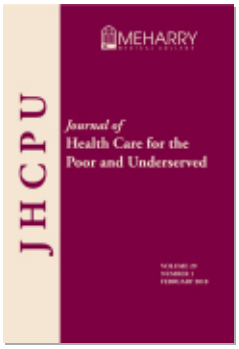
Affluence Does Not Influence Breast Cancer Outcomes in African American Women



Luisel J. Ricks-Santi, Brittany Barley, Danyelle Winchester, Dawood Sultan, John McDonald, Yasmine Kanaan, Amari Pearson-Fields, Arnethea L. Sutton, Vanessa Sheppard, Carla Williams

Journal of Health Care for the Poor and Underserved, Volume 29, Number 1, February 2018, pp. 509-529 (Article)

Published by Johns Hopkins University Press
DOI: https://doi.org/10.1353/hpu.2018.0034

ORIGINAL PAPER

Affluence Does Not Influence Breast Cancer Outcomes in African American Women

Luisel J. Ricks-Santi, PhD
Brittany Barley, BS
Danyelle Winchester, PhD
Dawood Sultan, PhD
John McDonald, PhD
Yasmine Kanaan, PhD
Amari Pearson-Fields, PhD, MPH
Arnethea L. Sutton, PhD, MLS(ASCP)
Vanessa Sheppard, PhD
Carla Williams, PhD

Abstract: The aim of this study was to determine the impact of race and socioeconomic status on breast tumor clinicopathological features and survival outcomes. This study used breast cancer data from the Washington D.C. Cancer Registry (2000–2010). Logistic regression and survival analysis assessed the association between race, socioeconomic (SES) variables, clinicopathological variables, recurrence-free survival and overall survival. African American (AA) breast cancer patients had an increased risk for stage III, ER-, and PR- breast cancer compared with White and Hispanic breast cancer patients. Additionally, D.C. geographical areas of lower socioeconomic status had higher incidences of stage III and stage IV breast cancer. A nested analysis demonstrated that AAs with higher median incomes compared with AAs with lower incomes revealed no differences for clinicopathological variables, nor

LUISEL RICKS-SANTI *is the Director at the Cancer Research Center, and Associate Professor, in the Department of Biological Sciences at Hampton University.* ***BRITTANY BARLEY*** *is a Master of Public Health Candidate, at Southern Illinois University-Carbondale.* ***DANYELLE WINCHESTER*** *is affiliated with Johns Hopkins Bloomberg School of Public Health.* ***DAWOOD SULTAN*** *is an Associate Professor in the Division of Social and Behavioral Sciences at Hampton University.* ***JOHN MCDONALD*** *is a Research Associate at the Cancer Research Center, Hampton University.* ***YASMINE KANAAN*** *is an Associate Professor of Microbiology, Microbiology Department & HoWard University Cancer Center.* ***AMARI PEARSON-FIELDS*** *is affiliated with the District of Columbia Cancer Registry, Bureau of Cancer and Chronic Disease, Community Health Administration, Department of Health.* ***ANETHEA SUTTON*** *is affiliated with Cancer Prevention and Control, Department of Health Behavior and Policy, School of Medicine, at Virginia Commonwealth University.* ***VANESSA SHEPPARD*** *is Professor and Chair, for the Department of Health Behavior and Policy, Theresa A. Thomas Memorial Chair in Cancer Prevention and Control, Associate Director for Disparities Research, Co-leader in the Cancer Prevention and Control Program, School of Medicine, at Virginia Commonwealth University.* ***CARLA WILLIAMS*** *is an Associate Professor of Medicine & Interim Director, at the HoWard University Cancer Center. Please address all correspondence to: Luisel J. Ricks-Santi, Department of Biological Sciences, Hampton University, Hampton, VA 23668. Phone: 757-728-6034; Email: Luisel.rickssanti@hamptonu.edu.*

were differences found between overall and recurrence-free survival. This study suggests that the biology of breast cancer in AAs could be driving breast cancer disparities.

Key words: Breast cancer, cancer disparities, triple negative breast cancer, ethnic disparities, cancer epidemiology, African American health.

Washington, D.C., (henceforth referred to as DC or the District) has the highest breast cancer (BCa) mortality in the United States, at 29.3 per 100,000 compared with a national rate of 21.2 per 100,000.[1] However, research has yet to adequately identify and determine the role of key factors that may influence the mortality rate in the DC population. Racial differences in breast cancer survival are apparent even after accounting for disease stage and known tumor characteristics,[2] suggesting that the disparity in breast cancer mortality may be attributable to social factors.[2–8] Being underinsured and having poor access to health care have been linked to disparate breast cancer outcomes between African American (AA) and White women.[9,10]

Breast cancer encompasses several subtypes, distinguishable with the use of genomic tools.[11–13] Molecularly, breast cancer is sub-categorized based upon its clinicopathological features such as invasiveness and size (stage), appearance (grade), and the presence or absence of three steroid hormone receptors, estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2/neu) which are targets for therapy; tumors not expressing the aforementioned receptors, ER, PR or HER2, are termed "triple negative" or "basal-like" tumors. Because of the absence or lower expression of the receptors, the triple negative breast cancer subtype does not respond to conventional endocrine therapy or to targeted therapeutic regimens, contributing to its overall aggressive clinical course leading to a poor prognosis and shortened survival.[14–18] Accounting for 10–20% of all breast cancers, triple negative breast cancer has a disproportionate incidence in women of African descent.[7,19–22] Previous studies have reported that socioeconomic status and the geographic location of a patient's residence may contribute to the development of tumor subtypes.[23–25] While these studies examined women within larger geographic areas (e.g., state level), the researchers also collected neighborhood data to further examine the role of SES and cancer risk and compare women of varying SES neighborhoods. Geographically, Washington, D.C. is divided into eight Wards. Wards 1 through 6 are located west of the Anacostia River while Wards 7 and 8 are located east of the river. Notably, the city's four cancer centers are located in Wards 1 and 2 reducing access to cancer care. It is also noteworthy that there is just one limited-service hospital located east of the Anacostia River (in Wards 8), serving 20% of DC's population. The inequitable distribution of accredited cancer centers in DC is reflected in the city's cancer incidence and mortality rates. However, in DC, little is known about whether geographic differences are associated with the clinicopathological features or outcomes of breast cancer.

In this study we used Washington, DC Department of Health (DCDOH) Cancer Registry data to determine if race/ethnicity, socioeconomic status, and geography are: 1) associated with breast cancer clinicopathological characteristics, such as stage, grade, molecular subtype; and 2) associated with overall and recurrence-free survival. Furthermore, to begin delineating the effect of socioeconomic status on cancer dispari-

ties, census tract-level median income for all DC residents was used to determine the association between low/high income, geography, and breast cancer clinicopathological features. We performed an analysis of AAs with high incomes (≥$64,773) compared with AAs with lower incomes (<$64,773) to determine if differences persist. This approach will provide a better understanding of the biological and social determinants in breast cancer disparities.

Methods

Data source and study sample. This study used data from the DC Department of Health (DCDOH) Cancer Registry. The analysis of these data was approved by the DCDOH IRB in 2012. Eligibility criteria for the current study included all histologically confirmed malignant breast cancers in Washington, DC, diagnosed between 2000 and 2010. All benign and stage 0 (Ductal Carcinoma In Situ) cases were excluded. Patients with duplicate records and multiple diagnoses were consolidated and coded as recurrences leaving 5,932 women with breast cancer diagnoses as the study sample.

