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Nakai Brown [Student's name typed] 12/5/2024 Date Disparities in Breast Cancer Mortality: Examining the Influence of Area-Level Socioeconomic Conditions and the Role of Individual-Level Socioeconomic Factors in Shaping Estimates

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Disparities in Breast Cancer Mortality: Examining the Influence of Area-Level Socioeconomic Conditions and the Role of Individual-Level Socioeconomic Factors in Shaping Estimates

By

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An abstract of A thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of Master of Public Health in Epidemiology 2024

Abstract

Disparities in Breast Cancer Mortality: Examining the Influence of Area-Level Socioeconomic Conditions and the Role of Individual-Level Socioeconomic Factors in Shaping Estimates

By Nakai Brown

In the United States breast cancer is the second leading cause of death in women, and while White women are more likely to be diagnosed with breast cancer, Black women are more likely to die. There are many drivers of breast cancer outcomes, like neighborhood and socioeconomic condition, that impact access to and quality of care. In this study we aimed to examine whether area-level neighborhood socioeconomic condition is associated with race-specific breast cancer mortality to understand how meaningful individual-level socioeconomic data is in improving risk estimation. Using the I Can Care survey cohort and the BRIDGE breast cancer surveillance cohort, there were 1,944 non-Hispanic Black and non-Hispanic White women, who were diagnosed with breast cancer between 2012 to 2015. Our exposure was neighborhood deprivation, and the outcomes of interest were all-cause and breast cancer mortality. Cox proportional hazards regression was used to perform our analysis. We observed that as the level of neighborhood deprivation increased, the risk of all-cause and breast cancer mortality also increased (Table 2). We also observed how neighborhood deprivation impacted Black and White women's breast cancer mortality risk differently (Table 3). Adjusting for individual socioeconomic status, we observed the most meaningful difference in risk when using education and household income (Table 5). When stratified by race we observed drastic differences in the impact of the education and household income variables by race on breast cancer mortality (Table 6). Our results suggest that living in neighborhoods that are more resource deprived has a harmful impact on all-cause and breast cancer mortality and that racial disparities exist for the impact of neighborhood deprivation. Adjusting for individual level socioeconomic factors, like education level and household income, appear to be much more meaningful for White women than they are for Black women, suggesting the presence of other factors like systemic and institutional racism that create barriers that perpetuate health disparities. Due to the small sample size, larger studies are needed to yield more statistically meaningful results and an expansion of the indicators used to create the neighborhood deprivation index variable may be beneficial to explore.

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Acknowledgments

I would like to start out by thanking Dr. Lauren E. McCullough for helping me embark on this journey. It has been a long one, but I am incredibly grateful for all the patience, support and guidance she has given me during this time. I knew I had an interest in exploring breast cancer disparities in black women and when I approached her, having never taken one of her classes or meeting her in person, she was so gracious and kind. She took the time to meet with me, got to know me and helped me explore my interests and using those interests, she helped me create a thesis topic that would be both challenging and beneficial. I want to thank her for introducing me to BRIDGE and allowing me to share spaces with some of the smartest and strongest people I have ever met.

I would also like to thank Dr. Lauren Barber for providing me with so much assistance in my data analysis phase. I'm thankful for her being so responsive, patient and supportive. I appreciate her taking the time to work with me and share her knowledge with me, I truly learned a lot! I also want to extend my thanks to the entirety of the BRIDGE Research and BRIDGE Community team, including Chava Bowden, Tsion Armidie, Alexis Smith, Breana Berry, Dr. Jacquelyn Anthony Bryant and Cindy Young. Working with and getting to know everyone in BRDIGE has truly helped me to grow both as a person and as a researcher. My time spent with the BRIDGE community focus group cohort members has opened my eyes and has left a lasting impact on my life. I am incredibly appreciative that I had the opportunity to get to know all of you and that you trusted me with your personal experiences as Black women with breast cancer in Georgia. Hearing your stories has helped me to contextualize the data and that has made the research so incredibly meaningful for me. I truly do appreciate them all for being vulnerable and for trusting me and the BRIDGE Community team with their stories. I hope that the research I've done will go on to affect positive changes in the breast cancer and health disparities research fields. Lastly, I would like to thank my friends and family, especially my mother, for continuously supporting me throughout the entirety of my educational career. I'm so incredibly appreciative of all of you and I hope I've made you proud!

Table of Contents

Introduction and Background	1
Methods	4
Results	6
Discussion	16
Tables	23
References	

Introduction and Background

In the United States, it's estimated that approximately 44,000 women will die from breast cancer in 2023. (National Breast Cancer Foundation, 2023) Behind only lung cancer, breast cancer is the second leading cause of cancer death in U.S. women, with an overall 2.5% chance of a woman dying from breast cancer. (National Breast Cancer Foundation, 2023) While we have seen improvements in breast cancer mortality over time, there are substantial differences by race.

Although White women have a higher incidence of breast cancer, Black women in the U.S. who are diagnosed, are 40% more likely to die than their White counterparts, a reality that has persisted for a decade. Furthermore, Black women less than 50 years old have a death rate that is twice as high as White women that age and Black women also have the lowest five-year breast cancer survival rate compared to all other racial and ethnic groups for every stage of diagnosis and every breast cancer subtype. (McDowell, 2023) In 2022 among non-Hispanic Black women in Georgia the age-adjusted female breast cancer death rate was 25.1 per 100,000 women compared to non-Hispanic White women in Georgia who had a breast cancer death rate of 18.7 per 100,000. (U.S. Cancer Statistics Working Group, 2024) An individual's socioeconomic status is an important driver of breast cancer outcomes – impacting both access to and quality of care. Nnorom and colleagues examined the impact of socioeconomic status and race and ethnicity on fiveyear breast cancer survival rates. When compared to White women in the lowest wealth quartile, 'Black women in the lowest, second and third quartiles, experienced the lowest five-year survival rates' and only in the most prosperous quartile do Black women 'achieve a similar outcome to the poorest quartile White women'. (Nnorom et al, 2022) These data

show that there are factors that increase the risk of breast cancer mortality among Black women beyond socioeconomic status.

