Mapping Hot Spots of Breast Cancer Mortality in the United States: Place Matters for Blacks and Hispanics

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Abstract

PURPOSE: The goals of this study were to evaluate geographic and racial/ethnic variation in breast cancer mortality, and evaluate whether observed geographic differences are explained by county-level characteristics.

METHODS: We analyzed data on breast cancer deaths among women in 3108 contiguous United States (US) counties from years 2000 through 2015. We applied novel geospatial methods and identified hot spot counties based on breast cancer mortality rates. We assessed differences in county-level characteristics between hot spot and other counties using Wilcoxon rank-sum test and Spearman correlation, and stratified all analysis by race/ethnicity.

RESULTS: Among all women, 80 of 3108 (2.57%) contiguous US counties were deemed hot spots for breast cancer mortality with the majority located in the southern region of the US (72.50%, p value <0.001). In race/ethnicity-specific analyses, 119 (3.83%) hot spot counties were identified for NH-Black women, with the majority being located in southern states (98.32%, p value <0.001). Among Hispanic women, there were 83 (2.67%) hot spot counties and the majority was located in the southwest region of the US (southern = 61.45%, western = 33.73%, p value < 0.001). We did not observe definitive geographic patterns in breast cancer mortality for NH-White women. Hot spot counties were more likely to have residents with lower education, lower

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household income, higher unemployment rates, higher uninsured population, and higher proportion indicating cost as a barrier to medical care.

CONCLUSIONS: We observed geographic and racial/ethnic disparities in breast cancer mortality: NH-Black and Hispanic breast cancer deaths were more concentrated in southern, lower SES counties.

Keywords

Breast Cancer; Health Disparities; Socioeconomic Factors; Geospatial Analysis

INTRODUCTION

Breast cancer is a leading cause of death among women in the United States (US), responsible for more than 41,000 annual deaths [1]. The overall survival for breast cancer has increased over the past few decades with an estimated 90.8% five-year relative survival rate among all US women, a 16.0% absolute increase since 1977 [2]. However, racial differences in breast cancer mortality persist as Non-Hispanic (NH)-Black (71% increased risk) and Hispanic (14% increased risk) women have poorer five-year cause-specific survival when compared with their NH-White counterparts [1, 2]. Though research suggests that many of these women with lower survival rates are more likely to have more aggressive forms of breast cancer, there is also evidence that suggest socioeconomic status is an integral factor in decreased survival rates [3].

NH-Black and Hispanic women have up to a 50% increased risk for late-stage breast cancer diagnoses [4, 5], and experience higher breast cancer mortality when compared with NH-Whites [6-11]. An increased risk of late stage breast cancer diagnosis is associated with residing in highly segregated areas and decreased access to mammography.[12]. In addition, Haas et al. (2008) reported that the mediating role of racial segregation on the association between Black race and adequate breast cancer care was responsible for nearly 10% of the total effect on adequate breast cancer care [13]. Prior research also suggests that Black and Hispanic women living in poor and/or racially segregated communities are more likely to be diagnosed with late-stage breast cancer and when compared with their NH-White counterparts [4-10, 12-18]. In addition, a recent analysis of data from Surveillance, Epidemiology, and End Results (SEER), showed that when compared with NH-White women, and after controlling for breast cancer hormone-receptor subtype, area-level socioeconomic status, and healthcare access, NH-Blacks and Hispanics had a 39% and 5% increased risk of breast cancer mortality, respectively [6]. These studies suggest that social and built environmental risk factors such as availability of quality cancer screening and treatment resources may lead to clustering of breast cancer mortality in specific regions, and partly explain racial disparities in mortality rates among US women.

While prior studies have reported on the influence of race and geographic residence on breast cancer outcomes in the US [19-27], these studies are limited in scope due to limited generalizability to the entire US population (i.e., few studies among the entire contiguous US), lack of granularity (i.e., many studies have been state-level analyses), and most have lacked data on specific county-level characteristics as potential explanations for observed

geographic patterns. Here, we will evaluate geographic variations in breast cancer mortality among US women by race/ethnic group, and evaluate the contribution of county-level characteristics important for breast cancer outcomes. Together, these data will add a nuanced view to our understanding of breast cancer mortality in the US, and highlight areas where targeted cancer prevention strategies are needed.

MATERIALS AND METHODS

Study Design and Data Source

This was a cross-sectional study of breast cancer mortality among women between 2000 through 2015 in counties within the contiguous US. County-level breast cancer mortality rates were obtained from the Center for Disease Control and Prevention (CDC) underlying causes of death file [28], while county-level characteristics were obtained from the 2014 County Health Rankings (CHR) and American Community Survey (ACS) [29, 30]. This study was considered exempt by the Institutional Review Boards of the University of Alabama at Birmingham and Washington University School of Medicine, as we used existing secondary data that are publicly available and non-identifiable.

Identification of Breast Cancer Deaths and Mortality

We defined breast cancer deaths as attributed to malignant neoplasms of the breast among women aged 15 and older for the years 2000 through 2015. Breast cancer deaths were identified from the underlying cause-of-death database produced by the CDC's National Center for Health Statistics (https://wonder.cdc.gov) [28]. The underlying cause-of-death defines attributable deaths as "the disease or injury which initiated the train of events leading directly to death, or the circumstances of the accident or violence which produced the fatal injury" [28]. Data from the underlying cause-of-death are derived from death certificates and include a record for every death of a US resident. We identified the county level total number, crude rates, and age-adjusted rates for breast cancer using the ICD-10 codes for breast cancer (**Supplemental Table 1**). We included breast cancer-related deaths for all persons aged 15 years or older during the observation period because the Underlying Causes of Death database uses a single reference standard population for ages 15 through 24, and therefore, the inclusion of the 15 to 19 year groups is necessary for the estimation of age-adjusted rates. Age adjusted rates were standardized to the year 2000 US population. We identified breast cancer deaths overall and by race/ethnicity for NH-Black, NH-White, and Hispanic Women.

County-Level Demographic Characteristics

We included the county-level data on age groups, sex, race, household income, population with college education, and Rural-Urban Commuting Area (RUCA) codes as study covariates. We obtained data on county-level proportion of race/ethnic groups for the five most populous racial groups in the US for the 15-year period including: NH-White, NH-Black and Hispanic. Hispanic women consisted of women that identified as having Hispanic, Latino, or Spanish origins including but not limited to: Mexican American, Chicano, Puerto Rican, Cuban, Argentinean, Colombian, Dominican, Nicaraguan, Salvadoran, and Spaniard. We classified counties as Urban or Non-Urban using the 2010

Rural-Urban Commuting Areas (RUCA) classifications. RUCA codes are based on population size and density, urbanization, and primary and secondary worker commuter flow patterns to larger urban areas and clusters [31]. The 10 RUCA codes were then aggregated into a dichotomized variable: (1) Urban (i.e., population centers with 50,000 or more residents) and (2) Non-Urban (i.e., towns or small cities with population centers with less than 50,000 residents) [31, 32]. We obtained all county-level demographic statistics from the 2014 ACS via National Historical Geographic Information System [29]. The 2014 ACS provided aggregated estimates for demographic statistics based on the preceding 5-year period (2010 – 2014).