Study variables. The study included a number of independent/explanatory variables: race/ ethnicity (WA= White American; AA= African American; HA= Hispanic American) and socioeconomic status (Ward). The dependent variables in this study are indicated by the clinicopathological characteristics of the patients such as age, stage, grade, estrogen receptor (ER) and progesterone receptor (PR) status, human epidermal growth factor receptor (HER2), molecular subtype, and survival. Socioeconomic status, demography, and medical histories were analyzed. Patient socioeconomic status was measured using the Washington, DC census tract annual median income, where income more than $64,773 indicated high socioeconomic status and income below $64,773 indicated lower socioeconomic status. Only the female gender was included in the study. Age at breast cancer diagnosis was measured as a categorical variable indicating ages 50 and younger or those older than 50 years of age (≤50 year and >50 years) and coded in binary terms with the older age code indicating higher risk for breast cancer. Race/ethnicity categories were as follows: White Americans (WAs), African Americans (AAs) and Hispanic Americans (HAs). Molecular subtype was indicated by estrogen receptor (ER), progesterone receptor (PR), and Human Epidermal Growth Factor 2 (HER2) status. These statuses were analyzed independently and together to determine the molecular subtype. Estrogen receptor and PR status were determined by immunohistochemistry; HER2 was determined by fluorescence *in situ* hybridization (FISH). The latter (FISH) is a method that uses fluorescence to probe for a marker such as HER2. If a marker, such as HER2, is present, a chemical reaction occurs and the probe fluoresces. If it is absent the probe will not fluoresce. In general, FISH should reveal two areas of fluorescence. In HER2 positive breast cancers, there are more than two areas of fluorescence and HER is defined as positive. If there are two or fewer areas of HER2 fluorescence, HER2 is defined as HER2 negative. For this study, tumors that were ER and/or PR positive and HER2 negative were coded as luminal A; tumors that were ER and/or PR positive and HER2 positive were coded as luminal B; tumors that were ER and/or PR negative and HER2 positive were coded as HER2 overexpressing/amplified; and tumors negative for ER, PR, and HER2 were

coded as triple negative. Tumor characteristics (size, stage, and grade) were included in the analysis. Size was measured in centimeters. Stage was measured in four categories (stage l, stage ll, stage lll, and stage lV). Grade was measured in terms of three categories: low, intermediate, and high. Vitality and recurrence were also measured as a binary yes/no (1,0) categorical variable. Patient family histories of breast cancer were collected by the registry and was measured herein as a binary (1,0) variable indicating the presence (1) or absence (0) of breast cancer in a family member.

In 2016, DC residents included 47.7% African Americans (AAs), 38.5% non-Hispanic Whites or WAs, and 10.9% Hispanics (HAs). Geographically, Washington, DC is divided into eight Wards. Wards 1 through 6 are located west of the Anacostia River while Wards 7 and 8 are located east of the river. Notably, the highest concentration of AAs lives in Wards 7 and 8, where they constitute 95% and 94% of the population, respectively. Wards 7 and 8 have the lowest median income and highest unemployment rates.[26] Most of the Hispanic population, the fastest growing segment in the city, resides in Wards 1 and 4.[26] Patient geographical location was defined by zip codes and categorized into two groups Wards 1–6 and Wards 7–8. For the cross-sectional analysis of African Americans, census tract-level median income for all DC residents was used to determine the association between low/high income, geography, and breast cancer clinicopathological features.

Statistical analysis. A descriptive analysis was initially performed to determine the frequencies of categorical variables. A chi-square or Fisher's exact test was used to compare characteristics between Whites (WAs), African Americans (AAs) and Hispanic Americans (HAs). The association of race, Ward, ZIP code, median income, and categorical variables was analyzed using logistic regression; odds ratios (OR) and 95% confidence intervals (CI) were calculated with adjustment for potential confounders (i.e., age at diagnosis and family history of cancer). Regression modeling allows for the analysis of categorical values; in this analysis, race, receptor status, stage, grade, Ward, and income were categorized and analyzed against each other. First, the association with race was assessed with clinicopathological variables; then clinicopathological variables were assessed against Ward while controlling for race, given that certain Wards were highly homogeneous. Student's t test was used to compare the means of the continuous variable, age. Kaplan-Meier Survival analyses were carried out to assess variables associated with survival. For survival analysis, time until one or more events happen, such as recurrence or death occurs is measured. Overall survival time was calculated from the date of diagnosis to the date of death from any cause. Disease-free interval was the time interval from diagnosis to loco-regional recurrence, distant recurrence, or death from any cause, whichever occurred first. Log-rank tests were used to compare unadjusted overall survival curves between the groups. All analyses were carried out using the IBM SPSS statistical program version 20 (SPSS Inc., Chicago, IL).

Results

The demographic, and tumor characteristics of breast cancer cases at diagnosis among African Americans (AAs), White Americans (WAs), and Hispanic Americans (HAs) can be seen in Figure 1. Hispanic Americans were younger, with a mean age of 57.80

± 14.048 compared with WAs (mean=60.06 ± 14.03) and AAs (mean=61.97 ± 14.19) (data not shown); additionally, there were a greater proportion of HAs (33.6%) who were younger than 50 years old compared with AAs (24%) and WAs (26%) (p<.0001) (data not shown). There were no significant differences among AAs, WAs, and HAs regarding self-reported family history (p=.614) (data not shown).

African Americans (AAs) were more likely to present at stage III (14.2%) and stage

