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Interrelationships of Sociodemographic and Biological Factors in Breast Cancer Mortality Disparity Affecting Young Black Women

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Abstract

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Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

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Abstract

Despite improved overall survival among breast cancer patients, race and biological subtype-specific disparities persist. Subsequently, this retrospective longitudinal study, guided by ecosocial theory, examined associations between biological subtypes of breast cancer and patient-level sociodemographic factors on survival outcomes in women 25 to 44 years of age. Using Surveillance, Epidemiology, and End Results (SEER) database, 34,007 breast cancer cases between 2013 and 2018 were extracted. Kaplan Meier method and Cox proportional hazards model were used to examine time to event and the adjusted mortality risk by race and breast cancer subtype. There was a statistically significant difference in survival among young Black women by biological subtype (χ^2 (1) = 13.031, $p < .05$. Young black women with triple-negative breast cancer (TNBC) had a significantly increased risk of breast cancer death than young Black women with non-TNBC (hazard ratio [HR] = 2.220, 95% CI [1.373, 3.589]). Additionally, young Black women with TNBC experienced worse survival outcomes than young White women with TNBC (adjusted HR = 3.613, $p = .001$). Statistically significant interactions between geographic location (GL), median household income (MHI), and tumor subtype were observed. Interactions between GL, MHI, and biological subtype are potential drivers of unequal survival outcome between Black and White women. Social change implications include increased knowledge of the breast cancer mortality disparity. Understanding the causes of poor survival outcomes will help develop evidence-based interventions and policies to address the socioeconomic and physical environment disadvantages affecting young Black women with breast cancer.

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Dedication

I want to dedicate my dissertation to my family and friends, who have been my anchor; this journey would not have been possible without your support. Thank you for believing in me and my dreams. I am indebted to my mother–Rhona Mutyabule, who has been my mentor since the beginning. Her support and encouragement have been unwavering and enabled me to realize my dreams. To my children, Kaitlyn, Zoe, and Matthew, my educational journey manifests that knowledge is infinite. Keep believing and never give up on your goals, aspirations, and dreams. And to my wife, I am forever grateful for rallying behind my causes and fostering my personal growth. I am eternally thankful that I've always been able to count on you when all seemed impossible.

This dissertation is in memory of Ms. Rosemary Lwande, one of my patients who lost her battle with breast cancer on February 4th, 2018. Her courage and resilience live on and are an inspiration to those who knew her. Like she used to say, "tomorrow will be another young Black woman with breast cancer experiencing these challenges unless we make a difference." We are……

Finally, I thank all my friends in Boston, San Francisco, Manchester USA, Kampala, and Jinja, Uganda, who supported and prayed for me. To God be the glory.

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Chapter 1: Introduction

Breast Cancer Mortality Disparity in the United States

In the United States, breast cancer is the second most common cause of cancer mortality among women after lung cancer (Ademuyiwa et al., 2017; Centers for Disease Control and Prevention [CDC], 2020; DeSantis et al., 2017). Approximately 250,000 new cases of breast cancer are diagnosed annually among women (CDC, 2020). The incidence rate of breast cancer is lower in Black and Hispanic women (121 and 95 women per 100,000 women, respectively) compared to White women (126 women per 100,000 women; CDC, 2019). However, despite the lower incidence rates of breast cancer among Black women compared to their White counterparts, Black women experience higher breast cancer mortality rates (CDC, 2020; DeSantis et al., 2017; Yedjou et al., 2019). Moreover, the mortality rate among young Black women (25–44 years) is disproportionately high compared to Black women 45 years and older (Hung et al., 2016; Sighoko et al., 2018; Yedjou et al., 2019). The disparities in breast cancer health outcomes among young Black women represent a significant and urgent public health concern in the United States.

Previous studies have attributed the observed racial disparities in breast cancer outcome to the increased incidence of triple-negative breast cancer (TNBC) subtype among Black women (Ademuyiwa et al., 2017; DeSantis et al., 2016; Hill et al., 2020). TNBC is a subtype breast cancer and derives its classification from the absence hormonal receptors. The TNBC has a negative expression of estrogen (ER), progesterone (PR), and human epidermal growth factor receptor-2 (HER2).

TNBC subtype represents about 15%–30% of all invasive breast cancer diagnosed in the United States with a higher prevalence among young Black women (Ademuyiwa et al., 2017; DeSantis et al., 2016; Doepker et al., 2018; Turkman et al., 2016). Women with TNBC breast cancer subtype experience a more aggressive clinical course, with worse outcomes within the first 3–5 years after diagnosis (DeSantis et al., 2016; Doepker et al., 2018; Hill et al., 2020). TNBC differs from other subtypes as they grow and spread faster with limited treatment options (Ademuyiwa et al., 2017; Prasad et al., 2016; Shepherd et al., 2017). The findings represent an urgent challenge for public health practitioners in addressing the potential determinants of the mortality disparities among Black subpopulations.

Additionally, despite the increased observed incidence of the aggressive forms TNBC subtype among Black women, Black women still experience worse outcomes of breast cancer after controlling for the breast cancer subtype, sociodemographic factors, breast cancer therapy received, access to quality healthcare and stage of the cancer (DeSantis et al., 2016; Hill et al., 2020; Yedjou et al., 2019). The findings suggest that the differences in race-specific mortality disparities in breast cancer may not be fully attributed to variation in breast cancer subtypes but rather a variety of factors that contribute to overall survival. A gap exists in understanding the role of the complex interrelationships of sociodemographic and biological factors in outcome disparities among young Black women that are beyond treatment differences in a clinical setting. Moreover, there is paucity of literature on the relationships between breast cancer subtype and sociodemographic factors in driving race-specific disparities in breast cancer

mortality among young Black women. Therefore, this study aimed to compare the association of biological subtype (TNBC vs n-TNBC) of breast cancer on prognostic factors (sociodemographic factors) that may influence survival outcome and will aid public health interventionists in developing risk assessment models that can better predict adverse outcomes in specific subpopulations and promote specific evidence-based interventions that will improve health outcomes among these subpopulations.

The race specific breast cancer mortality disparity trend remains a focus for public health research. The trend also highlights the need for a multifaceted approach to addressing health disparities that includes improving access to quality healthcare, increased participation of minority subgroups in research studies, and early screening/detection of aggressive forms of breast cancer disease.

In furtherance, differences in biological subtypes that influence breast cancer outcomes among subpopulations is a primary focus of the precision medicine initiative (CDC, 2020; DeSantis et al, 2016; Keenan et al., 2015; Richardson et al., 2016). According to CDC (2020), the precision medicine initiative approach helps to address health outcome disparities by promoting advances in research, and technology, that enable collaboration between clinicians, researchers, and patients in developing individualized care. The approach enables clinicians to understand how the molecular/biological characteristics of cancers interact with sociodemographic variables to influence health outcomes in certain subgroups. The study was aligned with the research agenda and objectives of the CDC and Healthy People 2030 that explore the

health disparity outcomes associated with social, economic, and environmental (micro and macro factors) disadvantages in the community.

Background

TNBC is a form of invasive breast cancer subtype that occurs at higher frequency in Black women compared to White women (Ademuyiwa et al., 2017; DeSantis et al., 2016; Doepker et al., 2018; Hill et al., 2020). The TNBC subtype is characterized by the absence of protein expression of the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2; CDC, 2021; Doepker et al., 2018). TNBC subtype has unique pathological, molecular, and clinical behavior (Prasad et al., 2016), being more aggressive in their clinical pathological course (Qiu et al., 2016; Sheppard et al., 2017), and are associated with a worse prognosis.

The TNBC subtype represents about 15%–30% of all invasive breast cancer diagnosed in the United States with a higher prevalence among young Black women (DeSantis et al., 2016; Doepker et al., 2018; Turkman et al., 2016). Additionally, women with TNBC breast cancer subtype experience a more aggressive clinical course, with worse outcomes within the first 5 years of diagnosis (DeSantis et al., 2016; Doepker et al., 2018; Hill et al., 2020). Disparities in survival outcome attributed to tumor biological differences represent an urgent public health challenge. With more than half of TNBC breast cancer patients experiencing poor 5-year overall survival (OS) and low disease-free survival (DFS) rates (Ademuyiwa et al., 2017; Qiu et al., 2016; Sheppard et al., 2017;). Particularly, young Black women are disproportionately affected compared to

older Black women (i.e., above 45 years; CDC, 2020; Doepker et al., 2018; Hill et al., 2020).

In this study, I examined the associations between TNBC and non-TNBC biological subtypes of breast cancer and patient level sociodemographic factors and how they influence survival outcomes. Race-specific disparities in survival outcomes among young women with breast cancer may be attributed to these associations.

TNBC largely affects young Black women ages 25–44 years (CDC, 2020; Doepker et al., 2018; Hill et al., 2020; Keenan et al., 2015). It is unclear if these predictors (biological subtype and sociodemographic factors) could explain the widening gap in breast cancer mortality disparity outcomes. The trends in race- and age-specific breast cancer mortality disparity remain a focus for public health interventions and inform designing appropriate preventive programs.

Social determinants of health—socioeconomic status (household income, and education attainment level), neighborhood disadvantages (crime rate, poor housing), unemployment, racial discrimination, lack of social support during cancer treatment, and social network deficiencies—play an important role in survival outcomes. The Healthy People 2020 was cognizant of the importance of promoting health by addressing ecological factors that contribute to poor health outcomes (Pronk et al., 2021). Pronk et al (2021) emphasized that the Healthy People 2030 initiatives highlight opportunities for states to use evidence-based interventions to promote health and foster equity and social justice. By utilizing ecological factors to address health inequity less emphasis is laid on

the traditional medical models hence reducing bias and racism built within these institutions.