Due to the lingering effects of racist and discriminatory practices that were introduced in many of the U.S. institutions, the Black community still navigates the effects of institutional and systemic racism and discrimination currently. Its effects are clearly observed in the criminal justice system, housing practices, educational opportunities, and in healthcare. Social determinants of health – the conditions in the environments where people are born, live, work, play, worship, and age – affect a wide range of health risks and outcomes, and are posited to drive the large disparities in health, including breast cancer. (Office of Disease Prevention and Health Promotion, 2023)

One social determinant of health that has been of primary interest due to ease of assessment through census and other publicly available data is one's neighborhood. The Population and Housing Census is taken every 10 years, with the intention that the data collected from it will help inform the government on how to distribute federal funds to local communities. Its data determines where schools, grocery stores, homes and hospitals are built, and how much federal assistance different state governments are given, which makes up state and local government budgets, which are then allocated to different areas like education, infrastructure, and housing. These procedures, in turn, largely drive the characteristics of a neighborhood and ultimately is a large determinate of how a person lives, what transportation they use, what type of foods they eat, what services they have access to and possibly what their earning potential is. According to recent data from the U.S. Census Bureau, 4 million Americans live in impoverished or disadvantaged neighborhoods. These neighborhoods are characterized as having high levels of poverty, high unemployment, physical dilapidation, a disproportionate number of single parent, often female-headed households and high crime rates. One-fifth of the residents in these types of neighborhoods live below the federal poverty line. Due to inaccurate or undercounted resident data, historical and modern housing discrimination and lack of government funds, certain neighborhoods end up with less and poorer quality resources resulting in increased poverty, crime, pollution, and many times less access to transportation, healthy foods, safe spaces to play, quality education and employment opportunities and healthcare. Black Americans are more likely to reside in disadvantaged neighborhoods, with 21% of Black Americans, compared to only 4.3% of White Americans living in these areas. (Christie-Mizell, 2022) This can lead to poorer health outcomes for Black Americans, and for Black women diagnosed with breast cancer, this could be a contributing factor to the persistent disparities in mortality we observe. There are numerous factors to consider at the intersection of race and socioeconomics in understanding health outcomes. It is worth examining further how a woman's neighborhood factors into her overall breast cancer mortality, especially when assessing the area-level economics compared to that individual woman's economic status.

There has been a dearth of literature examining the contextual role communitylevel socioeconomic status has on breast cancer mortality. One study of women residing in Wisconsin found that after adjusting for screening mammography, disease stage at diagnosis and lifestyle factors, the mortality disparity by income was eliminated but low community-level education '*was associated with increased breast cancer mortality even after adjusting for individual-level SES*.' (Sprague et al, 2011) This study highlights the importance of examining both individual and area-level economics of the neighborhood. The latter provides insights on neighborhood environment access while the former can yield important insights on possible barriers and stressors experienced by the individual daily. Having this type of multi-level information can inform interventions at both individual and neighborhood levels.

This thesis will examine whether area-level neighborhood socioeconomic condition, is associated with race-specific breast cancer mortality to understand how meaningful accounting for individual-level socioeconomic data is in improving the estimation of risk. The data used will be from the BRIDGE surveillance cohort, a subset of the I Can Care cohort and publicly available data.

Methods

Study Population

The Individualized Cancer Care or I Can Care patient survey was created to gather feedback from breast cancer patients on their treatment experiences and their decision making related to those cancer treatments. The data used for this study represents the overlap between the BRIDGE breast cancer surveillance cohort and the I Can Care cohort. Using this cohort, as well as publicly available data, we had a total of 1,944 non-Hispanic Black and non-Hispanic White female Georgia residents, with a stage I-IIIA breast cancer diagnosis occurring between the years 2012 to 2015.

Exposure and Outcome Assessment

Our exposure, neighborhood deprivation was measured by the Neighborhood Deprivation Index (NDI), created by Messer and colleagues. It comprised various domains including poverty, income, employment, occupation, housing and education. For our poverty indicators it was created with the inclusion of the percentage of individuals below the poverty line, percentage of households receiving public assistance and percentage of female-headed households with children who are less than 18 years old. For the income domain, the indicator we used was the percentage of the household income that is less than \$35,000. For the employment domain that was created with the percentage of individuals unemployed in the neighborhood. For occupation, included was the percentage of residents employed in managerial or administrative jobs. For our housing domain we included the percentage of housing crowding indicator and for the education domain we included the percentage of individuals who are 25 years old or older without a high school degree or a General Educational Development (GED). For the outcome of interest, we are using both all-cause mortality as well as breast cancer specific mortality. This was determined by use of the Georgia Cancer Registry. We only recorded all-cause and breast cancer specific deaths that occurred during the study follow-up period, through December 31st, 2022.

Covariates of Interest

Among the subset of the BRIDGE cohort and for race we subset our population to include only non-Hispanic Black women and non-Hispanic White women. For marital status, we included single, married or living together, divorced or separated, widowed or unknown. For neighborhood characteristics, we separated the subset into either urban or rural statuses. We also included the age at which they received their primary cancer diagnosis, as one of our covariates of interest.

Statistical Analysis

Cox proportional hazards regression was used to estimate the age-adjusted, age and race-adjusted and multivariable adjusted hazard ratios for the approximation of risk and

95% confidence intervals to estimate the association between neighborhood deprivation index and all-cause and breast cancer specific mortality. Person-time was accrued beginning at the breast cancer diagnosis and ending at breast cancer mortality, death from another cause, the end of the study person or when the participant was lost to follow-up. The multivariable adjusted model included race, urban-rural status and marital status. We performed the age-adjusted and multivariable-adjusted analysis again but stratifying by race and ethnicity. We performed the multivariable-adjusted analysis but adjusting for individual socioeconomic factors this time, including education, insurance status, employment before diagnosis, income lost, prescription coverage, and household income. Lastly, we performed the multivariable-adjusted analysis using only the education and household income variable and stratifying the results by race and ethnicity. All analyses were performed using SAS version 9.4. All statistical tests performed were two sided, and p-values that were less than 0.05 were considered statistically significant.

