10.1093/jnci/djv048
14. Bauer KR, Brown M, Cress RD, Parise CA, Caggiano V (2007) Descriptive analysis of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype: a population-based study from the California Cancer Registry. Cancer 109(9):1721–1728. https://doi.org/10.1002/cncr.22618
15. Trivers KF, Lund MJ, Porter PL, Liff JM, Flagg EW, Coates RJ et al (2009) The epidemiology of triple-negative breast cancer, including race. Cancer Causes Control 20(7):1071–1082. https://doi.org/10.1007/s10552-009-9331-1
16. Sineshaw HM, Gaudet M, Ward EM, Flanders WD, Desantis C, Lin CC et al (2014) Association of race/ethnicity, socioeconomic status, and breast cancer subtypes in the National Cancer Data Base (2010-2011). Breast Cancer Res Treat 145(3):753–763. https://doi.org/10.1007/s10549-014-2976-9
17. Akinyemiju TF, Pisu M, Waterbor JW, Altekruse SF (2015) Socioeconomic status and incidence of breast cancer by hormone receptor subtype. Springerplus 4:508. https://doi.org/10.1186/s40064-015-1282-2
18. Vona-Davis L, Rose DP (2009) The influence of socioeconomic disparities on breast cancer tumor biology and prognosis: a review. J Women's Health (Larchmt) 18(6):883–893. https://doi.org/10.1089/jwh.2008.1127
19. Dietze EC, Sistrunk C, Miranda-Carboni G, O'Regan R, Seewaldt VL (2015) Triple-negative breast cancer in African-American women: disparities versus biology. Nat Rev Cancer 15(4):248–254. https://doi.org/10.1038/nrc3896
20. Williams DR, Mohammed SA, Shields AE (2016) Understanding and effectively addressing breast cancer in African American women: unpacking the social context. Cancer 122(14):2138–2149. https://doi.org/10.1002/cncr.29935
21. SEER*Stat Database: NAACCR Incidence Data—CiNA Analytic File, 1995-2014, for NHIAv2 Origin, Custom File With County, Zahnd—Disparities in breast ca subtype (3-year increments) (which includes data from CDC's National Program of Cancer Registries (NPCR), CCCR's Provincial and Territorial Registries, and the NCI's Surveillance, Epidemiology and End Results (SEER) Registries), certified by the North American Association of Central Cancer Registries (NAACCR) as meeting high-quality incidence data standards for the specified time periods, submitted December 2016
22. United States Census Bureau. American Community Survey (ACS). https://www.census.gov/programs-surveys/acs/data.html. Accessed 9 Jan 2018
23. United States Department of Agriculture. 2016 Rural Urban Continuum Codes. http://www.ers.usda.gov/data-products/rural-urban-continuum-codes/documentation.aspx. Accessed 9 Jan 2018
24. National Cancer Institute. Mammography prevalence within 2 years (Age 40+)—small area estimates. https://sae.cancer.gov/nhis-brfss/estimates/mammography.html. Accessed 9 Jan 2018
25. Area Health Resources Files (AHRF). 2014-2015. Rockville, MD.: US Department of Health and Human Services, Health Resources and Services Administration, Bureau of Health Workforce
26. Anderson WF, Pfeiffer RM, Dores GM, Sherman ME (2006) Comparison of age distribution patterns for different histopathologic types of breast carcinoma. Cancer Epidemiol Biomarkers Prev 15(10):1899–1905. https://doi.org/10.1158/1055-9965.epi-06-0191
27. Phipps AI, Ichikawa L, Bowles EJA, Carney PA, Kerlikowske K et al (2010) Defining menopausal status in epidemiologic studies: a comparison of multiple approaches and their effects on breast cancer rates. Maturitas 67(1):60–66
28. Siu AL, United States Preventive Services Task Force (2016) Screening for breast cancer: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med 164(4):279–296. https://doi.org/10.7326/m15-2886
29. Zahnd WE, McLafferty SL (2017) Contextual effects and cancer outcomes in the United States: a systematic review of characteristics in multilevel analyses. Ann Epidemiol 27(11):739–748
30. Krieger N, Chen JT, Waterman PD, Soobader MJ, Subramanian SV, Carson R (2002) Geocoding and monitoring of US socioeconomic inequalities in mortality and cancer incidence: does the choice of area-based measure and geographic level matter?: the Public Health Disparities Geocoding Project. Am J Epidemiol 156(5):471–482
31. Akinyemiju TF, Genkinger JM, Farhat M, Wilson A, Gary-Webb TL, Tehranifar P (2015) Residential environment and breast cancer incidence and mortality: a systematic review and meta-analysis. BMC Cancer 15:191. https://doi.org/10.1186/s12885-015-1098-z