Previous researchers have also explored other aspects this social paradigm, like medical distrust among the Black subpopulation, cultural differences, immigration status, inadequate housing, food insecurity, and geographic factors such as neighborhood access to health services to explain differences in health outcome (Coughlin, 2019; DeSantis et al., 2016). However, beyond these social determinants of adverse health outcomes among Black women, a growing area of public health research is set on understanding the role of biological differences in disease outcomes (Ademuyiwa et al., 2017; Azim & Partridge, 2014; Wheeler et al., 2013). The heterogeneity that exists among the invasive breast cancers may be used to predict survival outcome.

Education Attainment Gaps and Neighborhood Disadvantages

With only 36% college participation rates for Blacks, educational attainment gaps persist and contribute to the growing socioeconomic gap (National Center for Education Statistics, 2019). Blacks and Latinos are more likely to attend high-poverty schools than their White counterparts and experience higher drop-out rates (Walker et al., 2016) presenting socioeconomic challenges in adulthood. Lack of employment and increased crime rate in some neighborhoods may interfere with access to care.

Social Network, Social Support and Family Dynamics

Two out of 10 Black women are single parents, exacerbating chronic psychosocial stress (Stafford et al., 2017; U.S Census Bureau, 2016). A large body of research has demonstrated evidence that psychological stress attributed to socioeconomic inequality

can significantly impact outcomes of patients with cancer (CDC, 2020; Coughlin, 2019; Walker et al., 2016). Additionally, the lack of social support due to family pressures may interfere with breast cancer treatment plans in clinical settings.

Overall, risk factors associated with racial and ethnic differences in breast cancer mortality remain largely unknown (DeSantis et al., 2016; Hu et al., 2016; Teng et al., 2016; Vidal et al., 2017; Teng et al., 2016; Hu et al., 2016; DeSantis et al., 2016). Therefore, examining risk factors linked to the relationship between breast cancer biological subtypes and sociodemographic factors is significant in understanding race-specific mortality disparities and this remains an active research area of social epidemiology.

Problem Statement

Breast cancer is the second most common cancer and the second leading cause of cancer mortality among women in the United States (CDC, 2020). Annually an estimated 250,000 cases of breast cancer are diagnosed in women in the United States (CDC, 2020). Of these new cases, the TNBC subtype represents 15%–30% (Ademuyiwa et al., 2017; DeSantis et al., 2016; Doepker et al., 2018; Turkman et al., 2016). TNBC has unique risk factors, which include young age, ethnic minorities, origin of ancestry, and Breast Cancer Gene 1 (BRCA1) mutations (CDC, 2020, Turkman et al., 2016). The TNBC risk profile may be attributed to the increased cases on TNBC among young Black women.

According to the CDC (2020), approximately 11% of all new cases of breast cancer are among women younger than 45 years of age. Hispanics and Blacks report a

lower incidence rates of breast cancer compared with their White counterparts, but their mortality rate is disproportionately higher (DeSantis et al., 2016; Newman, 2017; Teng et al., 2016). Additionally, an estimated 41,000 deaths from breast cancer occurred in 2015 making breast cancer the second leading cause of cancer death among women in the United States (Bollinger, 2018). The disproportionate trend of the high mortality rate and a lower incidence rate in the minority subpopulations (i.e., Blacks and Hispanics) represents the increased burden of female breast cancer in these subpopulations.

Overall, the female breast cancer mortality rate has decreased over time due to effective public health interventions of early detection through breast screening campaigns and an array of improved and effective therapeutic interventions (DeSantis et al., 2016; Yedjou et al, 2019). However, race-specific differences in breast cancer survival outcomes have persisted majorly affecting Black women aged 25–44 years (Ademuyiwa et al., 2017; DeSantis et al., 2016; Prasad et al., 2016). The disparity in survival outcome represents a significant public health burden.

The female breast cancer burden among young Black women continues to grow exerting tremendous physical, and emotional stress on an otherwise productive demographic for national development. Research has shown that parents with cancer have high rates of psychological morbidity, and their children are at an increased risk of poor psychosocial outcomes (Bollinger, 2018; Stafford et al., 2017), consequently producing a strain on families and communities where approximately 2 in 10 women is a single mother and sole provider of the family (U.S. Census Bureau, 2016). The age demographic 25–44 years is productive and a majority of women have families during

this age bracket (CDC, 2020). Hence psychosocial factors may play a role in the poor overall survival among Black women.

By understanding the role of sociodemographic factors (e.g., race, median household income, and geographical location) and breast cancer biological subtype (TNBC and n-TNBC) in outcome disparities among young women may inform the risk factors that explain differences in the survival outcome observed in clinical settings. The research study was pertinent to public health interventions in aiding the development of risk assessment tools that can better predict adverse outcomes in vulnerable subpopulations. The development of these risk assessment tools also provides better public health strategies for breast cancer prevention among vulnerable populations.

Purpose of the Study

Biological and sociodemographic factors are important prognostic determinants of breast cancer survival outcomes (Hu et al., 2016; Jimwook et al., 2017; Newman, 2017; Stiel et al., 2017). The patterns of race-specific breast cancer mortality rates may be attributed to the associations between sociodemographic determinants and breast cancer biological subtypes. The purpose of the study was to examine the associations between biological subtypes of breast cancer (TNBC and non-TNBC) and patient level sociodemographic factors (race, median household income, and geographical location) and how they influence survival outcomes in specific subpopulations.

The literature indicates that TNBC is associated with decreased survival outcome that majorly affects young Black women (CDC, 2020; Doepker et al., 2018; Hill et al., 2020; Keenan et al., 2015). However, the association between sociodemographic factors

(race, median household income, and geographical location) and specific biological subtypes (TNBC vs. n-TNBC) in contributing to the disproportionate survival outcome is largely unknown. An active area of research in the prevention of health outcome disparities seeks to understand the influence of the associations between sociodemographic factors and breast cancer biological subtypes to explain the differences in the race-specific mortality rate.

Epidemiological approaches to the race-specific cancer burden are essential in the analyzing the micro and macroeconomic impacts of early death in this subgroup and highlight the cost of illness in perpetuating the socioeconomic gap. The study will aid public health interventionists in developing risk assessment models that will form the basis for policy advocacy and setting priorities for allocation of resources to vulnerable groups experiencing higher breast cancer burden, thus developing targeted public health interventions aimed at reducing the mortality disparity gap.

The results of this study will aid in highlighting the risk factors that can be used to develop risk assessment models that better predict adverse outcomes in vulnerable populations, hence informing public health intervention strategies with potential to address disparities in survival outcomes among social, economic, and neighborhood disadvantaged communities.

Research Questions

The following research question was designed to guide this study: Do sociodemographic factors measured as median household income, and neighborhood factors (e.g., geographical location [metro vs. non-metro]) confound the survival rate

among young Black women with TNBC and non-TNBC biological subtypes? Investigating the effect of sociodemographic variables upon the survival rate among those with TNBC and the ones with other subtypes of breast cancer collectively referred to as non-TNBC (n-TNBC) in specific subpopulations is crucial to understanding the role of these associations in health disparity outcomes. The research questions and hypotheses below are based on answering this central question of the study:

Research Question 1: Do young Black women with TNBC biological type have poor survival outcome compared to other young Black women with the non-TNBC biological subtypes (Hormone Receptor (HR) +ve/HER2 +ve, HR +ve/HER -ve, HR -ve/ HER2 enriched) of breast cancer?

H_01: There is no difference in survival outcome based on the biological subtype of breast cancer (TNBC vs. non-TNBC) among young Black women diagnosed with breast cancer

H_a1: There is a difference in survival outcome based on the biological subtype (TNBC vs. non-TNBC) of breast cancer among young Black women diagnosed with breast cancer

Research Question 2: Is there a difference in survival rate among young Black women with TNBC subtype and non-TNBC subtypes (Hormone Receptor (HR) +ve/HER2 +ve, HR +ve/HER -ve, HR -ve/ HER2 enriched) when adjusted for sociodemographic factors?

H_02: There is no difference in survival rate among young Black women with TNBC subtype and non-TNBC biological subtypes when adjusted for sociodemographic factors

H_a2: There is a difference in survival rate among young Black women with TNBC subtype and non-TNBC biological subtypes when adjusted for sociodemographic factors

Research Question 3: Is there a difference in survival rate between young Black women and young White women with the same biological subtype-TNBC after controlling for sociodemographic factors?

H_03: There is no difference in survival rates between young Black women and young White women with the same biological subtype-TNBC after controlling for sociodemographic factors

H_a3: There is difference in survival times between young Black women and young White women with the same biological subtype-TNBC after controlling for sociodemographic factors

Theoretical and Conceptual Framework

The ecosocial theory, an emerging multilevel theory of disease production and distribution (Krieger, 2001), served as the framework for this study. The theory explains the shifting patterns of disease distribution in the population and examines the cumulative effects of proximate social, political, and economic processes in shaping disease biological profiles. The ecosocial theory was first proposed by Krieger in 1994 to explain population distributions of health and is used in social epidemiology to understand the

myriad of interrelated social and biological processes in causation of disease. This multiple causation model remains a widely acceptable model in epidemiology for examining population patterns of health.

According to Krieger (2001), the ecosocial theory also seeks to integrate social and biologic reasoning, along with a dynamic, historical, and ecological perspective, to address population distributions of disease and social inequalities in health. The central question in a study on disparities in health outcomes is "who and what is responsible for population patterns of health, disease, and well-being, as manifested in the present, past and changing social inequalities in health" (Krieger, 2012). Poor health outcomes in societies are mirrored in socioeconomic deprivation among minority ethnic/racial subpopulations in the United States (Hossain et al., 2019; Merlo, 2011). The findings are consistent with the theory that no aspect of our biology can be understood in the absence of knowledge on our life history and individual and societal ways of living.