Results

Descriptive Results

A total of 1,944 women were included in the study. Characteristics of the study population including race and ethnicity, marital status, type of insurance, breast cancer stage and molecular subtype according to tertiles of neighborhood deprivation are presented in Table 1. Most women resided in neighborhoods classified as 'low deprivation' (Tertile 1), with 1,008 women residing in this tertile, and Tertiles 2 and 3 each having 602 and 334 women, respectively. The mean age at diagnosis was the same for women residing in low and moderate deprivation neighborhoods at 59.1 years while for high deprivation neighborhoods the mean age was slightly higher at 61.0 years. The survival months, of the respondents in each category of neighborhood deprivation were very similar, but decreased from most to least deprived neighborhoods, with Tertile 1 having an average of 98.6 survival months, Tertile 2 having an average of 96.6 survival months and Tertile 3 having an average of 95.5 survival months.

Demographically, most of the respondents in the lower deprivation neighborhoods were Non-Hispanic White women, who accounted for 86.71% and 72.59% of respondents in the first two tertiles, respectively while Non-Hispanic Black women only accounted for 13.29% and 27.41% of respondents in these tertiles. However, for the highest deprivation neighborhoods, the respondents were much more evenly distributed between the two groups, with 49.1% of respondents being Non-Hispanic Black women and 50.9% being Non-Hispanic White women. Across all three tertiles a majority of women were married or living with a partner (69.54%, 56.81% and 43.71% respectively), with Tertile 3 having the largest proportions of respondents who were single (18.26%), divorced or separated (19.16%) or widowed (12.28%). For insurance status, most of the respondents had some form of insurance. In Tertile 1, the highest percentage of women had private insurance (63.19%), while 30.75% had Medicare. This pattern looks very similar amongst the second and third tertile, with 56.48% and 46.11% respectively who had private insurance and 33.55% and 39.82% respectively who had Medicare. In Tertile 3, we saw the highest percentage of respondents who had Medicaid (9.88%) compared to only 1.98% in Tertile 1 and 4.98% in Tertile 2. The usage of military insurance among respondents decreased with increasing neighborhood deprivation (2.28%, 1.5%, 0.9%) but the percentage of respondents who reported being uninsured increased in the same direction (0.6%, 1.33%,

1.80%). Most of the respondents across each tertile group had Stage I cancer (72.32%, 65.28% and 68.86%, respectively for low to high deprivation neighborhoods), while the largest percentage of respondents in Stage II were in the second tertile (33.89%). The percentage of respondents in Stage IIIA was incredibly small and very similar amongst all tertiles (0.3%, 0.33% and 0.3% respectively). Lastly, for breast cancer molecular subtype, Luminal A (HR+/HER2-) subtype was the most prominent subtype across all three tertiles (78.47% in Tertile 1, 70.27% in Tertile 2, and 76.65% in Tertile 3), while second tertile had the highest percentage of respondents with Luminal B (HR+/HER2+) and triple negative (HR-/HER2-) subtypes (11.3% and 11.46% respectively). HER2 overexpressing (HR-/HER2+) had the smallest percentage amongst all three groups (2.28%, 2.82% and 2.99% respectively).

Age- and Multivariable-Adjusted Results

In Table 2, we estimated hazard ratios for the association between neighborhood deprivation and both breast cancer mortality as well as all-cause mortality, adjusting for age at diagnosis, age at diagnosis and race and, age at diagnosis, race, urban-rural and marital status. There was a total of 213 deaths across all three tertile groups, with 83 deaths in low deprivation neighborhoods, 77 deaths in moderate deprivation neighborhoods and 53 in high deprivation neighborhoods. Adjusting for age, compared to our least deprived neighborhoods, our moderately deprived neighborhoods had a hazard ratio of 1.59 (95% CI, 1.17-2.17) and in our most deprived neighborhoods, we saw an even greater increased risk of all-cause mortality with a hazard ratio of 1.87 (95% CI, 1.32-2.64). After adjusting for both age and race, we accessed a similar trend of increased risk of all-cause mortality as we increased neighborhood deprivation, with a hazard ratio of 1.63 (95% CI, 1.19-2.23)

in moderate deprivation neighborhoods and an almost two-fold increase in risk in high deprivation neighborhoods (HR=1.99, 95% CI, 1.38-2.87), compared to low deprivation neighborhoods. Associations persisted upon additionally adjusting for urban-rural and marital status, where we continue to see increasing (though attenuated) risk in moderate deprivation neighborhoods (HR=1.52, 95% CI, 1.10-2.10) and in high deprivation neighborhoods (HR=1.84, 95% CI, 1.25-2.70), compared to our reference group.

We had a total of 75 breast cancer deaths, with 32 deaths in low deprivation neighborhoods, 27 deaths in moderate deprivation neighborhoods and 16 deaths in high deprivation neighborhoods. After adjusting for age, we accessed that compared to low deprivation neighborhoods, moderate deprivation neighborhoods have a 44% increased risk of breast cancer death (HR=1.44, 95% CI, 0.86-2.41) and in high deprivation neighborhoods we see a 57% increased risk of breast cancer death (HR=1.57, 95% CI, 0.86-2.86). When adjusting for both age and race, we see continue to see this trend, with breast cancer mortality risk highest amongst women living in high deprivation neighborhoods (HR=1.44, 95% CI, 0.76-2.71) but still increased for those in moderately deprived neighborhoods (HR=1.39, 95% CI, 0.83-2.34), compared to low deprivation neighborhoods. Accessing our multivariable adjusted model, we see that moderate deprivation neighborhoods have a hazard ratio of 1.31 (95% CI, 0.77-2.24) and high deprivation neighborhoods have a hazard ratio of 1.35 (95% CI, 0.69-2.64). We continue to see a similar pattern of those who live in the most deprived neighborhood, being most at risk of breast cancer mortality.