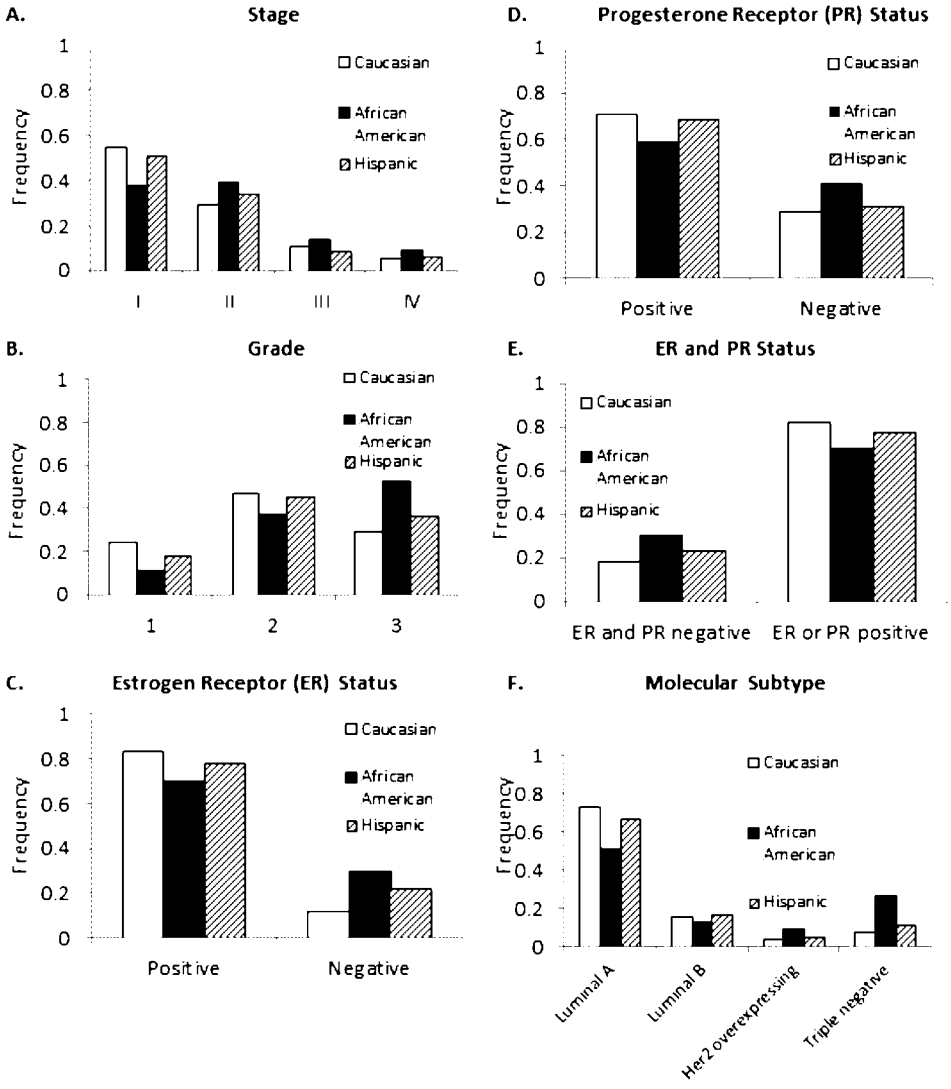


Figure 1. Frequency of clinicopathological characteristics by race/ ethnicity.
A) Frequency of stage by race/ethnicity.
B) Frequency of grade by race/ethnicity.
C) Frequency of estrogen receptor status by race/ethnicity.
D) Frequency of progesterone receptor status by race/ethnicity.
E) Frequency of estrogen and progesterone (combined) receptor status by race/ethnicity.
F) Frequency of molecular subtype by race/ethnicity.

IV (9.2%) compared with WAs (10.5% and 5.3%, stage III and IV, respectively) and HAs (8.4% and 6.3%, stage III and IV, respectively) (p<.0001) (Figure 1A). Additionally, AAs and HAs presented with different tumor features from WAs. White Americans (WAs) had a higher prevalence of grade 1 and 2 tumors compared with AA and HAs (p<.0001) (Figure 1B). Breast cancers in AAs were also more likely to be estrogen receptor (ER) negative (p<.0001), progesterone receptor (PR) (p<.0001) negative, ER negative/ PR negative (p<.0001), and triple negative (p=.01) (Figure 1C, 1D, 1E, and 1F).

The characteristics of breast cancer patients were also stratified by geographic location (Wards 1–6 and 7–8). Wards 1–6 and 7–8 have significantly higher percentages of African American breast cancer patients compared with White and Hispanic American patients (Figure 2A); therefore regression models were adjusted for race. Wards 1–6 have significantly more breast cancer patients across all race/ethnicity categories but Wards 7–8 reported a higher proportion of African American cases (p<.0001). Patients from Wards 7 and 8 were significantly younger (p=.01) (Figure 2B) and self-reported a significantly higher proportion of family history of breast cancer (p=.02) after adjusting for race/ethnicity (Figure 2C). No differences between Wards were found with stage, grade, ER receptor status, PR receptor status, HER2 receptor status, subtype or recurrence (Data not shown).

Association between race/ethnicity, Ward (socioeconomic status) and clinicopathological features. Table 1 shows the results of the logistic regression analysis and include statistically significant age-adjusted odds ratios (OR) and 95% CI for associations between receptor status, molecular subtypes, stage, grade, and race. As expected, AAs were at an increased risk for ER negative (OR = 2.24; p<.0001), PR negative (OR = 1.76; p<.0001), and ER negative/ PR negative (OR = 2.15; p<.0001) breast cancer compared with breast cancers in WAs and HAs (Table 1). African Americans (AAs) also had a higher risk for stage III and IV breast cancer (OR = 1.62; p<.0001) compared with WAs and HAs (Table 1). However, no statistically significant association between AAs and triple negative subtype was observed (OR = 3.22; p = .14). African Americans (AAs) (OR = 2.60) and HAs(OR = 1.48) had an increased risk for higher tumor grade compared with WAs (Table 1).

The association between breast cancer characteristics by Ward was also assessed. Because race was strongly associated with Ward and because Wards 7 and 8's population was largely AA, the analysis controlled for race (Table 1). Breast cancer patients from Wards 7 and 8 were younger (OR = 1.24; p = .006), reported a higher rate of family history (OR = 1.23; p<.019), and had higher incidences of Stage III cancer (OR = 1.43; p<.02) or Stage III and Stage IV breast cancer (OR = 1.26; p=.053) (Table 1).

Survival analysis. Survival analyses revealed that decreased overall survival was associated with race/ethnicity (log rank p<.0001), Ward (log rank p<.0001), older age (log rank p<.0001), higher stage (log rank p<.0001), higher grade (log rank p<.0001), family history (log rank p<.0001), ER negativity (log rank p<.0001), PR negativity (log rank p<.001), triple negative breast cancer (log rank p=.079), and ER/PR negative breast cancer (log rank p<.0001) (Table 2). However, neither race/ethnicity nor Ward was associated with recurrence-free survival (log rank p=.73 and .89, respectively) (Table 2). The mean survival for WAs, AAs and HAs was 66.56 ± 2.42, 55.21 ± 1.33, and 59.29