County-Level Characteristics

We included county-level prevalence of adult obesity, current smokers, mammography screening, physically inactivity as well as the proportion of adults that could not see doctor due to cost, had limited access to healthy foods, were unemployed or uninsured, the total number of primary care physicians, and region as county-level characteristics. We calculated the ratio of primary care physicians per 10,000 persons by dividing the total number of primary care physicians by the county population and then multiplied the quotient by 10,000. Geographic region was defined using the Census definition (i.e., Midwest, Northeast, South, and West) [33]. We obtained county-level characteristics from the 2014 County Health Rankings (CHR) [29, 30]. The CHR consists of nationally representative data collected from a variety of databases which all sample among the total non-institutionalized population over 18 years of age living within households. The CHR gathered and aggregated county level data from different resources such as the National Center for Chronic Disease Prevention and Health Promotion (e.g., data on adult obesity and physical inactivity), Behavioral Risk Factor Surveillance System (e.g., data on smoking and could not see doctor), USDA Food Environment Atlas (e.g., data on limited access to healthy foods), the Medicare/Dartmouth Institute (e.g., data on mammography screening), Bureau of Labor Statistics (e.g., data on unemployment rate), and the Area Health Resources Files (e.g., data on uninsured rate and number of primary care physicians). Detailed descriptions of county-level characteristics are described in **Supplemental Table 2**.

Geospatial Analysis and Identification of Breast Cancer Mortality Hot Spots

Geographic hot spots for disease can be described as the spatial aggregation of cases in an identifiable subpopulation [34]. While there is no formal and/or commonly accepted approach to identifying spatial disease clustering, there are several geospatial measures that account for the overall rate, county population, and spatial autocorrelation of designated areas of interest [35]. Further, the geospatial methods used in our analyses take into account geospatial differences on local (Getis Ord), global and local (LISA), and overall population sizes of each county (Empirical Bayes method). To avoid spurious results garnered from a singular geospatial measure, we used an aggregation of three separate spatial clustering methods to identify counties that were hot spots for breast cancer mortality [31]. We categorized county-level breast cancer mortality into two groups: "hot spots" or "non-significant" based on statistically significant higher observed vs. expected breast cancer mortality rate using the combination of three distinct methods. We considered a county to be a "hot spot" if it was identified as high risk for breast cancer mortality using all three

geospatial analyses: 1) fifth quintile of smoothed Empirical Bayes (EB) breast cancer mortality rates, 2) high-high cluster using Local Indicators of Spatial Association (LISA), and 3) as a hot spot defined by Getis-Ord Gi* statistic) [36, 37]. All other US counties were categorized as non-significant.

First, we estimated the smoothed Empirical Bayes (EB) breast cancer mortality rates using the proportion of women with deaths attributed to breast cancer, with smoothing performed using the EB tools in GeoDa 1.6.7.9 (http://geodacenter.asu.edu)[38]. Briefly, the smoothed EB rate method allows for more stable estimation of breast cancer mortality rates by accounting for the overall county population. EB smoothing includes the variance of each county by using the corresponding county population, and thus counties with higher populations have smaller variance and those with smaller populations had larger variance. Further, the EB rates are smoothed using an inverse function of the variance for shrinkage towards the overall mean for breast cancer mortality rates (i.e., counties with larger populations and smaller variance gave higher weights towards the observed weights). We categorized the EB smoothed breast cancer mortality rates into quintiles, and we defined counties as high-risk if the smoothed EB breast cancer mortality rates were in the fifth quintile. Secondly, we used Local Indicators of Spatial Association (LISA) to measure similarity of breast cancer mortality between counties and calculate values both within and across geographic boundaries, additionally identifying spatial outliers [36, 38, 39]. For each US county, we estimated Local Moran's I Statistic values, using associated z-scores and p-values to assess the magnitude of spatial autocorrelation and statistical significance, respectively[38]. Statistically significant (p value 0.05) positive z-scores indicate counties surrounded by areas with similar breast cancer mortality rates – either similarly high or similarly low (positive spatial autocorrelation) [38]. Lastly, we used the Gi* statistic to identify areas where breast cancer mortality rates with either high or low values clustered within the context of the neighboring county [37, 38, 40, 41].

For both the LISA and Gi* analysis we employed 1000 permutations and randomized data using the specific seed number 74 (an arbitrary number, but important for replication of study results). In contrast to LISA, the Gi* statistic are not related to the global statistic of spatial association [32]. Moreover, while the LISA statistic includes a diagnostic for outliers with respect to a measure of global association, the Gi* only examines associations for counties that share borders [32]. Further, the LISA analysis allows for examining local associations while accounting for the global spatial association (can be observed from the counties identified as either high-low or low-high outliers). Further details to the geospatial autocorrelation analysis were introduced by Nassel et al. (2014) and we have published similar analysis that are described elsewhere [30, 31]. We performed all geospatial analyses using GeoDa version 1.6.7.9, and mapping were performed using ArcGIS 10.5.

Statistical Analysis

We compared regional (i.e., Midwest vs. Northeast vs. South vs. West) differences in hot spot breast cancer categories (EB, LISA, Gi*, and Breast Cancer Mortality hot spot Category) using chi-square and Fisher's exact tests, as appropriate. We performed Fisher's exact tests for analyses with small cell sizes, and calculated Monte Carlo estimates of exact

p values using 10,000 samples with the random seed number 74. We compared differences in demographic and county-level characteristics between hot spot and non-significant counties using the Wilcoxon rank-sum test. We presented the medians and interquartile ranges for the sociodemographic and county-level characteristics due to the non-parametric distribution of continuous variables. Due to a large number of counties examined, there were many associations considered significant at α = 0.05. Therefore, in order to observe the magnitude of correlation between hot spots and county-level characteristics we additionally examined the correlation of demographic and county-level characteristics with being a county-level breast cancer mortality hot spot using a Spearmen correlation (positive values indicate positive correlation) (ρ). We obtained the mean crude and age-adjusted mortality rates standardized to the 2000 US standard population. We additionally estimated the crude and age-adjusted breast cancer mortality rates for the entire contiguous US. Lastly, to examine differences in breast cancer mortality and associated characteristics by race, we stratified all results by race/ethnicity. We performed statistical analyses using SAS version 9.4. All statistical tests were two-sided and p-values   0.05 were considered statistically significant.