Biological expression of social inequality occurs in our bodies (Krieger, 2012). Our bodies biologically express economic and social inequality experiences, from intrauterine life to death, thereby producing social disparities in health across a broad spectrum of disease. Blacks are disproportionately affected by socioeconomic challenges that translate into physical conditions like obesity, diabetes, and other chronic diseases (Tremmel et al., 2017; Rivera, 2014). Most of these conditions are risk factors for cancer development (Deshmukh et al., 2017). SES is a consistent and reliable predictor of a vast array of outcomes across the life span, including physical and psychological health. Thus,

SES is relevant to all realms of behavioral and social science, including research, practice, education, and advocacy.

In keeping with the ecosocial theoretical framework, the primary research aim was to measure the associations of breast cancer subtypes and sociodemographic determinants and their role in survival rate among Black women with breast cancer disease. Thus, I theorized that breast cancer biological subtypes like TNBC may have a sociodemographic link to the poor survival rate among young Black women.

Nature of the Study

The research study was premised on quantitative methods whose epistemological foundation is in logical positivism. Logical positivism contends that observations of the world are made through our senses and provide the sole foundation for knowledge. Anything that is not observable or is unconscious cannot be included in the realm of scientific knowledge (Burkholder et al., 2016). Hence, the methods used in this research are a gold standard for scientific knowledge generation.

The study design was a retrospective longitudinal cohort study design using secondary data from the Surveillance Epidemiology and End Results (SEER) program database of the National Cancer Institute (NCI). The SEER provides the most diverse sociodemographic characteristics that can be used to capture the differences that contribute to disparities in survival outcomes.

Statistical methods were used to quantify the associations and trends of the observations between the breast cancer biological subtype, sociodemographic variables (race, median household income, and geographical location), and survival times. The

study's survival outcomes were defined as the "time to event" to occur, with the primary endpoint as death. These outcomes were analyzed in the survival analysis models to examine the proportion of cancer patients with TNBC by race (Black vs. Whites) that experienced the event of death between 2013-2018 and also whether there were significant differences after adjusting for sociodemographic variables among young black women with TNBC and non-TNBC. The study evaluated the survival rate by the biological subtype (TNBC vs. n-TNBC) among Black women and examined whether statistically significant differences existed across different racial groups (Whites vs. Blacks) with TNBC, after adjusting for median household income, and geographic location (metro vs. non-metro). Interaction models were also used to determine any effect on the risk of mortality for a particular subgroup by race and biological subtype.

Definitions

Biological subtypes: TNBC is a subtype of breast cancer characterized by the absence of the three most targeted biomarkers considered for breast cancer treatment and derives its name from the lack of these three biomarkers (Dietze et al., 2015; Gonçalves et al., 2018,). TNBC has been found to affect young Black women (Doepker et al., 2017) and is the more aggressive breast cancer biological subtype (Prasad et al., 2016). The other biological subtypes of breast cancer are the breast tumor subtypes that include luminal A, luminal B, Human Epidermal growth factor Receptor 2 enriched (HER2-E). In the study, they are classified as non-TNBC subtypes.

Geographical location: Metro areas are counties in metropolitan areas with 1 million population, counties in metropolitan areas of 250,000 to 1 million population,

counties in metropolitan areas of 250,000 population. Nonmetropolitan areas may be counties adjacent to a metropolitan area, or nonmetropolitan counties not adjacent to a metropolitan area and the size of the population is less than 250,000.

Median household income: Income in the past 12 Months - Income of Households was taken as the average total income of a given household (CDC, 2020; Lehrer et al., 2016). The household income statistics cover the past 12 months, as reported at the time of the interview. The median household income was considered at two levels: those above $50,000 and those at $49,999 and below.

Assumptions, Limitations and Delimitations

For this study, I assumed that the data from the SEER registry 18 and Research Plus database would provide definitive, up-to-date information to answer the three research questions. I assumed that the data collected followed the established program guidelines that the NCI uses to support cancer surveillance activities. The information on cancer incidence and survival was representative of the general population in the United States.

The SEER data were collected though respondent surveys and may therefore have some information bias, such as self-reporting bias, especially for variables like the level of income. The median household income reported may not be a true reflection of the actual household income due to social desirability bias. Social desirability bias is a type of response bias in which there is a tendency by survey respondents to answer questions in a manner that will be viewed favorably by others (Szklo & Nieto, 2019). However, data triangulation was used to minimize this bias.

Limitations of the study also included the length of time the data were collected. Right censoring may have been apparent as some of the patients were censored before experiencing the event. The overall survival considered in the study is based on a well-defined time point and thus avoids interval censoring. Right censoring, due to incomplete follow-up may be a source of bias. Black women are more likely to be lost to follow-up due to social disadvantages in access to care (DeSantis et al., 2016; Doepker et al., 2018). This study was only conducted to determine if there is an interaction between the sociodemographic factors and breast cancer biological subtype and whether sociodemographic factors confound the survival times among young White and Black women. No causal nature of any identified relationship would be able to be determined, though the study provides preliminary data that can serve as a foundation for further research that can elucidate causal relationships.

Delimitations of the study included a sample of Black and White women with a diagnosis of breast cancer that was recorded with a biological subtype. The research study population was aged 25–44 years.

The study was quantitative in nature. The epistemological assumptions were that the researcher was independent of the observations used in the study and that the findings could only demonstrate an association and not causation.

Significance of the Study

The results of this study contribute to social change by highlighting the growing trend of disparities in health outcomes among breast cancer patients. Understanding the interactions of biological and nonbiological factors (sociodemographic) that contribute to

the excess mortality among young Black women with TNBC will potentially lead to evidence-based interventions and policy initiatives that address the socioeconomic and physical environment disadvantages prevalent among Black communities. This will improve survival outcomes among young Black women with aggressive biological subtypes of breast cancer.

According to literature, risk factors associated with racial and ethnic differences in breast cancer mortality remain largely unknown (DeSantis et al., 2016; Hu et al., 2016; Teng et al., 2016; Vidal et al., 2017). The research provides an empirical evidence of the nexus between TNBC biological subtypes and sociodemographic factors that may contribute to the excess age-specific breast cancer mortality rate among subcategories of Black women.

The research was also a continuum of socioecological research that highlights the nested hierarchies influencing behavior and disease risk across an individual's lifespan and examines the cumulative effects of environmental factors (socioecological) that disproportionately influence physiological processes (biology) in specific subpopulations hence contributing to intergenerational disease production.

Furthermore, the study provides compelling evidence to inform policymakers and public health practitioners of the need for increased access to genetic screening (biological) tests in early identification of tumor characteristics of aggressive forms of breast cancer that disproportionately affect young Black women.

Summary

This chapter provided the purpose, significance, and a brief background of the research study. A summary of the theoretical framework grounding this study was also discussed. The public health problem that this study addressed was the high mortality rate disparity among young Black women 25–44 years of age with TNBC. The research study was grounded in the ecosocial theory. I sought to examine associations in biological subtypes of breast cancer and sociodemographic determinants and their role on survival probabilities among young Black women. There is paucity of literature on race/ethnic specific differences in the risk factors associated with breast cancer mortality disparity.

Biological subtype of breast cancer and sociodemographic variables are important prognostic indicators that were used in the study to predict the survival outcome among breast cancer patients 25–44 years. Secondary data from the *SEER Registry 18 Research Plus* Database was used to answer the three research questions through hypothesis testing using Kaplan Meier Survival analysis method, log-rank test and Cox Proportional hazards method.

Chapter 2 provides a comprehensive review of the literature on TNBC biological subtype among Black women and the role of the association of sociodemographic and the breast cancer biological subtype variable in influencing health outcomes. Chapter 2 also provides a detailed theoretical and conceptual framework for the study based on the foundations of social epidemiology.

Chapter 3 provides detailed information of the methods used for this study. This chapter expanded on the research questions and hypotheses to include the statistical

analyses that were used. An explanation of the research population and research design, and operational definitions of the variables used for this study will also be provided. Chapter 4 presents the results of the study and Chapter 5 discusses the results and conclusions from this research, and offers directions for future research, the implications for public health policy and practice, and also discusses the limitations of the study.

Chapter 2: Literature Review

The purpose of this study was to examine the associations between biological subtypes of breast cancer (TNBC and non-TNBC) and patient-level sociodemographic factors and how they influenced survival outcomes in specific subpopulations. Chapter 2 provides an extensive review of the literature—the overview and classification of female breast cancer tumor biology. A conceptual definition of TNBC as a biological subtype of breast cancer used throughout the study is also presented. I discuss breast cancer epidemiology among young Black women, followed by a review of the relevant literature on TNBC breast cancer. What is known about biological subtypes and sociodemographic factors in influencing breast cancer survival outcomes was presented, followed by an in-depth discussion of the theoretical and conceptual frameworks used to provide context for the study.

The sources used for the literature review were EBSCO databases (Walden University Library), Google Scholar; Medline Plus; publications listed on the CDC Breast Cancer website; and a review of selected journal article citations. I used an extensive array of search terms to find publications related to this topic and the research questions. The key search terms were *survival outcomes*, *health disparities*, *sociodemographic factors*, *female breast cancer*, *triple-negative breast cancer*, *biological subtypes*, *genetics*, and *Black or Black women Ages 25—44 years* in the databases MEDLINE in full text, Academic Search Complete, Biomed Central, Cochrane Database for systematic reviews and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) database (EBSCO databases).