Age- and Multivariable-Adjusted Results Stratified by Race and Ethnicity

Next, we examined the age- and multivariable adjusted models for all-cause and breast cancer mortality stratified by race and ethnicity which is presented in Table 3. Among non-Hispanic White women there were a total of 165 all-cause mortality cases, with 72 deaths in low deprivation neighborhoods, 65 deaths in moderate deprivation neighborhoods and 28 deaths in high deprivation neighborhoods. Among non-Hispanic Black women there was a total of 48 cases of all-cause mortality with low deprivation neighborhoods accounting for 11, moderate deprivation neighborhoods accounting for 12 and high deprivation neighborhoods accounting for 25. For the age-adjusted model the hazard ratio for non-Hispanic White women who live in moderate deprivation neighborhoods was 1.85 (95% CI, 1.32-2.59) and for those in high deprivation neighborhoods the hazard ratio was 1.96 (95% CI, 1.26-3.03). For non-Hispanic Black women, in the age-adjusted model we see a 18% decreased risk of all-cause mortality (HR = 0.82, 95% CI, 0.36-1.87) for those living in moderate deprivation neighborhoods but in contrast, we saw 61% increased risk of all-cause mortality for women living in high deprivation neighborhoods (HR= 1.61, 95% CI, 0.78-3.32). When looking at our multivariable-adjusted model, in non-Hispanic White women, compared to our referent group, we observed a 66% increased risk of all-cause mortality amongst those living in moderate deprivation neighborhoods (HR= 1.66, 95% CI, 1.17-2.35) and a 77% increased risk amongst those living in high deprivation neighborhoods (HR= 1.77, 95% CI, 1.12-2.81). Looking at non-Hispanic Black women, we again found 18% decreased risk among women living in the moderately deprived neighborhoods (HR=0.82, 95% CI, 0.36-1.87)

but a 62% increased risk of all-cause mortality amongst those living in the most deprived neighborhoods (HR= 1.62, 95% CI, 0.76-3.43).

For breast cancer mortality, there were a total of 52 deaths amongst non-Hispanic White women and 23 deaths amongst non-Hispanic Black women. In non-Hispanic White women, looking at our model adjusting for age at diagnosis, we found a two-fold increase in breast cancer mortality risk in moderate deprivation neighborhoods (HR=2.01, 95% CI, 1.15-3.75) and a 94% increased breast cancer mortality risk in high deprivation neighborhoods (HR=1.94, 95% CI, 0.86-4.37), although estimates are imprecise. For non-Hispanic Black women, we observed a 60% decreased risk of breast cancer mortality for women in moderate deprivation neighborhoods (HR=0.40, 95% CI, 0.14-1.16) and a 33% decreased risk for women in high deprivation neighborhoods (HR=0.67, 95% CI, 0.26-1.72). For the multivariable adjusted model, in non-Hispanic White women we observe a hazard ratio of 1.9 for moderately deprived neighborhoods (95% CI, 1.03-3.53) and a hazard ratio of 1.83 in the most deprived neighborhoods (95% CI, 0.78-4.30), although these estimates are imprecise. For non-Hispanic Black women, we estimated a hazard ratio of 0.40 among women in moderate deprivation neighborhoods (95% CI, 0.14-1.18) and 0.70 among women in high deprivation neighborhoods (95% CI, 0.26-1.85), indicating a decreased risk of breast cancer mortality among Black women.

Age- and Multivariable-Adjusted Results by Breast Cancer Stage

We performed a sensitivity analysis to see the age- and multivariable-adjusted hazard ratios for the association between neighborhood deprivation and both breast cancer and all-cause mortality, among a subset of breast cancer stages I, II, and IIA, which is illustrated in Table 4. For all-cause mortality, when looking at our age-adjusted model, we observed that women residing in moderately deprived neighborhoods have a 53% increased risk of death (HR=1.53, 95% CI, 1.12-2.08) compared to the lowest deprived neighborhoods and women in the most deprived neighborhoods have an 82% increased risk of death (HR=1.82, 95% CI, 1.29-2.56) compared to the referent group. For our model adjusted by age at diagnosis, race, urban-rural status and marital status, we found that women in moderate deprivation have a 48% increased risk of death (HR=1.48, 95% CI, 1.07-2.05) compared to the referent group and women in the highest deprivation have an 85% increased risk of death (HR=1.85, 95% CI, 1.26-2.73) compared to the referent.

In age-adjusted models for breast cancer mortality, we observed a hazard ratio of 1.29 (95% CI, 0.77-2.15) amongst women in moderate deprivation neighborhoods and a hazard ratio of 1.42 (95% CI, 0.78-2.59) amongst those in high deprivation neighborhoods. The effect was slightly attenuated in multivariable-adjusted models where we found a hazard ratio of 1.2 for moderate deprivation (95% CI, 0.70-2.07) and a hazard ratio of 1.31 (95% CI, 0.67-2.56) for high deprivation, both compared to low deprivation. While our estimates are not statistically significant, we observed a consistent pattern where the highest risk of both all-cause and breast cancer mortality is among women who live in the most deprived neighborhoods.

Multivariable and Individual Socioeconomic Status-Adjusted Results

In Table 5, we additionally adjust for individual socioeconomic status variables including education, insurance status, employment before diagnosis, the amount of income a patient has lost since the initial breast cancer diagnosis, the amount of prescriptions that patients need to take for treatment that are covered by insurance and a patient's total household income. Using our previous multivariable-adjusted hazard ratio, we examine

For all-cause mortality, looking at our crude multivariable-adjusted model we see a hazard ratio of 1.52 (95% CI, 1.10-2.10) for moderate deprivation neighborhoods and a 1.84 hazard ratio (95% CI, 1.25-2.70) for high deprivation neighborhoods. When including our education variable into the model, we see hazard ratios of 1.32 (95% CI, 0.95-1.82) and 1.45 (95% CI, 0.98-2.15) for moderate and high deprivation respectively. Including insurance status in our model we see a hazard ratio of 1.49 (95% CI, 1.07-2.06) for moderate deprivation neighborhoods and for high deprivation neighborhoods a hazard ratio of 1.78 (95% CI, 1.21-2.62). With the inclusion of employment before diagnosis, we see hazard ratios of 1.49 (95% CI, 1.08-2.06) for the moderately deprived neighborhoods and 1.78 (95% CI, 1.21-2.62) for the most deprived neighborhoods. When including our income lost variable, we have a hazard ratio of 1.51 (95% CI, 1.09-2.09) for moderate deprivation neighborhoods and a hazard ratio of 1.82 (95% CI, 1.24-2.70) for high deprivation neighborhoods. Now including the prescription coverage variable, we see hazard ratios of 1.51 (95% CI, 1.09-2.09) and 1.83 (95% CI, 1.25-2.70) for moderate and high deprivation, respectively. Using the household income variables, we observed hazard ratios of 1.44 (95% CI, 1.04-2.00) for moderate deprivation neighborhoods and 1.60 (95% CI, 1.08-2.38) for high deprivation neighborhoods. Lastly, when we incorporate all our individual socioeconomic status variables into our multivariable adjusted model simultaneously, we see hazard ratios of 1.32 (95% CI, 0.94-1.83) and 1.42 (95% CI, 0.95-2.13) for our moderate and high deprivation neighborhoods, all compared to the referent group.