RESULTS

Mortality Rates by Hot Spot Areas

Between 2000 and 2015 there were 653,630 total deaths attributed to breast cancer (Table 1), corresponding to a mean age-adjusted breast cancer mortality rate of 29.2 per 100,000 6women (95% CI: 29.1 – 29.4). Age-adjusted mortality was higher in hot spot counties (34.6 per 100,000 women, 95% CI: 33.0 – 36.2) when compared with the remaining US counties (29.1 per 100,000 women, 95% CI: 29.0 – 29.3). Mortality rates were highest among NH-Black women (39.3, 95% CI: 39.0 – 39.6), compared with NH-White (29.3, 95% CI: 29.1 – 29.4) and Hispanic (18.1, 95% CI: 17.9 – 18.3) women.

All Race/Ethnicities

Among all women, we identified 80 of 3108 (2.57%) hot spot counties for breast cancer mortality with the majority (72.50%, p value <0.001) located in the southern US region (Table 2, Figure 1). Hot spot maps of each specific method (Gi* statistic, LISA, and EB) and stratified by race can be found in Supplemental Figures 1 – 12. Counties designated as hot spots had a higher proportion of NH-Black population (27.8% vs. 1.9%, p value <0.001, ρ correlation = 0.14), lower proportion of Hispanics (1.8% vs. 3.5%, p value <0.001, ρ correlation = −0.11), lower proportion of NH-White population (65.7% vs. 85.9%, p value <0.001, ρ correlation = −0.07), higher adult obesity (33.9% vs. 30.6%, p <0.001, ρ correlation = 0.12), lower proportion of adults with college education (13.7% vs. 18.0%, p <0.001, ρ correlation = −0.11), higher population with low income (27.8% vs. 20.5%, p <0.001, ρ correlation = 0.14), higher physical inactivity (33.1% vs. 28.1, p <0.001, ρ correlation = 0.13), and higher unemployment (9.4% vs. 7.5%, p <0.001, ρ correlation = 0.11) (Table 3).

NH-Black Women

Among NH-Black women, we identified 119 (3.83%) hot spot counties for breast cancer mortality with 117 (98.32%, p value <0.001) of those located in the southern US (Figure 2). When compared with non-significant counties, hot spots for NH-Blacks had a higher proportion of NH-Black residents (34.6% vs. 1.8%, p value <0.01, ρ correlation = 0.29), adult obesity (34.9% vs. 30.5%, p value <0.01, ρ correlation = 0.21), those that could not visit doctor due to cost (17.2% vs. 12.5%, p value <0.01, ρ correlation = 0.13), household incomes less than $20,000 (27.7% vs. 20.4%, p value <0.01, ρ correlation = 0.16), physical inactivity (32.4% vs. 28.0%, p value <0.01, ρ correlation = 0.16), unemployment (9.7% vs. 7.4%, p value <0.01, ρ correlation = 0.14), and uninsured residents (25.3% vs. 21.3%, p value, ρ correlation = 0.12) (Table 4). In addition, counties that were hot spots for NH-Blacks had lower proportion of adults with college education (14.3% vs. 18.0%, p value <0.01, ρ correlation = −0.11).

Hispanic Women

Among Hispanic women, we identified 83 (2.67%) hot spot counties for breast cancer mortality, with 51 (61.45%, p value <0.001) and 28 (33.73%) of those located in the southern and mid-western regions, respectively (Figure 3). When compared with non-significant counties, counties that qualified as hot spots for Hispanics had a higher proportion of Hispanic residents (50.2% vs. 3.3%, p value <0.01, ρ correlation = 0.26) and uninsured residents (29.3% vs. 21.3%, p value, ρ correlation = 0.17) (Table 3). In addition, hot spots for Hispanics had lower proportion of NH-White residents (42.2% vs. 86.4%, p < 0.001, ρ correlation = −0.23), adult obesity (28.8% vs. 30.8%, p <0.001, ρ correlation = −0.13), adult smoking prevalence (14.05 vs. 19.7%, p value <0.001, ρ correlation = −0.12), and mammography screening (55.4% vs. 61.5%, p value <0.01, ρ correlation = −0.11).

NH-White Women

Among NH-White women, we identified 57 (1.83%) hot spot counties for breast cancer mortality, with 27 (47.37%, p value <0.001) of the hot spot counties located in the Northeast (Figure 4). When compared with non-significant counties, counties that qualified as hot spots for NH-White women had a slightly higher proportion of unemployed residents (8.5% vs. 7.5%, p value <0.01, ρ correlation = 0.06), lower proportion of non-urban residents (37.3% vs. 59.7%, p <0.01, ρ correlation = −0.07), and slightly lower obesity (28.3% vs. 30.7%, p value <0.01, ρ correlation = −0.06).

DISCUSSION

The objectives of our analysis were to evaluate breast cancer mortality hot spots among US counties, identify the county-level characteristics of those counties, and delineate differences in breast cancer mortality hot spots by race. Overall, the age-adjusted breast cancer mortality rate was 18% higher for women living in hot spot counties compared with those in non-significant counties. Hot spot counties also had a higher proportion of NH-Black residents, higher prevalence of obesity, lower education and income, and higher unemployment and smoking prevalence. We observed distinct geographic patterns in hot spots for breast cancer mortality among NH-Black women (rural southern counties near the Mississippi River and

counties in the northern coastal North Carolina/southern Virginia areas) and Hispanic women (southwestern US, and central and southern Florida areas), but no geographic patterns were discernable among NH-White women. NH-Black women living in hot spots had a 15% higher risk of breast cancer mortality when compared with NH-Black women living in other geographic areas. Hispanic women living in hot spots had nearly a 26% higher risk of breast cancer mortality when compared with Hispanic women living in other geographic areas. For NH-White women, hot spots were more variably dispersed across the contiguous US, and thus we deem that there were no apparent geographic patterns or significant clustering.

Delineating geospatial patterns of breast cancer mortality, while additionally examining whether these patterns are modified by race and ethnicity, may provide utility in understanding areas where targeted mortality prevention strategies are needed, and may provide clues into etiological and/or prognostic risk factors for breast cancer in those areas. Moreover, limited research has investigated racial disparities in breast cancer mortality while taking into account the geographic variations and county-level characteristics using geospatial epidemiologic methodology [20, 24, 25, 42]. In this study we identified geographic areas of possible intervention for high breast cancer mortality for Hispanic and NH-Black women living in the US. Only a few studies have examined regional patterns of breast cancer mortality among US women [19-21, 23-27, 42, 43]. To our knowledge this is one of the first studies to utilize multiple geospatial analyses for identifying county-level hot spots for high breast cancer mortality among the entire contiguous US.