Overview and Classification of Female Breast Cancer

Breast cancer is a heterogeneous disease at molecular level with different clinical pathways determined by distinct gene expression patterns (Ademuyiwa et al., 2017). The genomic differences are secondary to somatic gene mutations that influence prognosis (Ademuyiwa et al., 2017; Eliyatkin et al., 2015; Partridge et al., 2016; Testa et al., 2020). Historically, breast cancer classifications have followed the traditional methods that involve histopathological characteristics of the tumor.

However, molecular taxonomy, the newer approach to breast cancer classification, utilizes tumor biological characteristics (Eliyatkin et al., 2015; Partridge et al., 2016; Testa et al., 2020). The approach helps clinicians evaluate tumor progression and other prognostic factors of cancer. Molecular taxonomy microarray technological applications in which genomic DNA is fluorescently labeled and used to determine the presence of gene loss or amplification (Khurana et al., 2019). Thus, enabling scholars to study the intrinsic characteristics of the tumor.

The breast cancer classification based on the tumor's molecular characteristics enables clinical profiling of the cancers based on their response to treatment. The breast tumor subtypes that include Luminal A, Luminal B, HER2-E, and basal-like luminal breast tumor subtypes were established based on gene microarray technological applications used in gene expression profiling (Dietze et al., 2015; Vidal et al., 2017). Most breast tumors diagnosed are luminal based on tumor biology characteristics (Vidal et al., 2017). The luminal tumors further exhibit heterogeneity in treatment response.

Luminal A tumors tend to be low grade and positively express ER and PR, but not HER2 receptors. Luminal A breast tumors respond favorably to hormonal therapies that target ER and PR (Vidal et al., 2017). Luminal B breast tumors majorly express ER and PR but may express HER2 and display a high Ki-67, a unique cancer cell division marker (Testa et al., 2020). Women with Luminal B tumors are often diagnosed at a younger age and have poorer outcomes than women with Luminal A tumors. In addition, 5%–15% of Breast cancer tumors are HER2-E (enriched) breast tumors, which are defined as ER-negative, PR negative, and HER2 positive. The HER2-E breast tumors are more amenable to HER2 receptor-targeted therapy like Herceptin (Vidal et al., 2017). The more common form of breast cancer among young Black women is the basal-like breast tumors that lack expression of ER, PR, and HER2 and are also referred to as *triple-negative breast cancer*, or *TNBC* (Doepker et al., 2018; Gonçalves et al., 2018; Vidal et al., 2017). TNBC disproportionately affects young Black women.

TNBC Among Black Women

TNBC is a subtype of breast cancer characterized by the absence of the three most targeted biomarkers considered for breast cancer treatment and derives its name from the lack of these three biomarkers (Dietze et al., 2015; Gonçalves et al., 2018). These are *estrogen receptor* (ER), *progesterone receptor* (PR), and *human epidermal growth factor receptor* (HER2). According to the CDC (2020), TNBC tends to be more common in women younger than age 50 years; the majority are Black and have a BRCA1 mutation (Doepker et al., 2018; Vidal et al., 2017). TNBC has also been found to affect young

Black women (Doepker et al., 2017). The occurrence may explain the differential factors associated with mortality outcome among these subpopulations.

Moreover, studies have also shown higher rates of local recurrence and invasion, visceral metastasis, and poorer prognosis that disproportionately affects young Black women (Prasad et al., 2016; Qiu et al., 2016; Vidal et al., 2017). Vidal et al. (2017) found that Black women with TNBC had the highest death rate at 26.7% than non-Hispanic White women, 16.5%. Additionally, Black women with TNBC and Luminal B/HER2- breast tumors had the highest mortality risk. However, mostly unknown from the literature is how racial/ethnic disparities in survival outcomes among young women with breast cancer are attributed to interrelations in breast tumor biological subtype and sociodemographic factors.

Studies comparing breast cancer among Black, White, and Hispanic women, have shown that Black women were more likely to have tumor progression with worse pathological characteristics (DeSantis et al., 2016; Doepker et al., 2018; Prakash et al., 2020; Vallega et al., 2016; Vidal et al., 2017). The inherent race-specific mortality rate disparities may be attributed to race-specific tumor biological differences, with increased prevalence of TNBC biological subtype (Doepker et a., 2018; Vidal et al., 2016). Thus, detailed scientific research needs to identify prognostic factors and potential therapeutic targets for TNBC biological subtype. Understanding the impact of tumor biology in breast cancer survival outcomes remains an active area of research.

Epidemiology of Breast Cancer Among Black Women

Black women have a 42% higher breast cancer mortality rate than White women, the highest of any U.S. racial or ethnic group (CDC, 2020; Vallega et al., 2016). Among women younger than 45, breast cancer incidence is higher among Black women than among White women (CDC, 2020; Vidal et al., 2017). Evidence from the literature shows that both biological and nonbiological factors contribute to the disparity in breast cancer survival outcomes (Danforth, 2013; DeSantis et al., 2016; Doepker et al., 2018; Prakash et al., 2020; Vallega et al., 2016). These factors may contribute to the excess burden of disease among young Black women.

Young Black women suffer a higher burden of basal-like breast cancers, which are aggressive and lack targeted therapy options (Ademuyiwa et al., 2017; DeSantis et al., 2016; Vidal et al., 2017). Basal-like breast cancers are generally TNBC subtype receptor forms which are highly proliferative with low overall and disease-free survival rates. Black women have a 78% 5-year breast cancer survival rate than White women with a 90% (Allicock et al., 2013; Vidal et al.,2017). Hence, showing a disproportionate burden of cancer disease across race with specific differences in tumor characteristics.

Moreover, Black women are less likely to be diagnosed with breast cancer at an early stage (Allicock et al., 2013; DeSantis et al., 2016; Prakash et al., 2020). The root cause of this trend is complex with underlying barriers in access to care (DeSantis et al., 2016). The literature also suggests factors like income inequality, lack of quality employment, cultural incongruence, health illiteracy, educational attainment gaps, inadequate housing, poor neighborhood factors, and barriers to high-quality cancer

prevention, early detection, and high impact therapeutic interventions may contribute to late diagnosis of disease and hence disparities in survival outcome.

The literature shows that associations in some of these nonbiological factors (i.e., cultural incongruence, health illiteracy, socioeconomic disadvantages) contribute to the disparity in health outcomes (Doepker et al., 2018, Prakash et al., 2020; Vidal et al., 2017). For example, predetermined pathways of associations between two or more sociodemographic factors namely- income level (socioeconomic status), education level (health literacy), neighborhood barriers (metro vs non-metro access to care), insurance status, comorbidities and breast cancer disease may contribute to excess disease burden in subpopulations.

Socioeconomic Status and Inadequate Access to Breast Cancer Care

Despite improvements in early detections and therapeutic interventions for breast cancer, Black women experience disproportionate mortality rates and lag in early screening participation rates (Walsh et al., 2019). Prior research has primarily focused on the broad core determinants of socioeconomic gaps, cultural, and ecological aspects that influence health outcomes (DeSantis et al., 2016; Kuzhan & Adli, 2015; Shariff-Marco et al., 2017). However, less is known about interactions of these sociodemographic variables with biological factors in influencing health outcomes, especially among vulnerable populations. Differences in health outcomes is an important area of public health research that aims to address health disparities and improve survival outcomes.

Psychobiological Stressors Based on Neighborhood Factors

Smoking and Diet

There is emerging evidence to suggest that psychosocial stress and toxicants may interact to modify health risks (Li et al., 2020; McEwen & Tucker, 2011; Merlo, 2011). Social disadvantages increase the risk of disease especially among vulnerable subpopulations (DeSantis et al., 2016). Black women exposed to environments infested with high crime rate and unfavorable physical conditions to live, play and grow in, may influence health outcomes (Smith & Erdogan-Madak, 2018). Physical environments present nested hierarchies of exposure to nonbiological factors that may influence disease patterns in subpopulations.

Smith and Erdogan-Madak (2018) further suggested that the increased exposure to tobacco smoke (both active and passive exposure), poor dietary choices (e.g., processed meats, lack of access to fruits and vegetables), excessive alcohol and recreational drugs consumption, as well as environmental carcinogens (e.g., in water sources) have also been associated with increased risk of cancer. The authors conducted a cross-sectional, cohort, and prospective studies, qualitative in nature that examined relationships neighborhood factors, socioeconomic status, residential segregation (racial discrimination), spatial access to mammography, and residential exposure to carcinogenic pollutants. And their analysis showed that Black women living in low socioeconomic status neighborhoods experienced greater odds of late-stage diagnosis and mortality. Moreover, the cumulative exposure to the stressors may influence our physiobiology. Smith and Erdogan-Madak provided a qualitative synthesis of the neighborhood factors

which the authors examined in-depth for meaningful associations that contribute to the excessive burden of disease mortality.

Additionally, stress–toxicant interactions could be meaningful in risk exposure that may influence tumors' biological characteristics. However, it is poorly understood as to whether the disproportionate distribution of psychosocial stressors has a role to play in the disproportionate distribution of TNBC in young Black women.

Research has shown that individual exposures to excessive stress measured by multiple periods of poverty are associated with a decline in physical and mental functioning (McEwen & Tucker, 2011). However, research on the influences of psychosocial stressors on tumor biology is poorly understood (Feller et al., 2019). Ademuyiwa et al. (2017) evaluated racial differences in the molecular pathology of TNBC. Their study involved evaluating the somatic mutations that revealed racial differences in the high prevalence of TNBC. The study demonstrated that modifiable factors exist that contribute to the racial disparity in TNBC. Public health interventions should aim to address these psychosocial and sociodemographic variables that influence the tumor microenvironment that cause carcinogenic somatic mutations. Stress-induced mutations from the psychobiological pathways may persist for generations and lead to prevalence of intergenerational diseases in some subpopulations (Ademuyiwa et al., 2017).