For breast cancer mortality our previously reported multivariable-adjusted hazard ratio was 1.31(95% CI, 0.77-2.24) for moderate deprivation neighborhoods and 1.35 (95% CI, 0.69-2.64) for high deprivation neighborhoods. We repeated our previous steps, with the inclusion of various individual SES variables and reported the following hazard ratios: for education 1.19 (95% CI, 0.70-2.04) and 1.09 (95% CI, 0.55-2.16), for insurance status 1.26 (95% CI, 0.73-2.15) and 1.24 (95% CI, 0.63-2.44), for employment before diagnosis 1.29 (95% CI, 0.76-2.21) and 1.31 (95% CI, 0.67-2.57), for income lost 1.32 (95% CI, 0.77-2.27) and 1.38 (95% CI, 0.71-2.69), for prescription coverage 1.26 (95% CI, 0.76-2.26) and 1.40 (95% CI, 0.71-2.72), and for household income 1.31 (95% CI, 0.76-2.26) and 1.22 (95% CI, 0.61-2.44), all for moderate deprivation neighborhoods and high deprivation neighborhoods, respectively. For the all-inclusive multivariable-adjusted model, we observed a hazard ratio of 1.20 (95% CI, 0.70-2.07) for the moderately deprived neighborhoods and a hazard ratio of 1.12 (95% CI, 0.55-2.26) for the highest deprived neighborhoods.

Multivariable and Individual Socioeconomic Status-Adjusted Results Stratified by Race and Ethnicity

In Table 6, we model the association between neighborhood deprivation and allcause and breast cancer mortality stratified by race and adjusting for individual socioeconomic status variables. First examining all-cause mortality among non-Hispanic White women, we previously estimated a race-stratified multivariable-adjusted hazard ratio of 1.66 (95% CI, 1.17-2.35) for moderate deprivation neighborhoods and 1.77 (95% CI, 1.12-2.81) for high deprivation neighborhoods. When including the education variable into our multivariable-adjusted model we observed a hazard ratio of 1.39 (95% CI, 0.971.98) for moderate deprivation neighborhoods and 1.40 (95% CI, 0.88-2.24) for high deprivation neighborhoods. For the inclusion of the household income variable, we reported hazard ratios of 1.59 (95% CI, 1.11-2.27) and 1.62 (95% CI, 1.02-2.59) for moderate and high deprivation neighborhoods, respectively. For non-Hispanic Black women, the previously reported race-stratified multivariable-adjusted hazard ratio without adjusting for individual level factors for moderately deprived neighborhoods is 0.82 (95% CI, 0.36-1.87) and for the highest deprived neighborhoods it's 1.62 (95% CI, 0.76-3.43). When we included the education variable, we observed hazard ratios of 0.79 (95% CI, 0.34-1.82) and 1.34 (95% CI, 0.62-2.87), for moderate and high deprivation neighborhoods, respectively and when we included the household income variable, we saw hazard ratios of 0.77 (95% CI, 0.33-1.81) and 1.28 (95% CI, 0.57-2.85) for moderate and high deprivation neighborhoods.

Lastly, when looking at breast cancer mortality, for non-Hispanic White women, we had a previously reported race-stratified multivariable-adjusted hazard ratio of 1.90 (95% CI, 1.03-3.53) and 1.83 (95% CI, 0.78-4.30) for moderate and high deprivation neighborhoods, respectively. When including the education variable to our model, we observed hazard ratios of 1.68 (95% CI, 0.89-3.15) and 1.48 (95% CI, 0.62-3.53) and when we included the household income variable in the model, the reported hazard ratios were 1.91 (95% CI, 1.01-3.58) and 1.71 (95% CI, 0.72-4.07), all for moderate and high deprivation neighborhoods, respectively. Among non-Hispanic Black women, the previously reported race-stratified multivariable-adjusted hazard ratio for moderate deprivation neighborhoods was 0.40 (95% CI, 0.14-1.18) and 0.70 (95% CI, 0.26-1.85) for high deprivation neighborhoods. Now, with the inclusion of the education variable we observed a hazard ratio of 0.41 (95% CI, 0.14-1.21) for the moderate deprivation neighborhoods and 0.59 (95% CI, 0.22-1.60) for the highest deprivation neighborhoods. Including the household income into the model we reported hazard ratios of 0.40 (95% CI, 0.13-1.21) and 0.62 (95% CI, 0.21-1.82) for moderately and highest deprived neighborhoods respectively. While our estimates are imprecise, we observed drastic differences in the impact of the education and household income variables, by race and ethnicity.

Discussion

In this study, we aimed to investigate the association between area-level socioeconomic conditions and breast cancer mortality and the extent to which the estimates change when using individual-level socioeconomic indicators, to examine whether using area-level socioeconomic conditions can serve as a proxy for individual socioeconomic status for breast cancer disparity research. As we know the economic conditions of the neighborhood where someone lives has a big impact on their health and from the results, we found that even after adjusting for age at diagnosis, race, marital status and urban-rural status, that the risk of both all-cause as well as breast cancer mortality increased as neighborhood deprivation increased. When we examine how neighborhood deprivation impacts non-Hispanic Black and non-Hispanic White women separately, we observed that for both Black and White women living in the most deprived neighborhoods severely increased their risk of all-cause mortality. When looking at breast cancer mortality however we observed greater heterogeneity. After adjusting for age, marital status and urban-rural status, we found increased risk of breast cancer mortality in moderate and high deprivation neighborhoods for non-Hispanic White women, whereas for non-Hispanic Black women

we observed a decreased risk of breast cancer mortality in these same deprived neighborhoods.

