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Breast Cancer Disparities and the Impact of Geography

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Abstract

Area of residence influences clinical outcomes due to its impact on access to and quality of care. For breast cancer patients, place of residence influences screening, stage, treatment, and mortality. Individuals residing in neighborhoods with high deprivation or rurality face significant hurdles to accessing and receiving care. Consequently, they experience later stages of disease at presentation, lower rates of guideline-concordant care, and higher mortality rates than their financially affluent or urban counterparts. With the evolving management of breast cancer, the implications of place on clinical outcomes warrant continued investigation. Moreover, literature gaps about geographic disparities in locoregional management and systemic treatment warrant further inquiry.

Keywords

Rural; Urban; Neighborhood; Breast Cancer; Disparities

Introduction

National discussions of health disparities and health equity have placed a spotlight on social determinants of health (SDHs). SDHs describe living and working conditions that affect overall health and influence one's ability to achieve health equity.^{1, 2} In the United States (US), place of residence has emerged as a powerful SDH with some scholars suggesting

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zip code is more significant for health outcomes than genetic code.³ This assertion is rooted in the effects of governmental policy, societal values, and cultural norms on the creation of neighborhoods and its subsequent implications for health and health outcomes.² For example, in the 1930's, systemic racism informed the practice of redlining by the Federal Housing Administration and the Home Owners' Loan Corporation.^{4,5} Redlining is the practice of systematic residential segregation by race in conjunction with disinvestment in Black neighborhoods secondary to mortgage lending biases.⁴ This historical practice has resulted in pervasive and persistent inequities and inequalities between predominantly Black versus White neighborhoods. {Richardson, 2020 #4357} Moreover, it has also adversely affected other SDHs such as education, employment, and homeownership in Black communities.⁵

The terms “neighborhood”, “place”, and “area of residence” all describe where people live. Neighborhood as a SDH can be viewed through its components of the built environment, services, and the people within the neighborhood.⁶ The built environment describes the infrastructure of a neighborhood such as buildings, streets, parks, and playgrounds.⁷ Examples of how the built environment can influence health outcomes include higher rates of obesity in neighborhoods with poor walkability.⁸ Services within a neighborhood include employment opportunities, schools, housing, and access to hospitals.⁶ Social relationships describe interactions between community members and how they leverage social cohesion and social capital within those relationships.⁹ These multidimensional components of the neighborhood influence health behaviors and psychosocial stressors and can even result in epigenetic changes (Figure 1).^{6, 10}

Social epigenetics is an emerging field evaluating the impact of the social and built environment on transcription of genetic information.⁶ Specifically, current research suggests epigenetic changes secondary to the social and built environment result in alterations in RNA silencing, protein fukumabaolding, DNA methylation, and histone modification.⁶ These epigenetic changes provide a plausible mechanism for how environmental exposures and chronic socioeconomic deprivation alter DNA and subsequently promote disease initiation and progression.⁶ For instance, epigenetic changes have been implicated in racial disparities in squamous cell carcinoma of the head and neck, depressive symptoms, and the development of hormone receptornegative breast cancers among black women.¹¹⁻¹³

The impact of place across the cancer continuum from prevention through survivorship is an area of active research. For breast cancer patients in particular, current studies suggest area of residence is a determinant of breast cancer stage of diagnosis, treatment, and mortality.^{14, 15} The objective of this paper is to provide a contemporary overview of the impact of place of residence on screening, stage, treatment, and mortality among breast cancer patients. Place will be examined through the lens of neighborhood and rural-urban status.