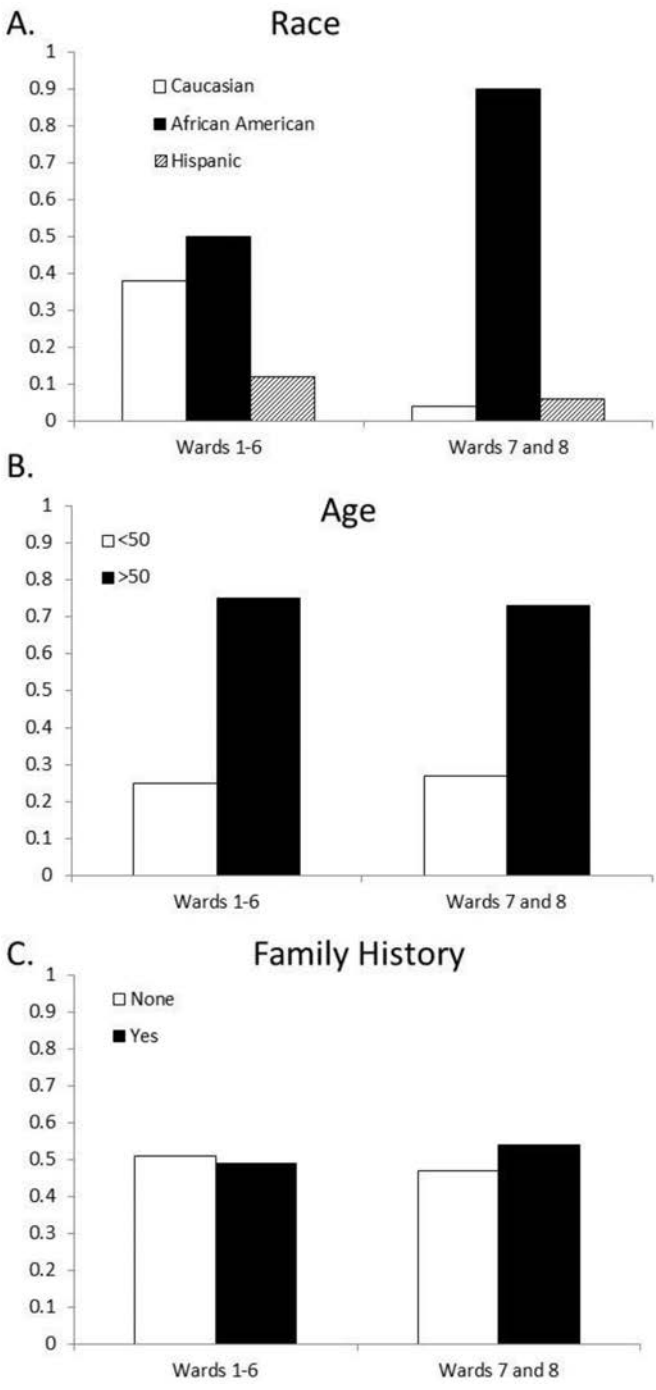


Figure 2. Frequency of demographic characteristics by Ward.
A) Frequency of race/ethnicity Ward.
B) Frequency of age group by Ward.
C) Frequency of family history status by Ward.

Table 1.

ADJUSTED ORS AND 95%CI FOR ASSOCIATIONS BETWEEN MOLECULAR SUBTYPES, STAGE, GRADE AND RACE

	N	ER Negative*	p-value	PR Negative*	p-value	ER- and PR-*	p-value	Grade*	p-value	Stage III and IV*	p-value	Age	p-value	Family History	p-value	Regional Invasion**	p-value
Caucasian	1735	1.00 (ref)		1.00 (ref)		1.00 (ref)		1.00 (ref)		1.00 (ref)							
African American	3304	2.24 (1.74-2.89)	<.0001	1.76 (1.42-2.19)	<.0001	2.15 (1.66-2.78)	<.0001	2.60 (2.19-3.08)	<.0001	1.62 (1.29-2.04)	<.0001						
Hispanic	647	1.22 (0.77-1.92)		1.09 (0.74-1.61)	.65	1.19 (0.75-1.89)	.46	1.48 (1.00-2.00)	.01	0.92 (0.59-1.43)	.7						
Wards 1-6	4575									1.00 (ref)		1.00 (ref)		1.00 (ref)		1.00 (ref)	
wards 7-8	1233									1.26 (0.99-1.59)	.053	1.24 (1.07-1.45)	.006	1.23 (1.04-1.47)	.019	1.40 (1.12-1.76)	.003

± 3.76 months, respectively (log rank p<.0001). Recurrence-free survival was lower in those over 50 years (38.23 ± 5.09) compared with those under 50 (20.01 ± 2.38) (log rank p=.002) (Table 2). Estrogen receptor (ER) negative (log rank p=.008), PR negative (log rank p=.007), and ER negative/PR negative (log rank p=.007) status were negatively associated with recurrence-free survival (Table 2). Recurrence-free survival was also not associated with stage, grade, HER2 status, or subtype (Table 2).

Cross-sectional analysis of AAs. Of the 5,852 female patients, 3,345 (56.4%) self-identified as Black or African American and 3,263 (97.5%) had ZIP code data available for analysis Table 3. Frequency analysis determined that 76.89% of the studied popu-

Table 2.

MEAN OVERALL AND RECURRENCE-FREE SURVIVAL BY DEMOGRAPHIC, SOCIOECONOMIC, AND TUMOR CHARACTERISTICS

		N	Mean Overall Survival (months)	Log rank p value	Mean Recurrence-free Survival (months)	p value
Race	White Americans	1735	66.66		24.25	
	African Americans	3304	55.21		25.34	
	Hispanics	647	59.28	<.0001	21.758	.733
Age	<50	1504	67.42		38.236	
	>50	4347	57.49	<.0001	20.012	.002
Ward	Wards 1–6	4575	61.36		24.446	
	Wards 7 and 8	1233	54.54	<.0001	24.49	.629
Stage	I	1100	48.77		12.43	
	II	898	47.03		16.07	
	III	308	38.34		13.3	
	IV	195	21.03	<.0001	1.48	.34
Grade	1+2	695	68.11		23.16	
	3	3830	57.12	.003	24.96	.89
Family History	Negative	1679	63.59		22.39	
	Positive	1717	55.98	<.0001	24.87	.56
ER	Positive	2185	49.48		20.413	
	Negative	729	39.09	<.0001	9.356	.008
PR	Positive	1850	46.86		19.681	
	Negative	1055	44.21	<.0001	7.848	.007
HER2	Negative	171			1.9	
	Positive	45			0.75	.29
Subtype	Other Subtype	177	28.28		1.39	
	Triple Negative	40	22.27	.002	4	.25
ER/PR	ER or PR positive	2199	49.1		21.462	
	ER and PR negative	701	39.46	<.0001	9.288	.007

lation lived within ZIP codes with incomes below the median, 76.40% were over the age of 50, 50.22% reported a family history of breast cancer, 76.57% had stage I or II breast cancer, 52.51% had grade 3 tumors, 70.25% were ER positive, 63.20% were PR positive, 27.36% were triple negative, and 71.33% were ER and PR negative (Table 3). There were no statistically significant differences among AA breast cancer patients in ZIP code areas with below-median income and above-median income in terms of age (p=.66), family history (p=.92), stage (p=.56), grade (p=.47), ER status (p=.71), PR status (p=.95), and ER/PR negative status (p=.39) (Table 3).

Overall and recurrence-free survival were compared in the two groups. There was no statistically significant difference in the median overall survival for those in below and above median income ZIP codes which was 48 months (±2.58 SE) and 59 months

Table 3.

CLINICOPATHOLOGICAL CHARACTERISTICS OF AFRICAN AMERICANS LIVING BELOW AND ABOVE THE MEDIAN INCOME

	Below Median Income	%	Above Median Income	%	p-value
Age					
<50	596	23.8	173	23.0	.66
>50	1913	76.2	580	77.0	
Family History					
Positive	772	50.2	238	50.4	.92
Negative	767	49.8	234	49.6	
Stage					
I	431	36.8	141	41.0	.56
II	461	39.4	127	36.9	
III	167	14.3	47	13.7	
IV	112	9.6	29	8.4	
Grade					
1	213	10.3	73	12.1	.47
2	763	37.0	217	35.9	
3	1085	52.6	315	52.1	
Estrogen Receptor					
Negative	387	30.0	114	29.0	.71
Positive	904	70.0	279	71.0	
Progesterone Receptor					
Negative	528	40.9	158	40.1	.95
Positive	762	59.1	236	59.9	
Estrogen and Progesterone receptor status					
ER negative and PR negative	376	29.2	106	27.0	.39
ER or PR positive	912	70.8	287	73.0	

(± 3.39 SE) (p=.98), respectively (Table 4 and Figure 3). The mean recurrence-free survival for those in below and above median income ZIP codes was 25.90 (95% CI: 19.67–32.12) and 23.95 months (95% CI: 14.01–33.90), respectively (Table 4 and Figure 3). Survival analysis also indicated no statistically significant differences between overall and recurrence-free survival between AA women living in below median income ZIP codes compared with those living in above median income ZIP codes (Table 4 and Figure 3).