After additionally adjusting for the individual socioeconomic status variables of education, insurance status, employment prior to diagnosis, the total amount of income lost since the initial breast cancer diagnosis due to having to take time off of or leave work, the amount of prescriptions that the patient need to take that are fully covered by their insurance and the patient's total household income, we observed some very interesting results. Compared to our previous multivariable-adjusted model, we observed that education and household income had the greatest impact on reducing the risk of both allcause mortality as well as breast cancer mortality. We found that for all-cause mortality, education and household income reduced the hazard of mortality for both non-Hispanic Black and non-Hispanic White individuals, throughout all neighborhood deprivation levels, when compared to our previously reported race-stratified multivariable adjusted hazard ratio. Compared to our previously reported race-stratified multivariable adjusted hazard ratios, we see that both education and household income decrease the risk of breast cancer mortality among non-Hispanic White women and appears to have the greatest effect on those women living in high deprivation neighborhoods. But for non-Hispanic Black patients, we found very little change in mortality risk for both education and household income. Examining the variables by level of neighborhood deprivation, we observe little to no change in hazard risk in moderately deprived neighborhoods and for the most deprived neighborhoods, although we observe slightly decreased mortality risk when compared to our race-stratified multivariable adjusted hazard ratios, we still see the same

pattern of increased breast cancer mortality risk as we increase neighborhood deprivation levels.

Our results suggest that living in neighborhoods that are more deprived of resources has a harmful impact on both all-cause mortality and breast cancer mortality. We also observed that there are disparities present when we look at the impact of neighborhood deprivation in non-Hispanic White versus non-Hispanic Black women. Upon adjusting for individual level socioeconomic factors, like education level and household income, these variables appear to be much more relevant for non-Hispanic White women than they are for non-Hispanic Black women. Given that the estimates for area-level socioeconomic conditions changes much more for non-Hispanic White women than they do for non-Hispanic Black women, we can say that accounting for individual socioeconomic variables is more meaningful for White women than it is for Black women, since we observe a reduced risk of mortality for White women when factoring in their education and household income. For Black women, since there was little to no observed change in specifically breast cancer mortality risk, there is indication that there are other factors that are impacting their breast cancer mortality.

Previous Literature

The results that we observed suggesting that living in deprived neighborhoods increases the risk of mortality, are consistent with results from previous studies like that performed by Connor et al; that when examining women in Maryland diagnosed with invasive breast cancer, concluded that the hazard of breast cancer mortality was 1.84 times higher for women living in the "least privileged quintile of racialized economic segregation..." compared to women living in the most privileged quintile (Connor et al.,

2022). This is also like the results found in a study analyzing the association between neighborhood deprivation index and clinical outcomes of locoregional breast cancer, which saw that breast cancer patients in areas with worse NDI "… have poor overall survival and disease-specific survival" (Roy et al. 2023).

When we adjusted for individual level socioeconomic factors, we found that education and household income were more relevant for mortality risk among non-Hispanic White women compared to non-Hispanic Black women. We know that an individual's economic status is associated with their access to care, which can impact what type of care they receive and how timely it is. One study in Canada found that, even in a universal health care system, "higher SES is associated with greater screening and treatments and with better overall survival after adjusting for screening, cancer stage at diagnosis and treatments" (Kumachev et al, 2016). It is therefore well-understood that one's socioeconomic status can greatly impact their chances of survival. This conclusion is only further supported by research showing that variations in treatment, socioeconomic status and clinicopathological factors "significantly explained 70% of excess breast cancer specific mortality among non-Hispanic Blacks compared to their non-Hispanic White counterparts." (Fwelo et al, 2023) This same study also saw that Black and Hispanic women both had higher odds of delayed treatment compared to White women and were significantly more likely to undergo more invasive treatments like mastectomies. Like in other research by Du et al. we saw that compared to white women with breast cancer, African Americans had a higher risk of breast cancer specific mortality, but they observed no racial disparities in overall survival for all-cause mortality between African American women and white women after controlling for treatment and socioeconomic status,

whereas we observed that those same disparities do exist even with all-cause mortality. In a research study done by Albert Okunade and Mustafa Karakus presenting the econometric model findings of the major drivers of breast cancer mortality among US women, they suggested that due to the higher mortality rate for Black women, implementing a culturally appropriate set of disease prevention and health promotion policies and programs to help. Their suggestion of designing region-specific programs would be beneficial to implement using neighborhood deprivation index of an indicator of program need.

Limitations

There are limitations present in this analysis. Our exposure, neighborhood deprivation index, while encompassing of various variables that can increase risk of mortality, it is not all encompassing and does not consider possible food scarcity, lack of green space for play or exercise, transportation services, access to healthcare facilities, the crime rate or the level environmental pollutants in the air or in the household materials that are present in those deprived neighborhoods that could potentially increase risk of both allcause and breast cancer specific mortality. To offer possible intervention ideas of social, political and commercial determinants it might be beneficial to expand the variables used to create the neighborhood deprivation index variable. Like Burwell et al., who examined poverty rate and percentage of SNAP benefits when examining geospatial associations between breast cancer mortality rates and environmental socioeconomic indicators in North Carolina, there was also inclusion of percentage of households below the poverty line and receiving public assistance in creation of the neighborhood deprivation index variable. Unlike that study however we didn't include percentage of minorities, which in the future, inclusion of this data could be beneficial for examining the effects of racialized

housing segregation on breast cancer mortality. Another challenge was the small sample size of women that were used in this cohort and there were a larger proportion of non-Hispanic White women than non-Hispanic Black women which led to small case numbers for Black women. These small cases did have an impact on the results but what is interesting to note is that for breast cancer mortality, in the high deprivation neighborhood, both non-Hispanic Black and non-Hispanic White women both have 8 breast cancer deaths and yet they have hazard ratios of 0.70 and 1.83 respectively. This suggests that the impact of being in high deprivation neighborhoods affects Black and White women differently. For future research, having a larger sample of participants or possibly matching might be beneficial to eliminate any possible bias so that our case numbers are much larger which would yield more statistically meaningful results. Also, it might be beneficial to expand the number of individual level socioeconomic status variables used in the analysis, to examine whether there are any more that have an effect breast cancer mortality risk for black women living in moderate and high deprivation neighborhoods, which could lead to potential for intervention.