Prior studies did not offer granular insight to the geographic areas most burdened with breast cancer mortality while delineating racial differences. For example, a prior analysis that supports our observed southern Mississippi River hot spots for breast cancer mortality utilized the same data source (national vital statistics data) although at a different spatial resolution (state-level) to examine changes in breast cancer by race between two time periods; 1986 through 1990 compared with 1991 through 1995 [19]. In this study, Canto et al (2001) reported that among states ranked in the top decile for breast cancer mortality in 1990, White women experienced a 9.85% reduction in mortality rate compared to only a 2.71% reduction in breast cancer mortality for Black women [19]. Mokdad et al (2017) similarly observed that from 1980 through 2014 clusters of high rates remained in the southern belt and along the Mississippi River [24]. Another study performed by Chien et al (2013) similarly utilized national mortality data between 1982 and 2004, to determine geographic disparities in breast cancer mortality by using the structured additive regression (STAR) model (i.e., similar to the current study's Gi* analysis) [20]. In contrast to our results, the authors observed that among Blacks and Whites the highest risk areas for breast cancer mortality were located in the Northeast US; showing up to a 2-fold increased risk of breast cancer mortality in these area [20]. In addition, approximately 67% and 25% of all US counties were categorized as high risk for White and African American women, respectively [20]. Possible explanations for the differences in our results may be: 1) regional differences in breast cancer mortality may have changed over past few decades, and 2) the use of more conservative cluster detection methodology using three separate statistical approaches in the current study.

We identified two specific hot spot areas for breast cancer mortality among NH-Black women: 1) rural southern counties near the Mississippi River and 2) counties in the northern coastal North Carolina/southern Virginia region. We also identified two unique areas of hot spots for Hispanic women: 1) in the southwestern states of Arizona, New Mexico, and southern Texas, and 2) in counties located in central to southern Florida area. Several factors likely contribute to racial differences in breast cancer mortality and in particular, the observed geographic clustering. However, studies suggest that the most significant causes relate to lack of adequate and timely screening necessary for early detection, and lack of access to adjuvant chemotherapy and/or surgical interventions [2, 6, 44-55]. Fedewa et al. (2011) reported that NH-Blacks were 25% to 106% more likely to have delayed breast cancer chemotherapy after 30-, 60-, and 90-days following breast cancer diagnosis [48]. Further, we previously observed that NH-Black women were 42% more likely to have late-stage breast cancer diagnosis, 45% less likely to receive surgical treatment after breast cancer diagnosis, 15% less likely to receive radiation therapy after breast cancer, and had a 39% higher risk of breast cancer mortality when compared with NH-White women [6]. In the current study, counties that were hot spots for breast cancer mortality also had county-level-characteristics that are likely barriers to receipt of screening and treatment. For instance, we observed that breast cancer mortality hot spot counties for NH-Black and Hispanic women were more likely to have lower household income and higher unemployment, and hot spot counties for NH-Black women had a higher proportion of adults that could not visit the doctor within the past year due to cost, and population with higher uninsured rates. These findings indicate that counties identified as hot spots for breast cancer mortality in the US, also had significant barriers to timely and quality healthcare due to lack of income and health insurance. Public health strategies focused on improving breast cancer screening among Hispanic women and reducing barriers to affordable treatment for NH-Black women may go a long way in preventing excess breast cancer deaths in the US.

We must note that the "southern Mississippi River" areas identified as hot spots in the current analysis have consistently been shown to be associated with poorer health outcomes using geospatial analyses in previous studies investigating varied diseases [56-61]. For example, studies have shown that the southern Mississippi River region has higher risks for lung cancer [60], coronary heart disease and stroke [61], and sepsis [58]. Consistent poverty and lower access to healthcare are likely significant contributors to the health disparities affecting this region, and targeted healthcare strategies focused on this geographic region are likely to have significant impact.

The results and discussion of this study should be interpreted with respect to a few limitations. First, the underlying causes of death file suppressed county-level data representing fewer than ten events, and as a result we were unable to ascertain estimates if counties had less than ten breast cancer deaths over the total fifteen-year period. Thus, counties with less than ten events were far more likely to be in areas of low clustering or non-significance during our analysis on geospatial autocorrelation. In addition, the geospatial hot spots when stratified by race were dependent on both prevalence of disease and number of persons living within a county. An inherent limitation is that the non-significant areas among NH-Blacks and Hispanic women may simply represent areas with lower populations of these specific minority groups. However, this still provides important

public health information regarding hot spot areas where targeted cancer prevention efforts may be more efficiently focused. By utilizing multiple geospatial methods to account for the county population size (i.e., empirical Bayes smoothed rates), global spatial associations (Getis-Ord analysis), and local spatial associations (i.e., Local Moran's I – LISA analysis), we reduced the likelihood of systematic bias in identifying hot spots. In general, it is reported that the latency period of breast cancer is between 8 and 15 years [62–64]. However, we examined breast cancer mortality using an ecologic study design, and thus our results are subject to temporality bias and ecological fallacy. Further, the objective of our study were not to ascertain causal inference, but rather to assess association between county-level factors and breast cancer mortality using similar dates: we used aggregated county demographic and characteristic data ranging from 2010 through 2014 and mortality data for years 2000 through 2015. Although we did not have data on specific breast cancer subtypes (e.g., estrogen receptor positive (ER+), negative (ER-), or triple negative), Hispanic subgroups, or individual level factors associated with breast cancer mortality in the current analysis, future studies focused on etiology would benefit from inclusion of these factors.

Additionally, there were benefits to the current study analyses that lead to more generalizable results. First, our results are likely less spurious than other studies that have employed fewer geospatial similar methods due to our conservative criteria for categorizing hot spots areas. Secondly, our results were derived from nationally representative sources including the underlying cause of death file from the CDC, ACS, and CHR. The ACS, CHR, and CDC datasources are nationally representative samples that have been used in studies examining sociodemographic and county-level characteristics [58, 65].