Discussion

This study found that unfavorable tumor characteristics, such as high stage, high grade, estrogen receptor (ER) negativity, progesterone receptor (PR) negativity, and ER negativity/ PR negativity were more prevalent in African American (AAs) breast cancer patients compared with WAs and HAs, although breast cancer in HAs presented at a statistically significant younger age. Adverse tumor characteristics were also associated with geographic variables specific to DC Wards 7 and 8. Additionally, we also found that overall survival was associated with hormone receptor positivity and recurrence-free survival was associated with younger age, ER positivity, PR positivity, and ER or PR positivity. Importantly, we did not find statistically significant differences in terms of clinicopathological characteristics such as stage, grade, ER status, PR status, and socioeconomic status between above and below median AAs. In addition, there were no significant differences in overall or recurrence-free survival between above and below median income AAs.

Demographic characteristics and tumor characteristics. Washington, DC has the highest age-adjusted breast cancer incidence and mortality rate in the United States [27] but it was not known what was contributing to the high incidence and mortality rates. It is well established that AAs will often present at later stage and will often have higher grade tumors.[2–7,22] Similarly, this study also found a statistically significant higher rate of later stage and high grade tumors in AAs potentially contributing to its high mortality rate.

It has also been reported that prognostic markers, such as hormone receptor status, have dissimilar incidence in AAs compared with other populations, and that hormone negativity is more prevalent in AA breast cancer, limiting treatment options since targets for endocrine therapy are absent.[22] Furthermore, AA women have a higher incidence of triple negative breast cancers (TNBCs) [7,19–22] which will not respond to endocrine therapy and are differentially responsive to chemotherapy. Important herein, the triple negative (TNBC) subtype has significant though incomplete overlap with immunohistochemical (IHC) ER, PR, and HER2/neu negativity and has a high proliferative index.[14,20,28–30]

Washington, DC also appears to have a high incidence of ER negative, triple negative, and ER negative/ PR negative breast cancer. Analysis of ER and PR status demonstrated that when stratified by race/ethnicity, AAs had a significantly higher rate of ER and PR negative tumors. Furthermore, almost one third of all AAs had triple negative breast cancer compared with 8% of WAs and 11% of HAs. However, analysis of molecular subtypes was limited by the lack of HER2 data. It is also important to mention that HER2 amplified tumors have a poorer prognosis compared with ER/ PR positive tumors.[31]

Table 4.

COMPARISON OF TREATMENT OUTCOMES IN AA WOMEN WITH BCA WITH INCOME AS A SES INDICATOR

	Mean				Median						
			95% Confidence Interval				95% Confidence Interval				
	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound	Chi-Square	df	Sig.
Overall Survival											
Below Median Income	56.12	1.52	53.12	59.11	48	2.58	42.93	53.06			
Above Median Income	60.28	3.72	52.99	67.58	59	3.39	52.35	65.64	0	1	0.98
Overall	56.72	1.4	53.96	59.47	51	2.17	46.74	55.25			
Recurrence-Free Survival											
Below Median Income	25.9	3.17	19.67	32.12	11	7.493	0	25.68			
Above Median Income	23.95	5.07	14.01	33.9	7	5.384	0	17.55	0.27	1	0.6
Overall	25.35	2.69	20.08	30.62	9	5.994	0	20.74			

Notes
AA= African American
BCa= Breast Cancer

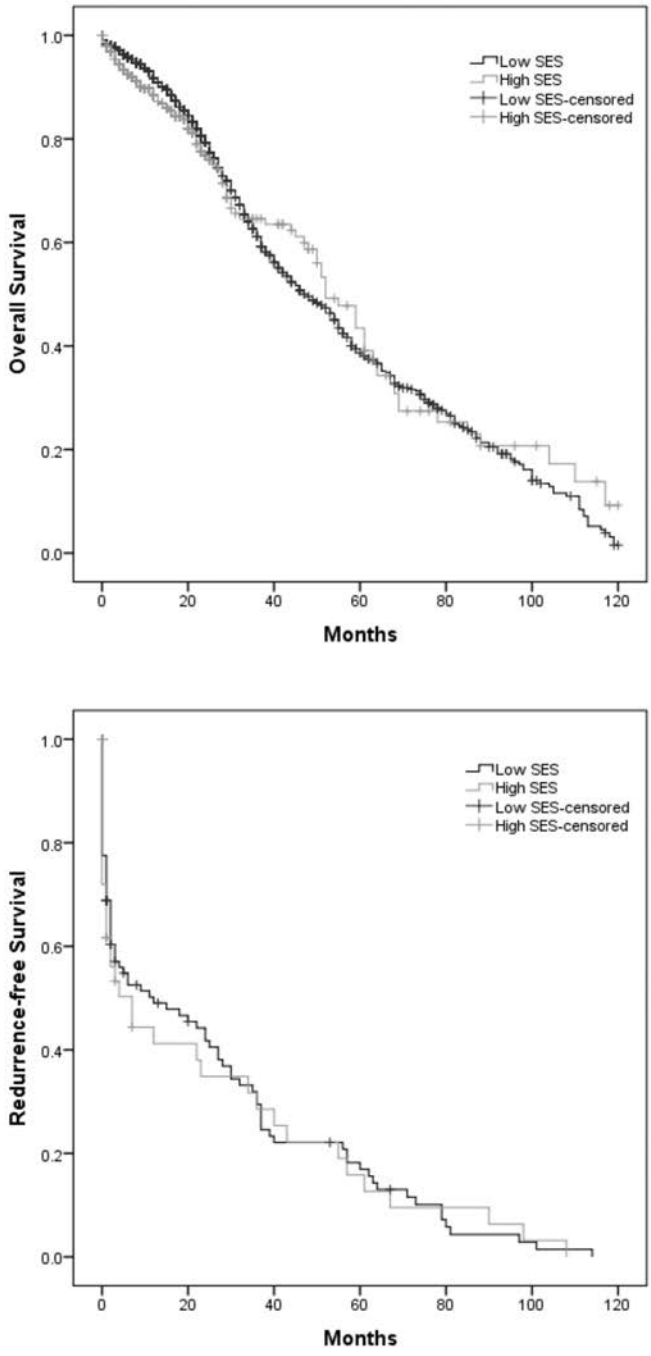


Figure 3. a. Overall and b. Recurrence-free survival analysis for African American patients with low and high SES.

However, monoclonal antibodies, such as Trastuzumab/ Herceptin, can target HER2 and may be concurrently used with chemotherapy to treat breast cancer resulting in improved outcomes for the group.[32] Herceptin was approved by the Food and Drug Administration (FDA) in 1998, but several years passed before FDA approved FISH detection for HER2 (2005) and before the American Society of Clinical Oncology (ASCO) released revised HER2 screening recommendations (2008). Therefore, HER2 screening may not have been available for a significant portion of our sample set.