Discussion

Neighborhood and Breast Cancer Screening, Stage, Treatment, and Mortality

Screening and Stage at Diagnosis—The Healthy People 2030 target for breast cancer screening among US women is 77.1% of women ages 50-74.¹⁶ However, current estimates project approximately 72.8% of women within that age range undergo screening.¹⁷ Factors affecting screening rates involve a combination of patient-related (e.g., cultural beliefs) and structural variables such as the availability of screening mammography facilities.^{18, 19} Neighborhood, as a determinant of health, influences screening rates by either mitigating or creating barriers in health care access, quality, and timeliness of care. Neighborhood characteristics associated with lower adherence to breast cancer screening guidelines include living in the inner city, rurality, high neighborhood socioeconomic deprivation, and no primary care facilities within a neighborhood.^{20, 21} Of note, patients living in neighborhoods with greater socioeconomic deprivation face longer times to diagnostic resolution after an abnormal mammogram compared to those in areas with low deprivation.²² In Beyer and colleagues' evaluation of perceived neighborhood quality and screening among Wisconsin residents, low levels of neighborhood stress were associated with increased odds of undergoing screening mammography.²³

Neighborhood-based disparities in screening could have significant repercussions for both stage at diagnosis, breast cancer tumor subtype, and mortality. A recent evaluation of non-metastatic breast cancer patients in SEER showed patients living in neighborhoods with low socioeconomic status (SES) were more likely to present with stage III breast cancer compared to their counterparts in more affluent neighborhoods.²⁴ Moreover, Black women are more likely to live in neighborhoods characterized by higher levels of socioeconomic disadvantage, and Black people are more likely to present with triple-negative breast cancer, an aggressive breast cancer subtype.²⁵ However, studies evaluating the relationship between neighborhood racial segregation and breast cancer stage suggest racial segregation may not influence breast cancer stage.²⁶

Treatment

Locoregional management: Surgery and Radiation therapy: A recent examination of neighborhood characteristics and locoregional management in the Missouri state registry revealed patients living in neighborhoods with higher deprivation were more likely to undergo mastectomy or have surgical management omitted altogether. Additionally, those in areas with higher deprivation had no or delayed radiation therapy after breast conserving surgery.²⁷ Among adolescent and young adult breast cancer patients (defined as ages 15-39) increased mastectomy use, as well as omission of radiation therapy after breast conserving surgery are associated with residency in neighborhoods with low SES.²⁸

Wakefield and colleagues conducted a study of radiation therapy interruptions in a cohort of cancer patients that included breast cancer patients. Their results suggest residing in a low-income neighborhood increased the likelihood of 5 unplanned radiation therapy appointment cancellations.²⁹

Unfortunately, there are very few contemporary studies evaluating the relationship between locoregional management and neighborhood. Consequently, there are gaps in the literature on the relationship between neighborhood and receipt of contralateral prophylactic mastectomy or breast reconstruction. Moreover, the influence of neighborhood on adherence to omitting low-value surgical procedures such as lymph node surgery in women age 70 with small hormone receptor-positive breast cancers warrants investigation.³⁰

Systemic Treatment: Significant advances have been made over the past half century on systemic therapies for breast cancer. With the advent of novel chemotherapeutic agents, endocrine therapy, and targeted therapies for the human epidermal growth factor receptor (HER2/neu), breast cancer management has transitioned from mostly local therapies to a combination of local and systemic treatments.^{31, 32} Regrettably, there is a dearth of literature on the effects of neighborhood on receipt of systemic therapies. Sadigh et al's review of the Trial Assigning Individualized Options for Treatment (Rx) (TAILORx trial) showed an association between high neighborhood deprivation and early discontinuation of endocrine therapy.³³ The study findings are noteworthy as they suggested that, after controlling for neighborhood deprivation, Black breast cancer patients in the trial had higher rates of adherence to hormone therapy than White women. The TAILORx trial evaluated the benefit of chemotherapy among hormone receptor-positive, HER2/neu-negative breast cancer patients stratified by Oncotype Dx Recurrence score.³⁴