The Ademuyiwa et al., study establishes a theoretical foundation for my research that inherent race-specific biological differences exist and that modifying the biophysiological environment can lead to cancer risk modifications. The study also

emphasizes the influence of genomics in breast cancer disparities. Therefore, to improve patients' survival time and outcome, there is a need to identify the influencing factors of clinical prognosis in breast cancer patients and their interactions. The nonbiological factors like physical environment, socioeconomic disadvantages may act directly to increase or decrease the consequences of the biological subtype. Hence, indirectly causing survival outcome disparities through associations between the breast cancer biological subtype, sociodemographic factors (nonbiological) and survival outcome.

Biological Subtypes of Breast Cancer and Sociodemographic Profiles

Breast cancer occurs at a lower frequency among Black women but is associated with poorer overall and breast cancer-specific survival rates (Ademuyiwa et al., 2017; CDC, 2020; DeSantis et al., 2016; Prasad et al., 2016; Yedjou et al., 2019). Bollinger's (2018) research highlighted the burdens of young women with female breast cancer disease. Bollinger used a qualitative study to show the unique biopsychosocial challenges of young Black women, including screening practices, access to mammography, and risk education- like encouraging breastfeeding, which has been associated with reduced breast cancer prevention and prevention services (Anstey et al., 2017). However, more pertinent to improving survival outcomes in vulnerable subgroups, the research does not address the fundamental aspects of whether improving these core components would be an excellent overall intervention approach without considering the biological subtype characteristics.

Partridge et al. (2016) further explored the increased risk of developing more aggressive subtypes of breast cancer among young women. The retrospective cohort

study involved examining outcomes breast cancer among various tumor subtypes by using the data from the National Comprehensive Cancer Network (NCCN) centers between 2000–2007. Multivariable Cox proportional hazards models were used to assess the relationships between the breast cancer subtype and breast cancer specific survival outcome while controlling for age. The study found a significantly increased risk of breast cancer death among the < 40 years group especially those with luminal A (Hazard Ratio = 2.1; 95% CI [1.4, 3.2]). The study provides empirical evidence to the effect of breast cancer subtype and age in being prognostic indicators of survival outcome. However, the study does not examine the differing risk factors and associations of biological and nonbiological factors in early disease recurrence and poor survival in the breast cancer subgroups.

Additionally, Vidal et al. (2017) conducted a retrospective study to investigate the extent to which racial/ethnic disparities in survival outcomes among Memphis women attributed to differences in breast tumor subtype and treatment outcomes. 3527 patients diagnosed with Stage I–IV breast cancer between January 2002 and April 2015 at Methodist Health hospitals and West Cancer Center in Memphis, TN, were included in a Kaplan Meier survival analysis model. Black women displayed increased mortality risk (adjusted hazard ratio HR = 1.65; 95% confidence interval CI [1.35, 2.03]) and were more likely to be diagnosed at advanced stages of the disease. The findings provide additional evidence that female breast cancer disparity gaps between Black and White women highlight the need for targeted interventions and public health policies to eliminate breast cancer disparities in Black populations. However, the research does not

largely address the influence of the interaction between biological factors and sociodemographic variables like age, ethnicity, socioeconomic status- [level of education and income, marital status, and family size- multiparity would contribute to the differences in survival outcomes].

Socioeconomic disparities pause significant risk factors for survival outcomes in breast cancer disease. Racial/ethnic inequities exist for late-stage diagnosis that disproportionately affects Black and Hispanic women with breast cancer (Krieger et al., 2020). Literature has shown that social injustice, socio-cultural differences, and poverty disproportionately affect Blacks (Krieger et al., 2020; Yedjou et al., 2019). The prevalent structural inequities, including racism, disproportionately affect Black racial/ethnic subgroups and contribute to disparities in health outcomes.

Role of Biological Profiling in Breast Cancer Screening Programs

Despite improved mammography screening in the United States, the incidence of late cancer diagnosis has not improved (CDC, 2020). Heller et al., 2019 conducted a quantitative study using the SEER database to compare Stage IV breast cancer's tumor biology with the commonly diagnosed tumor during routine mammography. Multivariable regression was used to assess the association between Stage IV breast cancer disease (late-stage disease according to the American Joint Committee on Cancer [AJCC] classification) and tumor biology controlling for the sociodemographic variables of race/ethnicity, education, and total household income level (Heller et al., 2019). The study found that Stage IV disease at presentation was more common among young Black women who were uninsured and with a low income/education and large and had

biologically aggressive tumors. The findings suggest the need to address deficiencies in screening programs that can capture the tumor's biological characteristics early, especially among vulnerable populations with increased risk presenting with aggressive forms of breast cancer like TNBC.

Similarly, Krieger et al. (2020) argued that although cancers have various etiological factors, neighborhood factors like the inability to access breast cancer screening services among racial/ethnic minority groups facing socioeconomic disadvantages may bias biological risk profiling. Studies are largely deficient in racial diversity due to less participation of Black women in cancer research (Vidal et., 2017). Some of the findings may lack the epidemiological hallmarks of generalizability.

The association between the biological subtypes of breast cancer and the sociodemographic factors (prognostic determinant of breast cancer) provide context of this study in examining disparities in survival outcome. Public health programs like breast cancer screening are intended to reduce health inequities. However, inadequate screening programs that do not address the associations between biological risk factors and sociodemographic determinants of the disease have reduced implications on population health (Zavala et al., 2021). Hence in public health prevention, developing breast cancer screening tools targeting vulnerable populations that are cognizant of the breast cancer risk based on biological and sociodemographic profiles are critical to addressing health inequities.

Disparities in Educational Attainment and Health Literacy Gaps

With a 36% college participation rate for Blacks, educational attainment gaps persist and contribute to the growing socioeconomic gap (National Center for Education Statistics, 2019). Blacks and Latinos are more likely to attend high-poverty schools than White counterparts and experience higher drop-out rates (Walker, Strom Williams, & Egede, 2016) presenting health literacy challenges.

Moreover, inadequate sensitization of Blacks on the cancer burden remains a challenge in some communities where mistrust and cultural differences are barriers to engagement in community health programs (Aleshire et al., 2021). Black women participate less in these programs. Musonda (2018) argued that the educational level and neighborhood barriers (racial discrimination) affect the levels of community engagement that might be beyond the perceived narratives of mistrust from these communities. Community engagement platforms are the cornerstone of successful public health interventions. By improving access to care through improved health literacy, communities benefit from appropriate public health programs that address cultural gaps and trust levels in communities.

Community engagement continuum that would address the fundamental aspects of the risk burden associated with the more aggressive forms of cancer in this subgroup. Public health efforts geared towards improving social factors and policies that influence breastfeeding rates at the individual and population levels. Such measures should give special consideration to Black mothers' needs, hence addressing disparities in breastfeeding among this group and possibly helping reduce breast cancer risk.

Community engagement processes are designed to promote self-empowerment that improves the quality of life and health outcomes (O'Mara-Eves et al., 2015). Sociodemographic factors studied that contribute to the poor outcomes experienced include limited access to care due to lack of health insurance, cultural challenges, and the higher limitations of access to primary care resources. The study provided a foundation to explore these sociodemographic predictors that influence survival outcomes.

Most research studies have been limited by the research approach, which was qualitative in nature and did not quantify the factors contributing to the high burden of care (Bollinger, 2018; Turkman et al., 2016). Additionally, literature has shown that multiparity and low breastfeeding levels were associated with the increased occurrence of TNBC among young premenopausal Black women. Hence inherent modifiable factors are important to explore, especially to understand attitude and behavioral practices that affect disease risks.

Biological Factors and Increased Breast Cancer Risk Burden

Obesity Burden and Breast Cancer Risk Among Black Women

The increasing obesity prevalence among Black women could be contributing to the rising incidence of breast cancer. Obesity and weight gain have also been directly correlated to increased breast cancer mortality (Fouad et al., 2018; Prakash et al., 2020; Vallega et al., 2016). Differences in obesity rates could also contribute to health disparities since Black women have higher levels of obesity (5 in 10) than White women (3 in 10) in the United States. The distinct epidemiological pattern of high obesity burden

among Blacks may have a role to play in the disproportionate number of aggressive subtypes of breast cancer.

Studies have shown that Black women with breast cancer express unique genes like resistin linked to inflammation and obesity (Vallega et al., 2016). Moreover, these resistin levels are higher in Blacks with TNBC (Fouad et al., 2018; Vallega et al., 2016). Additionally, studies have found higher methylation rates of tumor suppressor genes involved in malignant transformation among Blacks with breast cancers than other ethnic groups (Ademuyiwa et al., 2017; Vallega et al., 2016). Therefore, investigating differentially expressed genes between patient populations may explain racial health disparities and help in risk profiling. Prevention of obesity through lifestyle modification (healthy diet and increased physical activity) are essential in addressing disparities in health outcomes that are a result of the prevalent sociobiological disadvantages. These findings ultimately reinforce the need to investigate the role of biological differences and how they interact with the social and physical environment to cause disparities in health outcomes.

Hormonal Risk Factors in Breast Cancer Disparities

The breast cancer incidence rates under 45 years are higher among Black women than White women (Yedjou et al., 2019). However, the median age of breast cancer diagnosis is approximately 61 years, as most breast cancer screening campaigns target post-menopausal women (Surakasula, Nagarjunapu, & Raghavaiah, 2014). Age and prolonged hormonal exposure have been associated with breast cancer risks. Literature

shows that women who experience late natural menopause and those who begin menses at an early age experience a high risk of breast cancer.