32. Hall HI, Jamison PM, Coughlin SS, Uhler RJ (2004) Breast and cervical cancer screening among Mississippi Delta women. J Health Care Poor Underserved 15(3):375–389
33. Delta Regional Authority (2017) About. http://dra.gov/about-dra/mission-and-vision/. Accessed 9 Aug 2017
34. Moss JL, Liu B, Feuer EJ (2017) Urban/rural differences in breast and cervical cancer incidence: the mediating roles of socioeconomic status and provider density. Womens Health Issues 27(6):683–691
35. Palmer JR, Viscidi E, Troester MA, Hong CC, Schedin P, Bethea TN et al (2014) Parity, lactation, and breast cancer subtypes in African American women: results from the AMBER Consortium. J Natl Cancer Inst. https://doi.org/10.1093/jnci/dju237
36. Danielle K (2011) Cities where women are having the most babies. https://www.usnews.com/news/articles/2011/10/21/cities-where-women-are-having-the-most-babies. Accessed 10 Aug 2018
37. Shinde SS, Forman MR, Kuerer HM, Yan K, Peintinger F, Hunt KK et al (2010) Higher parity and shorter breastfeeding duration: association with triple-negative phenotype of breast cancer. Cancer 116(21):4933–4943. https://doi.org/10.1002/cncr.25443
38. Islami F, Liu Y, Jemal A, Zhou J, Weiderpass E, Colditz G et al (2015) Breastfeeding and breast cancer risk by receptor status—a

systematic review and meta-analysis. Ann Oncol 26(12):2398–2407. https://doi.org/10.1093/annonc/mdv379
39. DeSantis C, Ma J, Bryan L, Jemal A (2014) Breast cancer statistics, 2013. CA Cancer J Clin 64(1):52–62. https://doi.org/10.3322/caac.21203
40. Taylor TR, Williams CD, Makambi KH, Mouton C, Harrell JP, Cozier Y et al (2007) Racial discrimination and breast cancer incidence in US Black women: the Black Women's Health Study. Am J Epidemiol 166(1):46–54. https://doi.org/10.1093/aje/kwm056
41. Geronimus AT, Hicken M, Keene D, Bound J (2006) "Weathering" and age patterns of allostatic load scores among blacks and whites in the United States. Am J Public Health 96(5):826–833. https://doi.org/10.2105/ajph.2004.060749
42. Geronimus AT, Hicken MT, Pearson JA, Seashols SJ, Brown KL, Cruz TD (2010) Do US black women experience stress-related accelerated biological aging?: a novel theory and first population-based test of black-white differences in telomere length. Hum Nat 21(1):19–38. https://doi.org/10.1007/s12110-010-9078-0
43. Linnenbringer E, Gehlert S, Geronimus AT (2017) Black-White disparities in breast cancer subtype: the intersection of socially patterned stress and genetic expression. AIMS Public Health 4(5):526–556. https://doi.org/10.3934/publichealth.2017.5.526
44. Hébert JR, Braun KL, Kaholokula JK, Armstead CA, Burch JA, Thompson B (2015) Considering the role of stress in populations of high-risk, underserved community networks program centers. Prog Community Health Partnersh 9:71–82
45. Krieger N, Jahn JL, Waterman PD (2017) Jim Crow and estrogen-receptor-negative breast cancer: US-born black and white non-Hispanic women, 1992-2012. Cancer Causes Control 28(1):49–59. https://doi.org/10.1007/s10552-016-0834-2
46. Finerman R, Williams C, Bennett L (2010) Health disparities and engaged medical anthropology in the United States Mid-South. Urban Anthropol Stud Cult Syst World Econ Dev 39(3):265–297
47. Boscoe FP, Sherman C (2006) On socioeconomic gradients in cancer registry data quality. J Epidemiol Community Health 60(6):551
48. Krieger N, Chen JT, Ware JH, Kaddour A (2008) Race/ethnicity and breast cancer estrogen receptor status: impact of class, missing data, and modeling assumptions. Cancer Causes Control 19(10):1305–1318. https://doi.org/10.1007/s10552-008-9202-1
49. Howlader N, Noone AM, Yu M, Cronin KA (2012) Use of imputed population-based cancer registry data as a method of accounting for missing information: application to estrogen receptor status for breast cancer. Am J Epidemiol 176(4):347–356. https://doi.org/10.1093/aje/kwr512
50. Institute of Medicine National Cancer Policy Forum (2009) Ensuring quality cancer care through the oncology workforce: sustaining care in the 21st century: workshop summary. National Academies Press, Washington, DC
51. Meilleur A, Subramanian SV, Plascak JJ, Fisher JL, Paskett ED, Lamont EB (2013) Rural residence and cancer outcomes in the United States: issues and challenges. Cancer Epidemiol Biomarkers Prev 22(10):1657–1667. https://doi.org/10.1158/1055-9965.epi-13-0404