Conclusion

Systemic racism, which describes the ongoing racial inequities that are perpetuated by society leads to institutional racism which results in discriminatory practices and policies that are within institutions that create extra barriers that Black women face, leading to some of the health disparities that we are observing in our results. Systemic racism is the reason that the health disparities that we study exist within the social determinants of health. Historic policies and practices like redlining and housing discrimination have led to the deprived neighborhoods that we see much of the black community living in today.

Within these neighborhoods, Black people are exposed to higher levels of air pollution, they have less green space to exercise and play freely, they have less access to adequate health care services, the children are more likely to attend schools that are overcrowded, with less staff and adequate resources and these communities are more likely to be over policed and are less likely to have access to nutritious foods. All these factors contribute to inadequate health and can lead to increased risk of developing and dying from a variety of diseases, including breast cancer. Some of the institutional barriers include a delay in initial cancer diagnosis as well as in follow-up care, Black women being less likely to be informed of all treatment options including the opportunity to participate in clinical trials, their complaints and concerns of pain being ignored due to possible bias of the providers and an overall mistrust of providers due to perceived unfair treatment and lack of care and attention to their questions and concerns. As observed with the results of the study, regardless of education level or household income, these barriers will continue to exist and will continue to negatively impact Black women's health. Addressing these barriers at federal, state and local levels and eliminating the effect of systemic and institutional racism is imperative for Black women to achieve parity with their white counterparts in terms of individual level socioeconomic status improving their risk of breast cancer mortality.

<u>Tables</u>

	Neig	phorhood Deprivation Inc	dex
	Tertile 1 (Least)	Tertile 2	Tertile 3 (Most)
Characteristics	n=1,008	n=602	n=334
Patient characteristics	Mean (SD)	Mean (SD)	Mean (SD)
Age at diagnosis	59.1 (10.6)	59.1 (11.0)	61.0 (10.6)
Survival months	98.6 (17.6)	96.6 (20.1)	95.5 (20.3)
	%	%	%
Race/ethnicity			
Non-Hispanic Black	13.29	27.41	49.10
Non-Hispanic White	86.71	72.59	50.90
Marital Status			
Single	9.72	10.63	18.26
Married/living together	69.54	56.81	43.71
Divorced/Separated	10.71	15.78	19.16
Widowed	7.64	11.30	12.28
Unknown	2.38	5.48	6.59
Insurance type			
Uninsured	0.60	1.33	1.80
Private	63.19	56.48	46.11
Medicaid	1.98	4.98	9.88
Medicare	30.75	33.55	39.82
Military	2.28	1.50	0.90
Other/unknown	1.19	2.16	1.50
Stage			
I	72.32	65.28	68.86
II	27.18	33.89	30.84
IIIA	0.30	0.33	0.30
Unknown	0.20	0.50	0.00
Molecular subtype			
Luminal A (HR+/HER2-)	78.47	70.27	76.65
Luminal B (HR+/HER2+)	8.43	11.30	7.49
HER2 overexpressing (HR-/HER2+)	2.28	2.82	2.99
Triple negative (HR-/HER2-)	7.04	11.46	9.28
Unknown	3.77	4.15	3.59

 Table 1. Characteristics of the study population according to tertiles of neighborhood deprivation index, N=1,944.

 Neighborhood Deprivation Index

	Cases	Person- months	Age-adjusted HR (95% CI)	Age and Race-adjusted HR (95% CI)	MV-adjusted HR ^a (95% CI)
Neighborhood deprivation index			(X
All-Cause Mortality					
T1 (Least deprived)	83	99,405.30	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
T2	77	58,172.13	1.59 (1.17-2.17)	1.63 (1.19-2.23)	1.52 (1.10-2.10)
T3 (Most deprived)	53	31,909.03	1.87 (1.32-2.64)	1.99 (1.38-2.87)	1.84 (1.25-2.70)
Breast Cancer Mortality					
T1 (Least deprived)	32	99,405.30	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
T2	27	58,172.13	1.44 (0.86-2.41)	1.39 (0.83-2.34)	1.31 (0.77-2.24)
T3 (Most deprived)	16	31,909.03	1.57 (0.86-2.86)	1.44 (0.76-2.71)	1.35 (0.69-2.64)

Table 2. Age - and multivariable-adjusted hazard ratios for the association between neighborhood deprivation, breast cancer mortality and all-cause mortality.

HR, Hazard ratio; CI, Confidence interval; MV, Multivariable

^a Multivariable hazard ratio adjusted for age at diagnosis, race, urban/rural status, and marital status

	Cases	Person- months	Age-adjusted HR (95% CI)	MV-adjusted HR ^a (95% CI)	Cases	Person- months	Age-adjusted HR (95% CI)	MV-adjusted HR ^a (95% CI)			
			/	Race/et	hnicity ^b		· · · · · ·				
	Non-Hispanic White Patients Non-Hispanic Black Patients										
NDI											
All-Cause											
Mortality											
T1 (Least)	72	86,336.43	1.00 (Ref)	1.00 (Ref)	11	13,068.86	1.00 (Ref)	1.00 (Ref)			
T2	65	41,727.31	1.85 (1.32-2.59)	1.66 (1.17-2.35)	12	16,444.82	0.82 (0.36-1.87)	0.82 (0.36-1.87)			
T3 (Most)	28	16,216.68	1.96 (1.26-3.03)	1.77 (1.12-2.81)	25	15,692.35	1.61 (0.78-3.32)	1.62 (0.76-3.43)			
Breast Cancer Mortality											
T1 (Least)	22	86,336.43	1.00 (Ref)	1.00 (Ref)	10	13,068.86	1.00 (Ref)	1.00 (Ref)			
T2	22	41,727.31	2.01 (1.15-3.75)	1.90 (1.03-3.53)	5	16,444.82	0.40 (0.14-1.16)	0.40 (0.14-1.18)			
T3 (Most)	8	16,216.68	1.94 (0.86-4.37)	1.83 (0.78-4.30)	8	15,692.35	0.67 (0.26-1.72)	0.70 (0.26-1.85			

Table 3. Age- and multivariable-adjusted hazard ratios for the association between the neighborhood deprivation index (NDI), breast cancer mortality and all-cause mortality by race/ethnicity.