Mortality—Residing in neighborhoods with low SES or high rates of deprivation is associated with higher mortality among breast cancer patients.^{35, 36} To determine the association between neighborhood and survival, Shariff-Marco et al aggregated neighborhoods based on demographics and household composition, immigration, neighborhood SES, walkability, residential mobility, commuting, rural/urban status, land use, and food environment to create neighborhood archetypes. Study results suggest overall and breast cancer-specific survival are associated with neighborhood archetype. Specifically, patients in upper middle-class neighborhoods with high-SES had the highest survival.³⁷

The legacy of redlining has been implicated in increasing breast cancer mortality.³⁸ In a study by Collin's et al, both Black and White patients living in areas of high redlining had higher mortality compared to patients living in areas of low redlining.³⁸ Conversely, residency in a neighborhood with lending bias, defined as race-based systematic denial of mortgages, was associated with decreased breast cancer mortality.³⁸ Interestingly, for Black women, residing in neighborhoods with increasing proportions of Black people was associated with lower mortality.²⁶ These findings are in contrast to Russel and colleagues' work showing higher mortality rates among Black women in neighborhoods with higher percentages of Black residents.³⁹

Impact of Rural-Urban Status on Breast Cancer Screening, Treatment, and Mortality

Screening and Stage—Studies evaluating the relationship between rural/urban status and mammography use have been inconsistent about the effects of rurality on receipt of mammography. Examinations of both national and state databases suggest rural women are less likely to undergo screening mammography compared to women living in urban

odds of undergoing reconstruction compared to those in rural areas.⁵⁷ A possible driver of rural-urban disparities in reconstruction is the geographic availability of reconstructive surgeons.⁵⁸

Currently, the American Society of Breast Surgeons, the Society of Surgical Oncology, and Choosing Wisely guidelines discourage women with unilateral cancers without underlying genetic mutations from undergoing contralateral prophylactic mastectomy (CPM).³⁰ Nevertheless, there has been a significant increase in the utilization of CPM with young women as the main drivers of this trend.⁵⁹ This pattern of young age and increased CPM use has also been seen among rural patients. In an examination of CPM among breast cancer patients in Iowa, young (defined as age <40), rural women had the highest rate of contralateral prophylactic mastectomy (CPM) compared to metropolitan and non-metropolitan women. Notably, in the aforementioned study, rural women who traveled to metropolitan hospitals had higher rates of CPM than those who were treated at rural hospitals.⁶⁰

Locoregional management of breast cancer with breast conservation surgery in conjunction with radiation (i.e., breast conservation therapy) is effective in reducing recurrence.⁶¹ The receipt of radiation therapy after breast conservation therapy in early-stage breast cancer patients is considered guideline-concordant care.⁵⁴ Studies indicate the main barrier to utilization of radiation therapy among rural patients are long travel distances.⁵⁴

Systemic Treatment: Unfortunately, there is a paucity of literature on the relationship between rural-urban status and systemic treatments. In Andreason and colleagues' retrospective multi-institutional review, there was no difference in the use of hormone therapy based on rural versus urban residency.⁶² However, when stratified by Oncotype Dx recurrence score (RS), rural patients with an RS of 18-30 were less likely to undergo chemotherapy than urban patients with a similar score.⁶² With the results of the recent RxPONDER trial (examining benefit of chemotherapy in women with hormone receptor-positive, HER2-negative disease, 1-3 positive lymph nodes, and low-risk RS) and the aforementioned TAILORx trial, additional studies are needed to evaluate the dissemination and implementation of these trial results on systemic therapies in hormone receptor-positive patients across the rural-urban continuum.