Women who experience menopause after age 55 years have an increased risk of ovarian, breast, and uterine cancers (Oprean et al., 2020; Surakasula et al., 2014). The risk is even greater if a woman began menstruating before age 12. The long estrogen hormonal exposure is associated with an increased risk of breast cancer. Hence women who have been through natural menopause are more likely to develop cancer due to prolonged hormonal exposure.

Fouad et al. (2018) found that 44% of the women in their study reported natural menopause, with an average age of diagnosis being 61 years. However, the demographic profile significantly varies as most women were white. The median age of diagnosis for Black women is 58 years compared to White women, which is 62 years. Moreover, Black women tend to be diagnosed with late-stage disease (DeSantis et al., 2016; Yedjou et al., 2019). Implying that Black women tend to develop breast cancer disease at an early age but present with late disease at health facilities. The causes of the significant lag time are fear, lack of insurance, and lack of access to breast screening services (Fouad et al., 2019). Therefore, a breast cancer diagnosis for Black women below 50 years may be under-reported due to significant differences in access to health care. Understanding the challenges of this demographic is pertinent to early diagnosis of the biological subtypes like TNBC, which is prevalent in this age group.

Leveraging Genetics in Addressing the Disparity in Breast Cancer Survival Outcomes

Genetics plays an essential role in most cancers' clinical presentation and outcome (Smith et al., 2016). Black women are disproportionately affected by TNBC and have relatively poor survival outcomes than other ethnic races. The differences in the genetics of breast cancer incidence among Black women, as compared to White women, is well documented in the literature (Yedjou et al., 2019). Breast cancer risk increases with a first-degree relative who had breast cancer at a younger age.

Familial breast cancers are associated with mutations in the tumor suppressor genes BRCA1 and BRCA2 (Yedjou et al., 2019). Pal et al. (2015) conducted a quantitative study to evaluate BRCA pathogenic variants' frequency in a population-based sample of young Black women with breast cancer. The Pal et al. study utilized the Florida Cancer Registry for Black women less than 50 years diagnosed with invasive breast cancer. The study found eight recurrent mutations in the BRCA1, and two genes accounted for 49% of all mutations detected. The prevalence of mutations was about 43% in those less than 45 years, with 30% of these women having TNBC. BRCA1 and BRCA2 mutations increase the risk of breast cancer development.

BRCA carriers with mutations had a higher frequency of TNBC disease, and the disease occurred at < 45 years of age. Other studies also showed a higher prevalence of the TNBC disease among Blacks with BRCA1 and 2 mutations (Francies et al., 2015; Fulk et al., 2019; Shimelis et al., 2018). Therefore, expanded multipanel gene testing for patients with TNBC disease can help guide management by identifying other vulnerable

patients who may benefit from additional increased breast cancer surveillance. The approach will improve survival outcomes through early identification and treatment of at-risk family members.

Studies have also shown disparities in genetic testing. For example, Blacks and Hispanics are five times less likely to receive BRCA screening tests than white women (Dean et al., 2015). Thus, re-enforcing the need for wide-spread access to gene testing among the underserved populations disproportionately affected the breast cancer burden, especially among Blacks with TNBC. Hence enhancing access to genetic technologies among vulnerable populations may help address disparities in health outcomes associated with breast cancer disease.

Theoretical and Conceptual Framework

The basis for this study and the associated literature review is founded in ecosocial theoretical framework for understanding how the biological expressions of social inequality occur in our bodies and influence disease outcomes. Our bodies biologically express our experiences of socioeconomic inequalities, neighborhood disadvantages, cultural barriers, comorbidity, obesity, racial discrimination and lack of access to timely care have been discussed in the literature as increasing the likelihood of disparities in health outcomes across a broad spectrum of disease. The *Ecosocial theory* was well suited for grounding the study's theoretical framework. The historical development of the theory and conceptual framework were explained.

Ecosocial Theory

The *ecosocial theory* is an emerging multilevel theory of disease distribution and disparities in different populations' outcomes (Krieger, 2001). Krieger first proposed the theory in 1994 to explain population distributions of health and is used in social epidemiology to understand the myriad of interrelated social and biological processes that influence population health.

The theory emphasizes the shifting patterns of disease distribution in the population. It examines the cumulative effects of proximate ecological factors like neighborhood factors and socioeconomic disadvantages in shaping diseases' biological profiles. Krieger (2013) argues that thinking about biology in a societal, ecological, and historical context helps to frame the causes of disease and outcome disparities.

Krieger emphasized that understanding disease characteristics involved conceptualizing disease biomarkers in relation to the changing magnitudes of health inequities in the population. Our biological expressions are an embodiment of the socioeconomic disadvantages that our bodies experience (Krieger, 2001, 2012, 2013; Krieger et al., 2020). Biological expressions are central to the concept of "ecological evolutionary developmental biology," in which the genome is determined at an individual's conception (intrauterine). However, the argument is that the same genome at conception can generate different phenotypes, which is dependent on the environment that the individual grows in, akin to bodies expressing ecology.

The developmental plasticity that sees the prevalent phenotypic variations in adults with identical genotypes is seen among identical twins. Through developmental

trajectories, identical twins experience phenotypic variations dependent on the socioeconomic environment they grow in (Krieger, 2001). Similarly, breast cancer subtypes exhibit biological characteristics that influence survival outcomes. These biological characteristics are of clinical and public health importance as relevant prognostic determinants. For example, ER positive tumors are more amenable to hormonal therapy than ER-negative breast cancer tumors (DeSantis et al., 2016).

Krieger (2001) further draws on the *ecosocial theory* to focus on how societal disadvantages influence biology. The author builds on the constructs of evolution, pathology, society, and life course as integral to tumor biology development. Thus, presenting a scholarly argument that breast cancer incidence and mortality are closely linked to tumor biology. Variations in health outcomes at individual and population level may be attributed to interactions between tumor biology and sociodemographic factors.

According to Krieger (2001), the theory seeks to integrate social and biologic reasoning, along with a dynamic, historical, and ecological perspective, to address population distributions of disease and social inequalities in health. The central question in a study on disparities in health outcomes is "who and what is responsible for population patterns of health, disease, and well-being, as manifested in the present, past and changing social inequalities in health (Krieger, 2012). Poor health outcomes in societies are mirrored in socioeconomic deprivation among minority ethnic/racial subpopulations in the United States of America (Hossain et al., 2019; Merlo, 2011). The findings are consistent with the theory that no aspect of our biology can be understood in the absence of knowledge on our life history and individual and societal ways of living.

Application of the Ecosocial Theory Through a Modified Conceptual Model

The ecosocial theory conceptual approach to the study that maps out potential covariates that would act as confounders, mediators, and effect modifiers of the relationship between breast cancer biological subtypes and survival outcomes utilized in Figure 1 is further considered under the methodology section.

The modified conceptual model based on the ecosocial theory and explains the relationship between biology and sociodemographic factors in influencing health outcomes among breast cancer patients adopted from the Agénor, Krieger, Austin, Haneuse, & Gottlieb (2014) model. The sociodemographic factors (educational attainment, income level, employment status, insurance status, comorbidities, neighborhood factors) are considered potential confounders of the relationship between the biological subtype and survival outcome among patients with TNBC. The risk factors associated with breast cancer development were considered as potential mediators. According to literature, these include a strong family history of breast or ovarian cancer and related to genetic mutations (Yedjou et al., 2019), History of prolonged hormonal exposure- use of hormonal replacement therapy, early menarche, early menopause, late childbearing age above 35 years, not breastfeeding, History of mammary gland disease and the number of children (Brusselaers et al., 2018; Kamińska et al., 2015). And race as an effect modifier of the relationship between biological subtypes and survival outcome.

Social Production of Disease and Geopolitical Economy

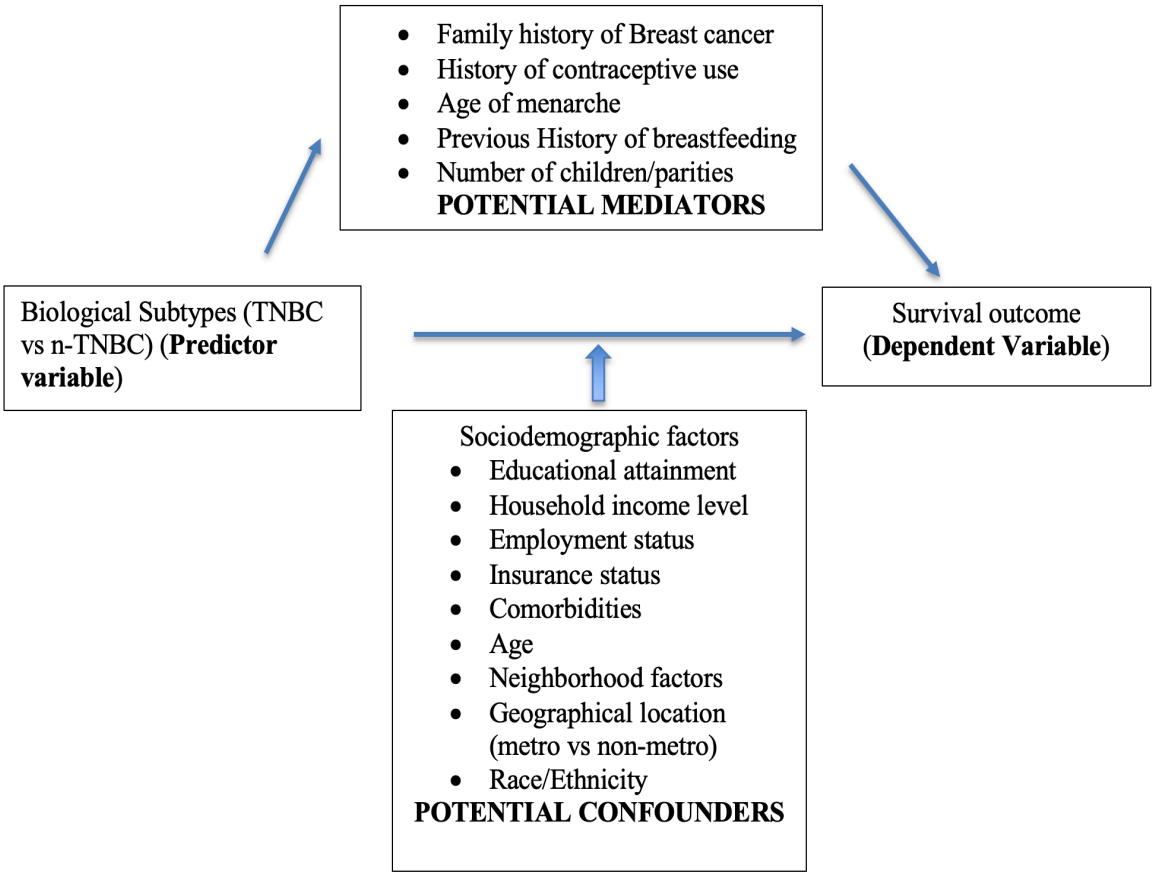
The socioeconomic and government policies are determinants of health and disease that influence subpopulations. The prevalent income inequality that affects