Given the missing HER2 information, the triple negative breast cancer data cannot be generalized to Washington, DC as a whole. Still, options for therapy are limited in AA women and those with triple negative breast cancer. Therefore, the high rate of deaths could be due to the high number of AAs with adverse prognostic tumors as demonstrated by DC's high rate of high grade tumors and hormone negative tumors in AAs and HAs which is consistent with other studies.[22,33–49]

Geography and tumor characteristics. Our results also show some differences in tumor characteristics when stratified by DC Wards, which may be linked to race/ethnicity and socioeconomic status. In fact, the highest concentration of AAs are found in Wards 7 and 8, where they constitute 95% and 94% of the population, respectively. Moreover, Wards 7 and 8 have the lowest median income and highest unemployment rates,[26] whereas most of the HA population, the fastest growing segment in the city, resides in Wards 1 and 4. Therefore, the differences in tumor characteristics found in our study could have been influenced by the varying racial distributions across the Wards in DC and aggressive tumor characteristics in the AA breast cancer patient population. However, after adjusting for race, and several factors such as stage and age, the differences persisted. Several studies also assert that where one lives is associated with outcomes. For example, several studies have shown that living in rural locations is associated with late-stage diagnosis.[50,51] Conversely, race and socioeconomic status was a better indicator of outcomes when comparing those who lived in Chicago with those who lived outside of Chicago.[52–55] What was not explored in the aforementioned study was whether other clinicopathological factors, such as hormone receptor status or grade were associated with geography. Given the lack of differences in outcomes between African American women with high and low SES, our studies demonstrate that biology may in fact be influencing the higher recurrence and mortality rates in the population. In the future, additional studies will be performed to identify geographical barriers to care and to determine if geography is a barrier to care in Washington, DC.

Survival and recurrence in African Americans by socioeconomic status. The most significant finding in this study is that despite differences in socioeconomic status and median income, there were no differences in tumor characteristics or survival, indicating that adverse tumor biology characteristics in the study population could be driving the higher cancer incidence among AAs and the observed outcomes disparities. This could be attributed to the general prognosis of breast cancer which may be partly driven by the underlying biology of the disease as has been demonstrated in other studies comparing tumors from AAs and WAs.[56–60] It may be the increased prevalence of aggressive disease driven by biologic, genetic, or epigenetic factors and not socioeconomic factors that are affecting breast cancer disparities.

While it was not possible to assess the demographic characteristics of the patients receiving care at the different facilities, it is likely that health system factors could be influencing outcomes in the group as well as differences in quality of health insurance, which could be associated with the types and the quality of providers and health facilities that are available to the local user population. Therefore, efforts to ameliorate the observed disparities should include a focus on increased understanding of the etiology and improved management and treatment of aggressive disease.

Study limitations. Limitations of this study include the retrospective nature of the data collection by tumor registrars and collection protocol at each of the collection sites. Additionally, despite highly consistent findings, the results of this study are not generalizable to other AA populations mainly due to the unique geographic and political structure of Washington, DC. Moreover, while the results demonstrated a high incidence triple negative breast cancer in AAs, much of the HER2 data are missing. Still, findings based on our data were consistent with other studies,[22,33–49] indicating that the District's triple negative breast cancer rates resemble rates found at other locations with large AA populations. Another major limitation was that the DC Cancer Registry does not link with National Death Index the lack of NDI linkage produces very low survival rates although giving us very consistent results. Additionally, for family history, almost half of the records do not have information on family history limiting our analysis. Regarding the categorization of Hispanic ethnicity and race, less than 3% of the records have Hispanic codes and more than 12% are coded as unknown Hispanic. It is important to note that "Hispanic" encompasses a heterogeneous group, which should be considered when identifying risk factors for breast cancer and survivorship. Finally, where the patient sought care was excluded from the data set inhibiting further analyses. However, inclusion of these data in the future will guide future efforts to examine additional factors contributing to our findings.

Summary. In summary, the District of Columbia has the highest mortality due to breast cancer of all U.S. states. Our findings suggest that the high rate of aggressive breast tumors, characterized by high grade and ER/PR negativity, may adversely affect mortality rates in the District. Our data show that negative tumor characteristics are more highly pronounced in AAs compared with WAs and that AAs and other underserved populations may benefit from early detection and behavioral risk reduction activities, such as collecting a family health history, which may greatly reduce late stage diagnosis and cancer mortality.

These findings also suggest the importance of additional community-based efforts to facilitate early detection of breast cancer and prompt linkage to care at cancer centers providing state-of-the-art therapy, as well as innovative research to identify the biologic drivers of aggressive disease in AAs. Community-based approaches, particularly within the African American community, have resulted in favorable outcomes in uptake of health care resources and motivating healthy behaviors.[61,62] As our findings indicate, higher incidence within this group regardless of income, community-based efforts, and interventions tailored for AAs may address this disparity. Developing tailored behavioral prevention messages aimed at risk reduction, improving use of cancer screening, increasing the use of chemopreventive options, and surgical intervention for aggressive tumors may have an additional impact on the District's cancer mortality rate.

References

1. American Cancer Society. Cancer Facts & Figures 2017. Atlanta, GA: American Cancer Society, 2017. Available at: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2017/cancer-facts-and-figures-2017.pdf.
2. Baquet CR, Horm JW, Gibbs T, et al. Socioeconomic factors and cancer incidence among Blacks and Whites. J Natl Cancer Inst. 1991 Apr 17;83(8):551–7. https://doi.org/10.1093/jnci/83.8.551 PMid:2005640
3. McWhorter WP, Schatzkin AG, Horm JW, et al. Contribution of socioeconomic status to Black/White differences in cancer incidence. Cancer. 1989 Mar 1;63(5):982–7. https://doi.org/10.1002/1097-0142(19890301)63:5<982::AID-CNCR2820630533>3.0.CO;2-I
4. Bradley CJ, Given CW, Roberts C. Race, socioeconomic status, and breast cancer treatment and survival. J Natl Cancer Inst. 2002 Apr 3;94(7):490–6. https://doi.org/10.1093/jnci/94.7.490 PMid:11929949
5. Brawley OW. Disaggregating the effects of race and poverty on breast cancer outcomes. J Natl Cancer Inst. 2002 Apr 3;94(7):471–3. https://doi.org/10.1093/jnci/94.7.471 PMid:11929941
6. Lannin DR, Mathews HF, Mitchell J, et al. Influence of socioeconomic and cultural factors on racial differences in late-stage presentation of breast cancer. JAMA. 1998 Jun 10;279(22):1801–7. https://doi.org/10.1001/jama.279.22.1801 PMid:9628711
7. Newman LA. Breast cancer in African-American women. Oncologist. 2005 Jun;10(1):1–14. https://doi.org/10.1634/theoncologist.10-1-1 PMid:15632248
8. Baquet CR, Commiskey P. Socioeconomic factors and breast carcinoma in multicultural women. Cancer. 2000 Mar 1;88(5 Suppl):1256–64. https://doi.org/10.1002/(SICI)1097-0142(20000301)88:5+<1256::AID-CNCR13>3.0.CO;2-3
9. Bigby J, Holmes MD. Disparities across the breast cancer continuum. Cancer Causes Control. 2005 Feb;16(1):35–44. https://doi.org/10.1007/s10552-004-1263-1 PMid:15750856
10. Williams DR, Jackson PB. Social sources of racial disparities in health. Health Aff (Millwood) . 2005 Mar–Apr;24(2):325–34. https://doi.org/10.1377/hlthaff.24.2.325 PMid:15757915
11. Perou CM, Sorlie T, Eisen MB, et al. Molecular portraits of human breast tumours. Nature. 2000 Aug 17;406(6797):747–52. https://doi.org/10.1038/35021093 PMid:10963602