Mortality: National mortality rates from cancer appear to be on the decline.⁶³ However, rural patients are not experiencing reductions in mortality rates comparable to their urban counterparts.⁶³ In breast cancer patients, the relationship between rural-urban status and mortality is unclear. Chu and colleagues' review of the Louisiana Tumor Registry suggest differences in overall and disease-specific survival among rural and urban breast cancer patients are driven by sociodemographic, clinical, and treatment rather than area of residence.⁶⁴ Conversely, an examination of the NCDB showed breast cancer patients living in large metropolitan areas have an 8% relative risk reduction in overall mortality compared to patients living in rural areas after controlling for sociodemographic, clinical, and treatment factors.⁵³ The inconsistency in these results may be reflective of the patient populations utilized in each study. The NCDB represents approximately 70% of cancers in

the United States and consequently may have a more heterogeneous population compared to the registry of the state of Louisiana.⁶⁴

Summary

Area of residence has significant implications for breast cancer screening, stage of diagnosis, treatment, and mortality. However, there are significant gaps in the literature on the impact of neighborhood on the receipt or completion of systemic therapies. Moreover, additional research needs to be conducted on how place influences emerging changes in surgical management such as implementation of axillary surgery de-escalation, elimination of low-value surgical procedures, and the utilization of oncoplastic reconstruction. Health systems need to incorporate population health into their healthcare delivery paradigms to help identify and address the effects of place on breast cancer outcomes.

Abbreviation/Glossary List

SDH	Social determinants of health
TAILORx trial	Trial Assigning Individualized Options for Treatment (Rx)
BRFSS	Behavioral Risk Factor Surveillance Systems
SEER	Surveillance, Epidemiology, and End Results Program

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Clinical Care Points

1. Routinely collect social determinants of health as part of clinic workflow to identify barriers faced by patients in rural or high-deprivation neighborhoods
2. Incorporate social work or patient navigation to help mitigate barriers.

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KEY POINTS

- Neighborhood is a powerful social determinant of health with significant implications for breast cancer outcomes.
- High neighborhood deprivation is associated with advanced stages of disease at presentation and disparities in locoregional and systemic treatment.
- Rural breast cancer patients face barriers in screening and treatment of breast cancer that adversely affect their survival.

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SYNOPSIS

Neighborhood has significant implications for breast cancer screening, stage, treatment, and mortality. Patients residing in neighborhoods with high deprivation or rurality face barriers and challenges to accessing and receiving care. Consequently, they experience higher mortality rates than their financially affluent or urban counterparts. There are multiple gaps in the literature on the relationship between place of residence and the use of systemic therapies or emerging surgical strategies for disease management. As the management of breast cancer continues to evolve, additional studies are needed to understand the implications of place on the implementation and dissemination of new and emerging treatment modalities.

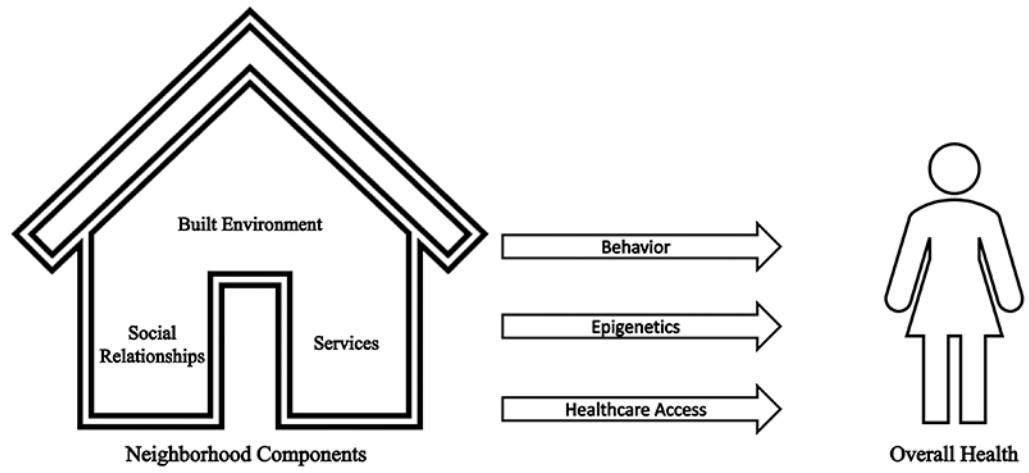


Figure 1: The influence of neighborhood on health. This figure depicts the pathways through which neighborhood can influence health.