CONCLUSION

The results of this study suggest that breast cancer mortality for NH-Black and Hispanic American women are geographically clustered in specific regions in the US. Specifically, for NH-Black women the high-risk areas of breast cancer mortality are located in the rural south of counties near the Mississippi River and counties in the northern coastal North Carolina/southern Virginia areas, and for Hispanic women, the hot spot areas are located in the southwestern US, and central and southern Florida areas. Targeted cancer prevention strategies, including transportation, increased availability of affordable screening, and quality treatment facilities in these specific areas are likely to be highly efficient in reducing disparities in breast cancer mortality in the US.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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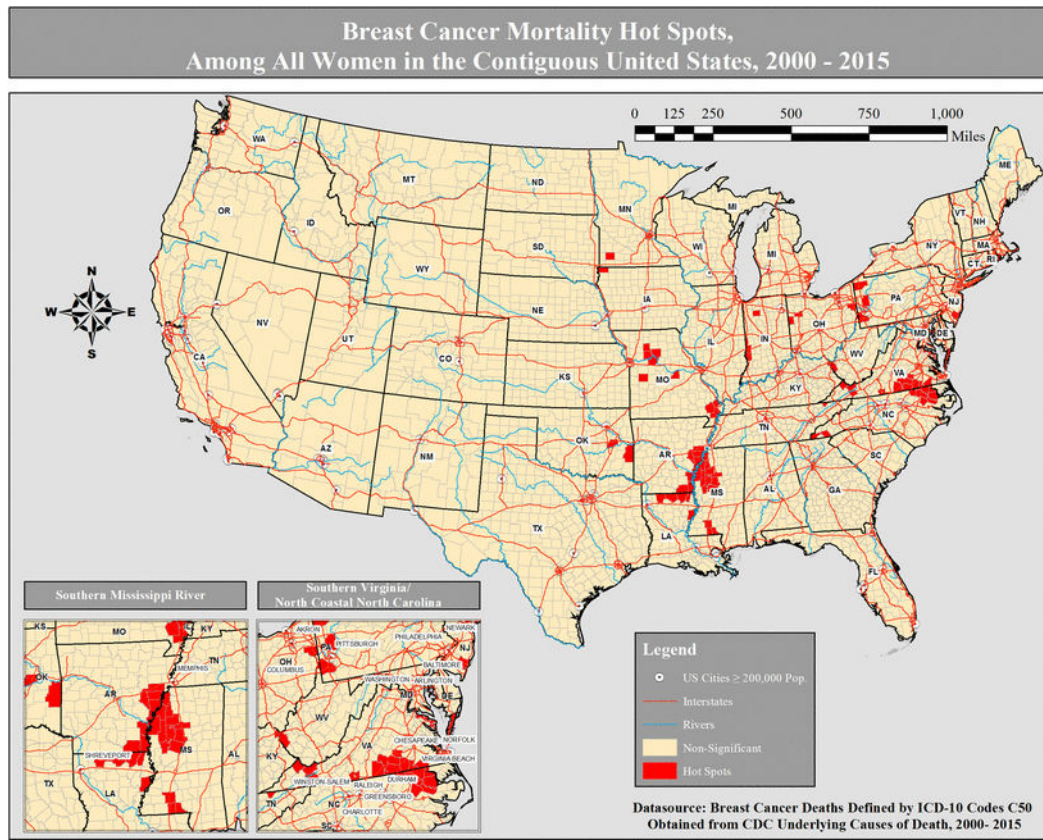
Figure 1:
Breast cancer mortality hot spots, among all women in the contiguous United States, 2000 – 2015.
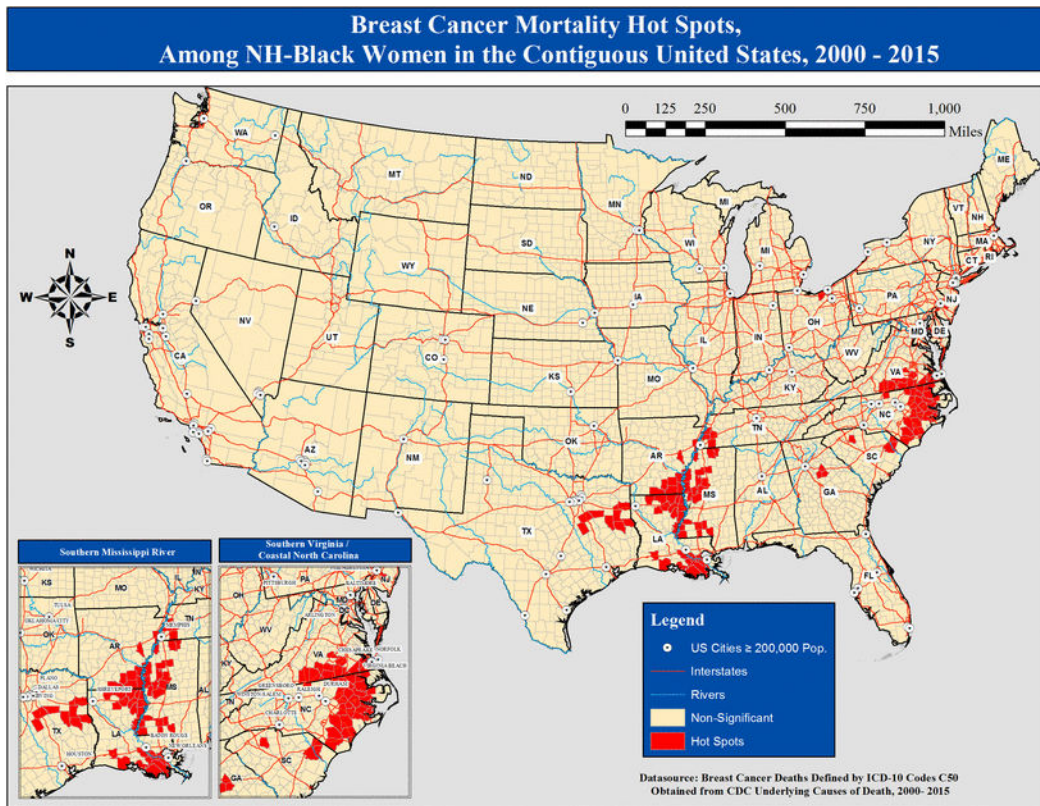
Figure 2:
Breast cancer mortality hot spots, among all NH-Black women in the contiguous United States, 2000 – 2015.