minority subpopulations has negative consequences on affordability and access to medical care. Researchers have linked income inequality to health (Doepker et al., 2018; Fouad et al., 2018; Krieger, 2020; Williams et al., 2010). To effectively address racial disparities in health requires an understanding of the contributing factors that importantly affect the racial patterning of disease distribution. The link between income inequality and geopolitics is evident by the low levels of economic investments in minority neighborhoods (Yonto, & Thill, 2020). These structural causes of inequalities as a result of systematic under investment across these communities impacts public infrastructure like hospitals, schools and transportation. Thus, generating clusters of poor health with increased chronic disease risk burden. The conceptual model examined these sociodemographic factors and their association with mortality risk among the breast cancer biological subtypes.

The approach lays a foundation for the study. I hypothesized that social demographic factors may confound survival outcomes among Black women with TNBC breast cancer. Figure 1 below introduces the conceptual model with main relationship between biological subtypes and survival outcome. And the sociodemographic factors as confounders of the association between biological subtype of breast cancer and survival outcome. The potential mediators though not measured will provide a basis for further research in understanding the modifiable factors that may contribute to the disproportionate mortality rate in subpopulations.

Figure 1

Modified Ecosocial Theory Conceptual Framework



Summary

The disparity in mortality outcome for breast cancer is a significant public health objective. The study aims to highlight risk factors that contribute to the excess burden of mortality among vulnerable subpopulations. The high mortality rate among young Black women with TNBC is of public health importance. The literature is consistent about the role of sociodemographic factors in influencing survival rate among breast cancer patients. However, little is not known about the associations that contribute to the disproportionate burden of mortality among young Black women with TNBC disease.

Research is sparse on the associations between the TNBC biological subtype and the sociodemographic factors on influencing survival rate among young Black women. Through the ecosocial theory the study is used to explain the known relationships. The study proposed to fill the gap by further understanding the role of the association between sociodemographic factors and the TNBC biological subtype of breast cancer in contributing to the disparity in survival times by race. In Chapter 3, I reintroduce the research questions and hypotheses for the study. And I further describe the methods and variables selected to answer the research questions and the statistical aims that were used to test the hypotheses.

Chapter 3: Research Method

The purpose of this study was to examine the associations between biological subtypes of breast cancer (TNBC and non-TNBC) and patient level sociodemographic factors and how they influence survival outcomes in specific subpopulations. Measuring these associations will help to predict the likelihood of adverse outcome. Sociodemographic and biological factors (tumor subtype) are known prognostic indicators of breast cancer (Fouad et al., 2019; Vidal et al., 2017; Zavala et al., 2021). However, little is known about their associations in influencing survival outcomes among breast cancer patients of specific subpopulations. Differences in these associations could explain the growing disparities in mortality outcome among young Black women compared to other racial/ethnic groups in the United States.

Disparity in breast cancer survival outcomes among Black women represent a significant and urgent public health concern in the United States, and the trend remains a focus for public health research. This chapter describes the methods used in this study. A quantitative, retrospective longitudinal study of using secondary data from the *SEER 18 Registry and Research Plus Database*. SEER databases are supported by the Surveillance Research Program (SRP) in the NCI, a Division of Cancer Control and Population Sciences (DCCPS). The datasets provide the most diverse sociodemographic and biological characteristics that can capture the differences that contribute to disparities in survival outcomes (CDC, 2020). The SEER database is the most appropriate data source with extensive cancer surveillance statistics in the United States (NCI, 2020).

In this chapter, I discuss the study design used to answer the research questions, followed by the target population and sampling procedures. Survey procedures and informed consent undertaken by SEER to collect the data are covered in detail. The measures selected for the dependent, independent variables and the covariates are described in depth. Furthermore, the statistical analysis to be applied for each research question and associated hypotheses described in Chapter 1 are presented in this chapter.

Research Design

The approach in this study was quantitative in nature with a retrospective cohort design, which were used to study whether the associations between sociodemographic factors and the biological subtype are predictive of breast cancer survival outcomes and whether there are differences in survival rates between young Black and White women with TNBC subtype. I also investigated the effect of several sociodemographic variables upon the survival rate among those with TNBC and the ones with other subtypes of breast cancer collectively referred to as non-TNBC (n-TNBC) in specific subpopulations. The population, sampling procedure, ethics, study questions, data collection methods, the operationalization of variables, and data analysis are outlined in the following sections.

Methodology

Study Population

The population for this study included young Black and White women (female) diagnosed with TNBC and non-TNBC (for the other biological subtypes -Hormone Receptor (HR) +ve/HER2 +ve, HR +ve/HER -ve, HR -ve/ HER2 enriched). Ages 25–44 years of age. Using the *SEER 18 registry* and the Census Tract-Level Socioeconomic

Status and Rurality *Research Plus* database, the inclusion criterion was applied, and breast cancer cases diagnosed from 2013 to 2018 were extracted. Study exclusion criteria included cases from the registry that were less than 25 years or greater than 44 years of age. Survival times were compared by race and breast cancer biological subtype. Sociodemographic variables of neighborhood geographical location (metro vs. non-metro), race, age and median household income levels were used.

Sampling Methods and Statistical Power

Records were extracted from the *SEER 18 Registry and Research Plus database* based on the defined criteria. The inclusion criteria were race (White and Black), age (25–44), and year of initial diagnosis (2013–2018). The biological subtypes were included by confirmed diagnosis. Other variables considered from the data were geographical location-a proxy for neighborhood factors, and median household income level. The sample was restricted to age 25–44, and I used stratified random sampling for the attribute of race and breast cancer biological subtype to ensure proportional representation.

The statistical power of the study was a function of the population effect size at which there was likelihood of rejecting the null hypothesis to achieve statistical significance with an assumed alpha level (α) of .05. The sample size was calculated using Freedman and Schoenfeld approaches. Sample size required n = Total number of events/Probability of an event. The probability of experiencing the event of death (denominator) was expressed as *1-p* and the value was estimated by number ratios between the number of participants of each group and survival functions from previous

studies (Bollinger, 2018; Gonçalves et al., 2018; Watkins et al., 2017; Zavala et al., 2021).

Using Freedman and Schoenfeld approach, with the assumption that a randomly selected individual experiences an event during the observation time which depends on the accrual time and duration of follow up (Abel et al., 2015; Kohn & Senyak, 2021; Schoenfeld, 1988), the sample size was calculated. The sample size prediction was adequate with a statistical power of 80% and significance level alpha (α) 0.05 that resulted in the 3283-requisite sample.

Data Access

To access the SEER database, an online request for the data from the NCI was completed after approval from the Walden University Institutional Review Board (IRB)-IRB approval number 05-17-21-086425. A SEER Research data use agreement was completed under SEER ID 20184-Nov 2019. The purpose of the data was for my capstone study and the data were not used beyond its primary purpose. As a scholar at Walden University, I had the privileges to access the SEER *Research Plus* database**.**

Ethical Considerations

I requested and was granted approval from the Walden University IRB. I further received approval from the National Council Institute Surveillance Epidemiology and End Results program to conduct the study upon execution of the data use agreement.

There was no direct contact with human subjects for this research study. Data obtained were deidentified to protect patient identities that would present more than the minimum risk if the data were compromised. In this study, I adhered to the Health

Insurance Portability and Accountability Act (HIPAA) Privacy Rule that establishes national standards to protect individuals' medical records and other personal health information as applies to health plans, health care clearinghouses, and those health care providers that conduct certain health care transactions electronically.

Some of the actions undertaken to safeguard patient data included: (a) encryption of the hard drive, (b) storing extracted data on my laptop and generating a password to ensure an extra layer of security, (c) retaining the encrypted data extracted for 6 years as per Code of Federal Regulations involved in the conduct of research- 45 CFR 164.528., and (d) destroying the data at the expiration of 6 years, using approved overwriting software that erases the computer hard drive.

Further I adhered to the agreement terms of use as described in the Data Access Request for SEER data (attached in the appendix). I followed all necessary safeguards not to share passwords/keys involved in access of the database.