NDI, Neighborhood deprivation index; HR, Hazard ratio; CI, Confidence interval; MV, Multivariable

^a Multivariable hazard ratio adjusted for age at diagnosis, urban/rural status, and marital status

^b P _{interaction} = 0.05

Table 4. Age- and multivariable-adjusted hazard ratios for the association between neighborhood deprivation, breast
cancer mortality and all-cause mortality for breast cancer stages I - IIIA.

	Cases	Person-months	Age-adjusted HR (95% CI)	MV-adjusted HR (95% CI)
Neighborhood deprivation index				
All-Cause Mortality				
T1 (Least deprived)	83	99,405.30	1.00 (Ref)	1.00 (Ref)
T2	77	58,172.13	1.53 (1.12-2.08)	1.48 (1.07-2.05)
T3 (Most deprived)	53	31,909.03	1.82 (1.29-2.56)	1.85 (1.26-2.73)
Breast Cancer Mortality				
T1 (Least deprived)	32	99,405.30	1.00 (Ref)	1.00 (Ref)
T2	27	58,172.13	1.29 (0.77-2.15)	1.20 (0.70-2.07)
T3 (Most deprived)	16	31,909.03	1.42 (0.78-2.59)	1.31 (0.67-2.56)

HR, Hazard ratio; CI, Confidence interval; MV, Multivariable

^a Hazard ratio additionally adjusted for urban-rural status and marital status

	MV- Adjusted HR ^a (95% CI)	MV- Adjusted + Education HR (95% CI)	MV- Adjusted + Insurance Status HR (95% CI)	MV- Adjusted + Employme nt Before Diagnosis HR (95% CI)	MV- Adjusted + Income Lost HR (95% CI)	MV- Adjusted + Prescription Coverage HR (95% CI)	MV- Adjusted + Household Income HR (95% CI)	MV-Adjusted + All Individual SES Variables HR (95% CI)
Neighborhood Deprivation Index								
All-Cause Mortality								
T1 (Least)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
T2	1.52	1.32	1.49	1.49	1.51	1.51	1.44	1.32
	(1.10-2.10)	(0.95 - 1.82)	(1.07-2.06)	(1.08-2.06)	(1.09-2.09)	(1.09-2.09)	(1.04-2.00)	(0.94-1.83)
T3 (Most)	1.84	1.45	1.78	1.78	1.82	1.83	1.60	1.42
	(1.25 - 2.70)	(0.98-2.15)	(1.21-2.62)	(1.21-2.62)	(1.24-2.70)	(1.25 - 2.70)	(1.08-2.38)	(0.95 - 2.13)
Breast Cancer Mortality								
T1 (Least)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
T2	1.31	1.19	1.26	1.29	1.32	1.26	1.31	1.20
	(0.77 - 2.24)	(0.70 - 2.04)	(0.73 - 2.15)	(0.76 - 2.21)	(0.77 - 2.27)	(0.74 - 2.16)	(0.76 - 2.26)	(0.70 - 2.07)
T3 (Most)	1.35	1.09	1.24	1.31	1.38	1.40	1.22	1.12
	(0.69-2.64)	(0.55 - 2.16)	(0.63 - 2.44)	(0.67 - 2.57)	(0.71 - 2.69)	(0.71 - 2.72)	(0.61 - 2.44)	(0.55 - 2.26)

 Table 5. Multivariable - and individual socioeconomic status variable - adjusted hazard ratios for the association between neighborhood deprivation, breast cancer mortality and all-cause mortality

HR, Hazard ratio; CI, Confidence interval; MV, Multivariable; SES, Socioeconomic Status

^a Multivariable hazard ratios adjusted for age at diagnosis, race, urban/rural status, and marital status.

	Cases	Person- months	Race- Stratified MV-adjusted HR (95% CI) ^a	MV- Adjusted + Education HR (95% CI)	MV- Adjusted + Household Income HR (95% CI)	Cases	Person- months	Race- Stratified MV- adjusted HR (95% CI) ^a	MV- Adjusted + Education HR (95% CI)	MV- Adjusted + Household Income HR (95% CI)
					Race/	ethnicity ^b				
		Non	-Hispanic Whit	e Patients			Non-	Hispanic Black	x Patients	
NDI										
All-Cause										
Mortality										
T1 (Least)	72	86,336.43	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	11	13,068.86	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
	65	41,727.31	1.66	1.39	1.59	12	16,444.82	0.82	0.79	0.77
T2			(1.17 - 2.35)	(0.97 - 1.98)	(1.11-2.27)			(0.36 - 1.87)	(0.34 - 1.82)	(0.33 - 1.81)
	28	16,216.68	1.77	1.40	1.62	25	15,692.35	1.62	1.34	1.28
T3 (Most)			(1.12-2.81)	(0.88-2.24)	(1.02-2.59)			(0.76-3.43)	(0.62-2.87)	(0.57-2.85)
Breast										
Cancer										
Mortality										
T1 (Least)	22	86,336.43	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	10	13,068.86	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
. ,	22	41,727.31	1.90	1.68	1.91	5	16,444.82	0.40	0.41	0.40
T2			(1.03 - 3.53)	(0.89-3.15)	(1.01 - 3.58)			(0.14 - 1.18)	(0.14 - 1.21)	(0.13 - 1.21)
	8	16,216.68	1.83	1.48	1.71	8	15,692.35	0.70	0.59	0.62
T3 (Most)		<i>.</i>	(0.78 - 4.30)	(0.62 - 3.53)	(0.72 - 4.07)			(0.26 - 1.85)	(0.22 - 1.60)	(0.21 - 1.82)

Table 6. Multivariable - and individual socioeconomic status variable - adjusted hazard for the association between the neighborhood deprivation index (NDI), breast cancer mortality and all-cause mortality by race/ethnicity

NDI, Neighborhood deprivation index; HR, Hazard ratio; CI, Confidence interval; MV, Multivariable;

^a Multivariable hazard ratios adjusted for age at diagnosis, urban/rural status, and marital status.

^b P _{interaction} = 0.05

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