Figure 3:
Breast cancer mortality hot spots, among all Hispanic women in the contiguous United States, 2000 – 2015.
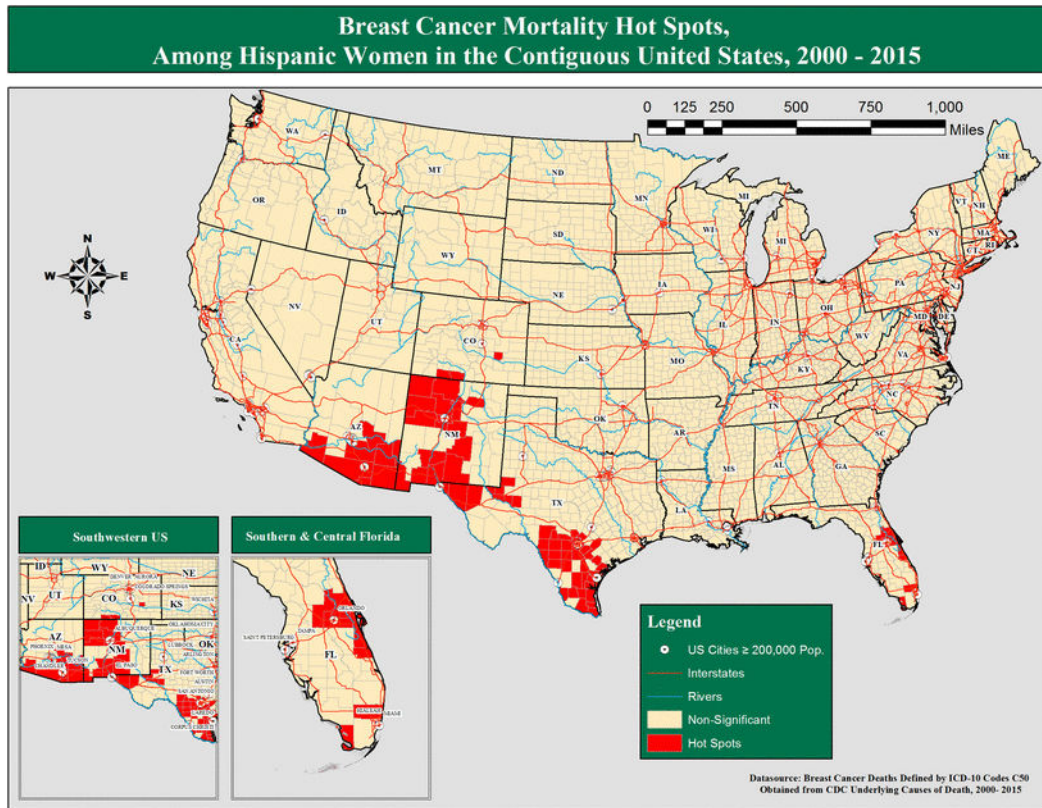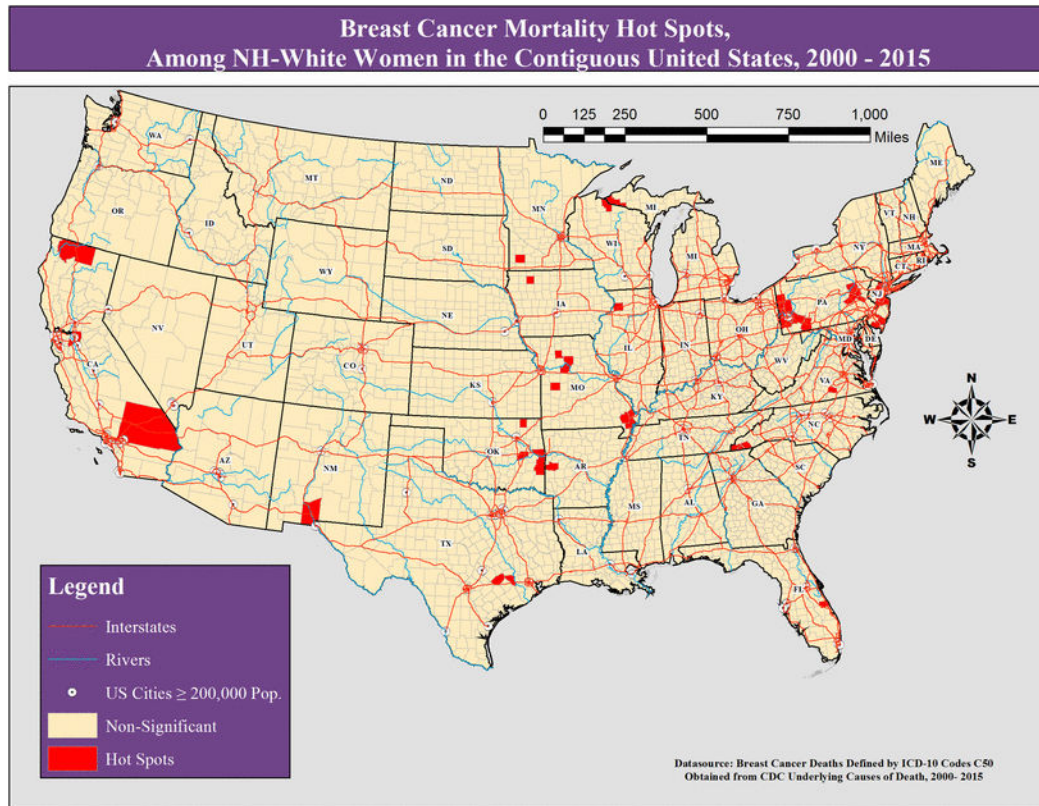
Figure 4:
Breast cancer mortality hot spots, among all NH-White women in the contiguous United States, 2000 – 2015.

Table 1:

Breast Cancer Mortality[a] in the United States by Hot Spot Category, 2000 – 2015, excluding Alaska and Hawaii.

	Breast Cancer Deaths[b]	Mean Crude Breast Cancer Mortality per 100,000 women[c] (95% CI)	Mean Age-Adjusted Breast Cancer Mortality per 100,000 women[c] (95% CI)
Entire United States			
Hot Spot ($n = 80$)	8,209	44.5 (42.0 – 47.0)	34.6 (33.0 – 36.2)
Non-Significant ($n = 3,028$)	645,421	32.8 (32.6 – 33.1)	29.1 (29.0 – 29.3)
Overall ($n = 3,108$)[d]	653,630	32.9 (32.7 – 33.1)	29.2 (29.1 – 29.4)
Among NH-Black Women			
Hot Spot ($n = 119$)	6,049	44.2 (42.7 – 45.8)	44.7 (43.3 – 46.2)
Non-Significant ($n = 2,989$)	83,703	35.8 (35.4 – 36.2)	38.9 (38.6 – 39.3)
Overall ($n = 3,108$)[e]	89,752	36.3 (35.9 – 36.6)	39.3 (39.0 – 39.6)
Among Hispanic Women			
Hot Spot ($n = 83$)	8,806	18.5 (18.1 – 18.9)	21.6 (21.2 – 22.0)
Non-Significant ($n = 3,025$)	23,635	12.2 (12.0 – 12.4)	17.2 (17.0 – 17.4)
Overall ($n = 3,108$)[f]	32,441	13.4 (13.3 – 13.6)	18.1 (17.9 – 18.3)
Among NH-White Women			
Hot Spot ($n = 57$)	30,268	46.6 (45.4 – 47.8)	29.1 (28.9 – 29.2)
Non-Significant ($n = 3,051$)	479,420	37.0 (36.8 – 37.3)	33.2 (32.5 – 33.9)
Overall ($n = 3,108$)[g]	509,688	37.5 (37.2 – 37.8)	29.3 (29.1 – 29.4)

[a] Deaths per 100,000 women.

[b] Total number of deaths, identified using *International Classification of Diseases*, 10th Version codes for breast cancer.

[c] Weighted by county population of women aged 18+ (weighted by NH-Black, Hispanic, and NH-White populations for race/ethnicity stratified mortality rates).

[d] The row that indicates "overall mortality rate" should be interpreted as the county-level mean mortality rate per 100,000 women for all women

[e] NH-Black women

[f] Hispanic women

[g] NH-White women.