12. Sorlie T, Perou CM, Tibshirani R, et al. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proc Natl Acad Sci USA. 200 Sep 11;98(19):10869–74.
13. Weigelt B, Baehner FL, Reis-Filho JS. The contribution of gene expression profiling to breast cancer classification, prognostication and prediction: a retrospective of the last decade. J Pathol. 2010 Jan;220(2):263–80.
PMid:19927298
14. Rios J, Puhalla S. PARP inhibitors in breast cancer: BRCA and beyond. Oncology (Williston Park). 2011 Oct;25(11):1014–25.
15. Dent R, Trudeau M, Pritchard KI, et al. Triple-negative breast cancer: clinical features and patterns of recurrence. Clin Cancer Res. 2007 Aug 1;13(15 Pt 1):4429–34.
https://doi.org/10.1158/1078-0432.CCR-06-3045
PMid:17671126
16. Haffty BG, Yang Q, Reiss M, et al. Locoregional relapse and distant metastasis in conservatively managed triple negative early-stage breast cancer. J Clin Oncol. 2006 Dec 20;24(36):5652–7. Epub 2006 Nov 20.
https://doi.org/10.1200/JCO.2006.06.5664
PMid:17116942
17. Yu KD, Zhu R, Zhan M, et al. Identification of prognosis-relevant subgroups in patients with chemoresistant triple-negative breast cancer. Clin Cancer Res. 2013 May 15;19(10): 2723–33. Epub 2013 Apr 2.
https://doi.org/10.1158/1078-0432.CCR-12-2986
PMid:23549873 PMCid:PMC3655097
18. Metzger-Filho O, Tutt A, de Azambuja E, et al. Dissecting the heterogeneity of triple-negative breast cancer. J Clin Oncol. 2012 May 20;30(15):1879–87. Epub 2012 Mar 26.
https://doi.org/10.1200/JCO.2011.38.2010
PMid:22454417
19. Stead LA, Lash TL, Sobieraj JE, et al. Triple-negative breast cancers are increased in black women regardless of age or body mass index. Breast Cancer Res. 2009;11(2):R18. Epub Mar 25.
20. Carey L, Winer E, Viale G, et al. Triple-negative breast cancer: disease entity or title of convenience? Nat Rev Clin Oncol. 2010 Dec;7(12):683–92. Epub 2010 Sep 28.
https://doi.org/10.1038/nrclinonc.2010.154
PMid:20877296
21. Bowen RL, Duffy SW, Ryan DA, et al. Early onset of breast cancer in a group of British black women. Br J Cancer. 2008 Jan 29;98(2):277–81. Epub 2008 Jan 8.
https://doi.org/10.1038/sj.bjc.6604174
PMid:18182985 PMCid:PMC2361454
22. Bauer KR, Brown M, Cress RD, et al. 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. 2007 May 1;109(9):1721–8.
https://doi.org/10.1002/cncr.22618
PMid:17387718
23. Banegas MP, Tao L, Altekruse S, et al. Heterogeneity of breast cancer subtypes and survival among Hispanic women with invasive breast cancer in California. Breast Cancer Res Treat. 2014 Apr;144(3):625–34. Epub 2014 Feb 28.

https://doi.org/10.1007/s10549-014-2882-1
PMid:24658879 PMCid:PMC4045012
24. Parise CA, Bauer KR, Brown MM, et al. Breast cancer subtypes as defined by the estrogen receptor (ER), progesterone receptor (PR), and the human epidermal growth factor receptor 2 (HER2) among women with invasive breast cancer in California, 1999–2004. Breast J. 2009 Nov–Dec;15(6):593–602. Epub 2009 Sep 17.
https://doi.org/10.1111/j.1524-4741.2009.00822.x
PMid:19764994
25. Carvalho FM, Bacchi LM, Pincerato KM, et al. Geographic differences in the distribution of molecular subtypes of breast cancer in Brazil. BMC Womens Health. 2014 Aug 29;14:102.
https://doi.org/10.1186/1472-6874-14-102
PMid:25174527 PMCid:PMC4153008
26. Washington, DC Economic Partnership. DC Neighborhood Profiles 2013. Washington, DC: Washington, DC Economic Partnership, 2013. Available at: http://wdcep.com/wp-content/uploads/2010/08/np.pdf.
27. DeSantis CE, Fedewa SA, Goding SA, et al. Breast cancer statistics, 2015: convergence of incidence rates between Black and White women. CA: Cancer J Clin. 2016 Jan–Feb;66(1):31–42. Epub 2015 Oct 29.
https://doi.org/10.3322/caac.21320
PMid:26513636
28. Foulkes WD, Smith IE, Reis-Filho JS. Triple-negative breast cancer. N Engl J Med. 2010 Nov 11;363(20):1938–48.
https://doi.org/10.1056/NEJMra1001389
PMid:21067385
29. Lachapelle J, Foulkes WD. Triple-negative and basal-like breast cancer: implications for oncologists. Curr Oncol. 2011 Aug;18(4):161–4.
https://doi.org/10.3747/co.v18i4.824
PMid:21874112 PMCid:PMC3149541
30. Bertucci F, Finetti P, Cervera N, et al. How basal are triple-negative breast cancers? Int J Cancer. 2008 Jul 1;123(1):236–40.
https://doi.org/10.1002/ijc.23518
PMid:18398844
31. Slamon DJ, Clark GM, Wong SG, et al. Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene. Science. 1987 Jan 9;235(4785):177–82.
https://doi.org/10.1126/science.3798106
PMid:3798106
32. Tovey SM, Brown S, Doughty JC, et al. Poor survival outcomes in HER2-positive breast cancer patients with low-grade, node-negative tumours. Br J Cancer. 2009 Mar 10;100(5):680–3. Epub 2009 Feb 17.
https://doi.org/10.1038/sj.bjc.6604940
PMid:19223897 PMCid:PMC2653773
33. McBride R, Hershman D, Tsai WY, et al. Within-stage racial differences in tumor size and number of positive lymph nodes in women with breast cancer. Cancer. 2007 Sep 15;110(6):1201–8.
https://doi.org/10.1002/cncr.22884
PMid:17701948
34. Kurian AW, Fish K, Shema SJ, et al. Lifetime risks of specific breast cancer subtypes

among women in four racial/ethnic groups. Breast Cancer Res. 2010;12(6):R99. Epub 2010 Nov 19.
https://doi.org/10.1186/bcr2780
PMid:21092082 PMCid:PMC3046442