Table 2:

Comparison of Breast Cancer Mortality Geospatial Hot Spot[a] by Counties within United States Region, stratified by race/ethnicity years 2000 – 2015.

	Midwest Counties[b] (N = 1,055)	Northeast Counties[b] (N = 217)	Southern Counties[b] (N = 1,422)	Western Counties[b] (N = 414)	Total (N = 3108)	P value[c]
	Presented as N (%)[d]				N (%)[e]	
Among All Women						
Breast Cancer Hot Spot[a]	18 (22.50)	4 (5.00)	58 (72.50)	0 (0.0)	80 (2.57)	<0.001
LISA High-High Cluster	87 (37.66)	29 (12.55)	112 (48.48)	3 (1.3)	231 (7.43)	<0.001
EB 5th Quintile	279 (44.87)	42 (6.75)	260 (41.80)	41 (6.59)	622 (20.01)	<0.001
Gi* Hot spot	69 (19.49)	15 (4.24)	268 (75.71)	2 (0.56)	354 (11.39)	<0.001
Among NH-Black Women						
Breast Cancer Hot Spot[a]	1 (0.84)	1 (0.84)	117 (98.32)	0 (0.0)	119 (3.83)	<0.001
LISA High-High Cluster	1 (0.69)	1 (0.69)	143 (98.62)	0 (0.0)	145 (4.67)	<0.001
EB 5th Quintile	104 (16.72)	35 (5.63)	473 (76.05)	10 (1.61)	622 (20.01)	<0.001
Gi* Hot Spot	26 (5.15)	49 (9.70)	412 (81.58)	18 (3.56)	505 (16.25)	<0.001
Among Hispanic Women						
Breast Cancer Hot Spot[a]	0 (0.0)	4 (4.82)	51 (61.45)	28 (33.73)	83 (2.67)	<0.001
LISA High-High Cluster	2 (1.68)	4 (3.36)	63 (52.94)	50 (42.02)	119 (3.83)	<0.001
EB 5th Quintile	98 (15.76)	89 (14.31)	257 (41.32)	178 (28.62)	622 (20.01)	<0.001
Gi* Hot Spot	16 (5.59)	51 (17.83)	110 (38.46)	109 (38.11)	286 (9.20)	<0.001
Among NH-White Women						
Breast Cancer Hot Spot[a]	13 (22.81)	27 (47.37)	13 (22.81)	4 (7.02)	57 (1.83)	<0.001
LISA High-High Cluster	68 (35.98)	37 (19.58)	62 (32.80)	22 (11.64)	189 (6.08)	<0.001
EB 5th Quintile	261 (41.96)	45 (7.23)	234 (37.62)	82 (13.18)	622 (20.01)	<0.001
Gi* Hot Spot	144 (41.62)	43 (12.43)	136 (39.31)	23 (6.65)	346 (11.13)	<0.001

[a]Defined as counties estimated as a hot spot by all three geospatial methods (local indicators of spatial association, empirical Bayes, and Gi*). EB = empirical Bayes.

[b]US regions as determined by the US Census Bureau.
Midwest counties are in the states of IN, IL, IA, MI, MN, MO, NE, ND, OH, SD, and WI.
Northeast counties are in the states of CT, ME, NH, NJ, NY, PA, RI, and VT.
Southern counties are in the states of AL, AR, DE, DC, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA, and WV.
Western counties are in the states of AZ, CA, CO, ID, MT, NM, NV, OR, UT, WA, and WY.

[c]p values determined using chi-square or Fisher's exact tests (exact p values calculated using Monte Carlo estimation).

[d]Denotes row percentages.

[e]Denotes column percentages.

Table 3:

County-Level Characteristics Comparisons by Breast Cancer Mortality Hot Spot Category, Among All Women 2000 – 2015.

	Hot Spot[a] (N = 80)	Non-Significant (N = 3,028)	P value[b]	ρ[c]
	Presented as Median (IQR)[d]			
Race				
% NH-White	65.7 (41.4 – 94.2)	85.9 (67.6 – 94.0)	<0.001	−0.07
% NH-Black	27.8 (2.4 – 52.5)	1.9 (0.5 – 9.4)	<0.001	0.14
% Hispanic	1.8 (1.2 – 3.1)	3.5 (1.7 – 8.8)	<0.001	−0.11
% Female Sex	51.1 (49.6 – 52.1)	50.4 (49.5 – 51.1)	<0.001	0.06
% Age				
<18	22.0 (20.0 – 24.2)	22.9 (20.9 – 24.6)	0.05	−0.04
18 – 29	13.9 (12.7 – 15.1)	14.0 (12.3 – 16.0)	0.77	−0.01
30 – 44	17.5 (16.4 – 18.4)	17.7 (16.3 – 19.0)	0.26	−0.02
45 – 64	28.8 (27.0 – 29.9)	28.0 (26.3 – 29.6)	0.10	0.03
65 – 79	12.9 (11.5 – 14.5)	12.1 (10.3 – 13.9)	0.005	0.05
80+	4.4 (3.8 – 5.1)	4.2 (3.4 – 5.2)	0.09	0.03
% Completed college	13.7 (12.1 – 17.2)	18.0 (14.0 – 23.9)	<0.001	−0.11
% Household income <$20,000	27.8 (23.3 – 34.5)	20.5 (16.4 – 25.4)	<0.001	0.14
County-level characteristics				
% Obesity	33.9 (31.4 – 36.9)	30.6 (28.3 – 33.1)	<0.001	0.12
% Smoking	22.6 (20.2 – 26.5)	19.4 (14.4 – 24.1)	<0.001	0.09
% Could not see doctor due to cost	17.1 (13.2 —21.5)	12.6 (5.0 – 17.4)	<0.001	0.09
% Limited access to healthy foods	6.3 (3.4 – 12.0)	6.1 (3.4 – 10.2)	0.36	0.02
% Mammography screening	58.0 (51.6 – 63.0)	61.4 (55.9 – 66.7)	0.003	−0.05
% Physical inactivity	33.1 (29.4 – 34.6)	28.1 (24.5 – 31.2)	<0.001	0.13
% Unemployment	9.4 (7.7 – 11.3)	7.5 (5.7 – 9.3)	<0.001	0.11
% Uninsured	23.0 (20.1 – 26.0)	21.4 (16.8 – 26.1)	0.02	0.04
PCP[e] per 10,000 persons	4.3 (2.5 – 6.0)	4.9 (3.1 – 7.0)	0.02	−0.04
Non-Urban	68.8 (50.8 – 88.4)	59.1 (32.9 – 87.0)	0.006	0.05

[a] Defined as counties estimated as a hot spot by all three geospatial methods (local indicators of spatial association, empirical Bayes, and Gi*).