35. Lund MJ, Trivers KF, Porter PL, et al. Race and triple negative threats to breast cancer survival: a population-based study in Atlanta, GA. Breast Cancer Res Treat. 2008 Jan;113(2):357–70. Epub 2008 Mar 7.
https://doi.org/10.1007/s10549-008-9926-3
PMid:18324472
36. Khanna KK, Jackson SP. DNA double-strand breaks: signaling, repair and the cancer connection. Nat Genet. 2001 Mar;27(3):247–54.
https://doi.org/10.1038/85798
PMid:11242102
37. Carey LA, Perou CM, Livasy CA, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. JAMA. 2006 Jun 7;295(21):2492–502.
https://doi.org/10.1001/jama.295.21.2492
PMid:16757721
38. Huo D, Ikpatt F, Khramtsov A, et al. Population differences in breast cancer: survey in indigenous African women reveals over-representation of triple-negative breast cancer. J Clin Oncol. 2009 Sep 20;27(27):4515–21. Epub 2009 Aug 24.
https://doi.org/10.1200/JCO.2008.19.6873
PMid:19704069 PMCid:PMC2754904
39. Morris GJ, Naidu S, Topham AK, et al. Differences in breast carcinoma characteristics in newly diagnosed African-American and Caucasian patients: a single-institution compilation compared with the National Cancer Institute's Surveillance, Epidemiology, and End Results database. Cancer. 2007 Aug 15;110(4):876–84.
https://doi.org/10.1002/cncr.22836
PMid:17620276
40. Lin NU, Vanderplas A, Hughes ME, et al. Clinicopathologic features, patterns of recurrence, and survival among women with triple-negative breast cancer in the National Comprehensive Cancer Network. Cancer. 2012 Nov 15;118(22):5463–72. Epub 2012 Apr 27.
https://doi.org/10.1002/cncr.27581
PMid:22544643 PMCid:PMC3611659
41. Christiansen N, Chen L, Gilmore J, et al. Association between African American race and outcomes in patients with nonmetastatic triple-negative breast cancer: a retrospective analysis by using results from the Georgia Cancer Specialist Database. Clin Breast Cancer. 2012 Aug;12(4):270–5. Epub 2012 Jun 8.
https://doi.org/10.1016/j.clbc.2012.04.007
PMid:22683281
42. Clarke CA, Keegan TH, Yang J, et al. Age-specific incidence of breast cancer subtypes: understanding the Black-White crossover. J Natl Cancer Inst. 2012 Jul 18;104(14):1094–101. Epub 2012 Jul 5.
https://doi.org/10.1093/jnci/djs264
PMid:22773826 PMCid:PMC3640371
43. O'Brien KM, Cole SR, Tse CK, et al. Intrinsic breast tumor subtypes, race, and long-term survival in the Carolina Breast Cancer Study. Clin Cancer Res. 2010 Dec 15;16(24):6100–10.
https://doi.org/10.1158/1078-0432.CCR-10-1533

PMid:21169259 PMCid:PMC3029098
44. Joslyn SA. Racial differences in treatment and survival from early-stage breast carcinoma. Cancer. 2002 Oct 15;95(8):1759–66.
https://doi.org/10.1002/cncr.10827
PMid:12365025
45. Joslyn SA. Hormone receptors in breast cancer: racial differences in distribution and survival. Breast Cancer Res Treat. 2002 May;73(1):45–59.
https://doi.org/10.1023/A:1015220420400
PMid:12083631
46. Li CI, Malone KE, Daling JR. Differences in breast cancer hormone receptor status and histology by race and ethnicity among women 50 years of age and older. Cancer Epidemiol Biomarkers Prev. 2002 Jul;11(7):601–7.
PMid:12101106
47. Li CI, Daling JR, Malone KE. Incidence of invasive breast cancer by hormone receptor status from 1992 to 1998. J Clin Oncol. 2003 Jan 1;21(1):28–34.
https://doi.org/10.1200/JCO.2003.03.088
PMid:12506166
48. Rizzo M, Lund MJ, Mosunjac M, et al. Characteristics and treatment modalities for African American women diagnosed with stage III breast cancer. Cancer. 2009 Jul 1;115(13):3009–15.
https://doi.org/10.1002/cncr.24334
PMid:19466698
49. Trivers KF, Lund MJ, Porter PL, et al. The epidemiology of triple-negative breast cancer, including race. Cancer Causes Control. 2009 Sep;20(7):1071–82. Epub 2009 Apr 3.
https://doi.org/10.1007/s10552-009-9331-1
PMid:19343511 PMCid:PMC4852686
50. Johnson A, Shulman L, Kachajian J, et al. Access to care in Vermont: factors linked with time to chemotherapy for women with breast cancer—a retrospective cohort study. J Oncol Pract. 2016 Sep;12(9):e848–57. Epub 2016 Aug 30.
https://doi.org/10.1200/JOP.2016.013409
PMid:27577620 PMCid:PMC5022113
51. Huang B, Dignan M, Han D, et al. Does distance matter? Distance to mammography facilities and stage at diagnosis of breast cancer in Kentucky. J Rural Health. 2009 Fall;25(4):366–71.
https://doi.org/10.1111/j.1748-0361.2009.00245.x
PMid:19780916
52. Wang F, Luo L, McLafferty S. Health care access, socioeconomic factors and late-stage cancer diagnosis: an exploratory spatial analysis and public policy implication. Int J Public Pol. 2010;5(2–3):237–58. Epub 2009 Dec 28.
https://doi.org/10.1504/IJPP.2010.030606
https://doi.org/10.1504/IJPP.2010.035127
53. McLafferty S, Wang F. Rural reversal? Rural-urban disparities in late-stage cancer risk in Illinois. Cancer. 2009 Jun 15;115(12):2755–64.
https://doi.org/10.1002/cncr.24306
PMid:19434667 PMCid:PMC2774239
54. Wang F, McLafferty S, Escamilla V, et al. Late-stage breast cancer diagnosis and health care access in Illinois. Prof Geogr. 2008 Feb;60(1):54–69.

https://doi.org/10.1080/00330120701724087
PMid:18458760 PMCid:PMC2367325

55. McLafferty S, Wang F, Luo L, et al. Rural-urban inequalities in late-stage breast cancer: spatial and social dimensions of risk and access. Environ Plann B Plann Des. 2011 Aug;38(4):726–40.
https://doi.org/10.1068/b36145
PMid:23335830 PMCid:PMC3547633
56. Shiao YH, Chen VW, Lehmann HP, et al. Patterns of DNA ploidy and S-phase fraction associated with breast cancer survival in Blacks and Whites. Clin Cancer Res. 1997 Apr;3(4):587–92.
PMid:9815724
57. Joslyn SA, West MM. Racial differences in breast carcinoma survival. Cancer. 2000 Jan 1;88(1):114–23.
https://doi.org/10.1002/(SICI)1097-0142(20000101)88:1<114::AID-CNCR16>3.0.CO;2-J
58. Crowe JP Jr, Gordon NH, Hubay CA, et al. The interaction of estrogen receptor status and race in predicting prognosis for stage I breast cancer patients. Surgery. 1986 Oct;100(4):599–605.
PMid:3764686
59. Chen VW, Correa P, Kurman RJ, et al. Histological characteristics of breast carcinoma in Blacks and Whites. Cancer Epidemiol Biomarkers Prev. 1994 Mar;3(2):127–35.
PMid:7519506
60. Beverly LN, Flanders WD, Go RC, et al. A comparison of estrogen and progesterone receptors in Black and White breast cancer patients. Am J Public Health. 1987 Mar;77(3):351–3.
https://doi.org/10.2105/AJPH.77.3.351
PMid:3812846 PMCid:PMC1646891
61. Davis C, Darby K, Moore M, et al. Breast care screening for underserved African American women: community-based participatory approach. J Psychosoc Oncol. 2017 Jan–Feb;35(1):90–105. Epub 2016 Aug 11.
https://doi.org/10.1080/07347332.2016.1217965
PMid:27662263
62. Santos SL, Tagai EK, Scheirer MA, et al. Adoption, reach, and implementation of a cancer education intervention in African American churches. Implement Sci. 2017 Mar 14;12(1):36.
https://doi.org/10.1186/s13012-017-0566-z
PMid:28292299 PMCid:PMC5351199