[b] Significance determined using Wilcoxon test, p values <0.05.

[c] Spearman correlation with being a county-level breast cancer mortality hot spot.

[d] IQR = interquartile range.

[e] PCP = Primary care physicians

Table 4:

County-Level Characteristics Comparisons by Breast Cancer Mortality Hot Spot Category, Stratified by Race/Ethnicity years 2000 – 2015

	Race/Ethnicity								
	NH-Blacks			**Hispanics**			**NH-Whites**		
	Hot Spot[a] (N = 119)	**Non-Significant (N = 2,989)**	**ρ[b]**	**Hot Spot[a] (N = 83)**	**Non-Significant (N = 3,025)**	**ρ[b]**	**Hot Spot[a] (N = 57)**	**Non-Significant (N = 3,051)**	**ρ[b]**
	Presented as Median (IQR)[c]			**Presented as Median (IQR)[c]**			**Presented as Median (IQR)[c]**		
Race									
% NH-White	58.8 (45.1 – 66.1)	86.6 (69.2 – 94.2)	−0.23	42.2 (19.5 – 58.4)	86.4 (68.4 – 94.2)	−0.23	79.2 (60.9 – 93.0)	85.8 (67.2 – 94.0)	−0.03
% NH-Black	34.6 (25.8 – 50.9)	1.8 (0.5 – 8.0)	0.29	1.4 (0.5 – 4.1)	2.1 (0.5 – 10.6)	−0.03	3.9 (1.4 – 9.6)	2.0 (0.5 – 10.1)	0.05
% Hispanic	3.0 (2.0 – 6.0)	3.4 (1.7 – 8.7)	−0.03	50.2 (27.6 – 70.4)	3.3 (1.7 – 7.7)	0.26	6.9 (1.7 – 16.7)	3.4 (1.7 – 8.4)	0.03
% Female Sex	51.2 (50.2 – 52.1)	50.4 (49.5 – 51.1)	0.11	50.4 (49.0 – 51.0)	50.4 (49.6 – 51.2)	−0.01	51.1 (50.4 – 51.4)	50.4 (49.5 – 51.1)	0.06
% Aged 80+	3.8 (3.1 – 4.3)	4.2 (3.4 – 5.2)	−0.07	3.6 (2.9 – 4.5)	4.2 (3.4 – 5.2)	−0.07	4.7 (3.9 – 5.9)	4.2 (3.4 – 5.2)	0.05
% Completed college	14.3 (12.0 – 18.6)	18.0 (14.1 – 24.0)	−0.11	16.2 (12.1 – 24.4)	17.9 (14.0 – 23.7)	−0.02	19.5 (14.9 – 27.4)	17.9 (13.9 – 23.6)	0.04
% Household income < $20,000	27.7 (22.1 – 33.9)	20.4 (16.4 – 25.3)	0.16	23.4 (18.2 – 29.6)	20.6 (16.5 – 25.6)	0.06	19.9 (16.9 – 25.2)	20.7 (16.5 – 25.7)	−0.01
County-level characteristics									
% Adult obesity	34.9 (32.7 – 37.2)	30.5 (28.3 – 33.0)	0.21	28.8 (24.5 – 29.9)	30.8 (28.4 – 33.2)	−0.13	28.3 (25.9 – 31.9)	30.7 (28.4 – 33.2)	−0.06
% Adult smoking	22.2 (19.2 – 25.6)	19.3 (14.3 – 24.1)	0.08	14.0 (0.0 – 18.8)	19.7 (14.7 – 24.2)	−0.12	19.9 (16.3 – 24.3)	19.5 (14.4 – 24.1)	0.01
% Could not see doctor due to cost	17.2 (13.8 – 21.5)	12.5 (4.6 – 17.3)	0.13	13.6 (0.0 – 17.7)	12.7 (5.8 – 17.5)	0.02	13.2 (10.4 – 17.7)	12.7 (5.0 – 17.5)	0.02
% Limited access to healthy foods	6.2 (3.4 – 10.9)	6.1 (3.4 – 10.3)	0.01	10.5 (5.9 – 17.1)	6.1 (3.4 – 10.1)	0.09	5.0 (2.3 – 7.5)	6.2 (3.4 – 10.4)	−0.05
% Mammography screening	61.3 (54.6 – 66.6)	61.4 (55.8 – 66.7)	−0.01	55.4 (48.8 – 60.9)	61.5 (56.0 – 66.7)	−0.11	59.1 (56.1 – 62.5)	61.4 (55.8 – 66.7)	0.04
% Physical inactivity	32.4 (29.4 – 34.2)	28.0 (24.4 – 31.1)	0.16	25.9 (23.3 – 27.8)	28.3 (24.6 – 31.5)	−0.10	27.7 (24.2 – 30.8)	28.1 (24.5 – 31.4)	−0.01

	Race/Ethnicity								
	NH-Blacks			**Hispanics**			**NH-Whites**		
	Hot Spot[a] **(N = 119)**	**Non-Significant (N = 2,989)**	ρ[b]	**Hot Spot**[a] **(N = 83)**	**Non-Significant (N = 3,025)**	ρ[b]	**Hot Spot**[a] **(N = 57)**	**Non-Significant (N = 3,051)**	ρ[b]
	Presented as Median (IQR)[c]			**Presented as Median (IQR)**[c]			**Presented as Median (IQR)**[c]		
% Unemployment	9.7 (7.7 – 11.2)	7.4 (5.7 – 9.2)	0.14	7.1 (5.6 – 8.9)	7.5 (5.8 – 9.3)	0.02	8.5 (7.3 – 10.5)	7.5 (5.8 – 9.3)	0.06
% Uninsured	25.3 (21.9 – 28.0)	21.3 (16.7 – 25.9)	0.12	29.5 (24.9 – 33.2)	21.3 (16.7 – 25.9)	0.17	20.1 (14.8 – 25.7)	21.5 (16.9 – 26.1)	−0.03
PCP per 10,000 persons	4.0 (2.7 – 5.5)	4.9 (3.1 – 7.0)	−0.05	4.2 (2.9 – 6.3)	4.9 (3.1 – 7.0)	−0.04	5.9 (4.4 – 7.6)	4.9 (3.1 – 7.0)	0.04
Non-Urban[e]	60.8 (38.5 – 82.9)	59.4 (33.1 – 88.2)	0.00	31.8 (10.7 – 60.7)	60.1 (34.4 – 87.8)	−0.09	37.3 (5.8 – 67.1)	59.7 (33.8 – 88.2)	−0.07

[a] Defined as counties estimated as a hot spot by all three geospatial methods (local indicators of spatial association, empirical Bayes, and Gi*).

[b] Spearman correlation with county-level breast cancer hot spot category.

[c] IQR = interquartile range.

[e] Presented as N (Column %)