Research Questions and Hypothesis

The central research question was: Do associations between TNBC breast cancer biological subtype and sociodemographic factors like median household income level, race, and neighborhood-geographic factors contribute to the increased mortality rate (decreased survival rate) among young Black women? The research questions and hypotheses below will guide the study.

Research Question 1: Do young Black women with TNBC biological type have poor survival rate compared to other young Black women with the non-TNBC

biological subtypes (Hormone Receptor (HR) +ve/HER2 +ve, HR +ve/HER -ve, HR -ve/ HER2 enriched) of breast cancer?

$H_0$1: There is no difference in survival rate based on the biological subtype of breast cancer (TNBC vs non-TNBC) among young Black women diagnosed with breast cancer

H_a1: There is a difference in survival rate based on the biological subtype (TNBC vs non-TNBC) of breast cancer among young Black women diagnosed with breast cancer

Research Question 2: Is there a difference in survival rate among young Black women with TNBC subtype and non-TNBC subtypes (Hormone Receptor (HR) +ve/HER2 +ve, HR +ve/HER -ve, HR -ve/ HER2 enriched) when adjusted for sociodemographic factors?

$H_0$2: There is no difference in survival rate among young Black women with TNBC subtype and non-TNBC biological subtypes when adjusted for sociodemographic factors

H_a2: There is a difference in survival rate among young Black women with TNBC subtype and non-TNBC biological subtypes when adjusted for sociodemographic factors

Research Question 3: Is there a difference in survival rate between young Black women and young White women with the same biological subtype-TNBC after controlling for sociodemographic factors?

H_03: There is no difference in survival rates between young Black women and young White women with the same biological subtype-TNBC after controlling for sociodemographic factors

H_a3: There is difference in survival times between young Black women and young White women with the same biological subtype-TNBC after controlling for sociodemographic factors

Statistical Approach

Kaplan Meier survival analysis and log rank test were used to estimate the probability of surviving. By using the Kaplan Meier's method, I made assumptions that

- at any time, breast cancer patients who were to be censored would have the same survival prospects as those who continued to be followed;
- the survival probabilities were the same for subjects included early and late in the research study; and
- the event of death happened at the time specified.

Cox proportional hazards model was used to investigate the associations between the breast cancer biological subtype and survival time of breast cancer among young Black women with breast cancer controlling for sociodemographic factors. This model gives an expression for the hazard (death) at a time (t) for an individual given specification of a set of explanatory variables like the biological subtype. The model assumptions Cox proportional hazards analysis were assessed:

- Each covariate had a multiplicative effect in the hazards function that was constant over time. The approach helped to show statistical significance of the

relationship between biological subtype and survival times among young Black women with breast cancer disease after adjusting for the covariates.

- The individuals in the study and the events were independent of each other.
- Censoring was non-informative.
- Ln(h)(t) was linear function of the outcome variable.
- Proportional hazards-relative differences between groups were constant overtime and the survival curves did not cross and were assessed using the clog-log plot.
- The baseline hazard was unspecified in the equation.

Data Collection

Secondary data were used for the analysis. I analyzed data using SPSS (Version 27) with Walden University IBM software license. The data of the study were from *SEER 18 Registry and Research Plus* database.

SEER 18 Registry and SEER Research Plus Database

SEER 18 Registry. The SEER 18 registry comprises all cancer cases diagnosed from 2000 through the current data year (2019) and includes expanded races (NCI, 2020). The data is collected from population-based cancer registries in the United States that participate in the NCI's SEER program contains patient demographics that identify the cancer patient. These include the patient's name (de-identified in raw data), age, gender, race, ethnicity, and birthplace. Tumor (cancer) characteristics include the biological and clinical aspects of cancer and genomic information. The stage of the disease, treatment information, and outcome, including survival times, are captured in the dataset.

The SEER research program, led by the NCI, has collected cancer incidence and survival data from a collection of U.S. cancer registries since 1973. The original SEER program involved nine cancer registries and has since expanded to 18 registries throughout the United States (NCI, 2020). The SEER expansions were done to diversify the study population and increase heterogeneity by race/ethnicity, thus improving the SEER database's external validity. The SEER program covers approximately 28% of the total U.S. population, and the registries participating in SEER are selected to ensure that included cancer cases are representative of the general U.S. population in terms of education and poverty level and that minority races and ethnicities are adequately represented.

However, SEER tends to have slightly higher proportions of urban and foreign-born persons than the total U.S. population (NCI, 2020). Additionally, because the SEER program is a collection of cancer registries, all incident cancer cases diagnosed in participating areas are reported to SEER by local hospitals, clinicians, and pathology laboratories. SEER database may have selection bias. To control for the selection bias, SEER requires that each registry report all cases within 2 years of diagnosis, after which cases are followed for demographic, clinical, and mortality data. The process results in a complete population of all cancer cases within participating geographical areas that together are representative of the general U.S. population. In total, the SEER program captures incidence and survival data for over 7.7 million cancer cases throughout an almost 40-year study period, making the SEER program the largest and most

comprehensive population-based cancer epidemiologic data source in the country (NCI, 2020).

Under the *SEER 18 Registry*, areas covered include the Alaska Native Tumor Registry, Connecticut, Detroit, Georgia Center for Cancer statistics, Greater Bay Areas Cancer Registry, Greater California, Hawaii, Iowa, Kentucky, Los Angeles, Louisiana, New Mexico, New Jersey, Seattle-Puget Sound, and Utah (NCI, 2020). The details of data collected from these areas is summarized in the Table 1 below.

Table 1

SEER 18 Registry Data Collected 2000–2019

	All cases	Malignant cases	Malignant + in situ cases
1975–2017 data (Nov 2019 Submission)	10,985,942	9,885,885	10,650,516
1975–2016 data (Nov 2018 Submission)	10,450,709	9,428,053	10,146,162
Increase from 2018 to 2019 submission	535,233	457,832	486,207
Number of 2017 cases for SEER 18	512,101	440,933	504,354

Note. Adapted from *Registry Groupings in SEER Data and Statistics,* by National Cancer Institute, 2020 (https://seer.cancer.gov/registries/terms.html). In the public domain.

SEER Research Plus Database. The database includes Census Tract-Level Socioeconomic Status and Rurality database is a specialized database of the NCI. The database consists of three variables:

- The Socioeconomic Status index is constructed using a factor analysis from seven variables that measure different aspects of the SES of a census tract

(NCI, 2020). These seven variables include Median household income, Median house value, Median rent, Percent below 150% of poverty line, Education Index as calculated from the Percent working class, and Percent unemployed (NCI, 2020). The indices are estimated from the data collected through the 2000 U.S. Decennial Census long form survey, and a series of American Community Survey (ACS) with 5-year estimates from 2006 to 2016. American Community Survey (ACS).

- Rural Urban Commuting Areas (RUCA) is census tract level rurality variable and is coded by urban area commuting and non-urban area commuting.
- Census based measure of the population living in the non-metro areas and metro areas.

The database is critical to understanding the impact of sociodemographic variables in driving disparities in Breast cancer mortality outcome.

Operationalization of the Variables

The following are the study variables that were operationalized in this study:

- Breast cancer survival rate will reflect the percentage of women who are alive at a given time interval. The dependent variable is continuous.
- Biological subtype: a categorical variable in which the biological subtypes will divided into TNBC subtype and non-TNBC (n-TNBC) subtype to represent the subtypes of Hormone Receptor (HR) +ve/HER2 +ve, HR +ve/HER -ve, HR -ve/ HER2 enriched.
- Race; a categorical variable with two levels Black and White

- Sociodemographic factors to be considered are median Household income level, and geographical location
- Median Household Income level: categorical variable with 2 levels was used; <$49,999 and > $50,000
- Geographical location, categorical variable with two levels Metro and non-metro

Data Cleaning and Screening Procedures

Data cleaning were conducted in SPSS (Version 27), and the data transformation for missing values were handled using multiple imputation procedures. The sample dataset obtained were weighted to adjust for race to account for limitations that may occur in the access to care among the Black subpopulation.

Data Analysis

Data were analyzed using SPSS (Version 27), which is licensed through Walden University. Descriptive statistics were summarized using frequency tables. To examine the relationships between breast cancer survival and predictors of interest biological subtype and sociodemographic factors, the following analyses were performed, Kaplan Meier survival analysis, log-rank tests and Cox proportional hazards.

Kaplan Meier's method estimated differences in survival curves of different subgroups- the TNBC and n-TNBC groups and by race for Blacks versus Whites. The Log-rank tests was used to test if there was statistical significance in the difference in survival functions. Cox proportional hazards model was used to determine the effect of

the different predictors (sociodemographic factors) on survival rate after controlling for the biological subtype of breast cancer.

The Wald and Chi square tests were used to determine if the effects of the predictor are significant in the model. Turkey-Kramer method were used to control for the family wise error rate when two predictor variables produced statistically survival curves. The assumptions of the Cox proportional hazards model were tested using the log-log plot to look for divergence, convergence or crossing of the curves.

Threats to Validity

The SEER data were collected though respondent surveys and may therefore have some information bias like self-reporting bias especially for variables like the level of income. To reduce the threat of self-reporting bias, data triangulation using two datasets (*Research Plus database and SEER 18 Registry*) to validate information were used. Additionally, medical surveillance bias may have occurred. Medical surveillance bias is a type of information bias that occurs when one group of subjects (White subpopulation) is followed up more closely than the others (Black subpopulation), for example, if they undergo a specific medical intervention (Szklo, & Nieto, 2019). Stratification of the data was used reduce these bias effects.

Further to control bias, measurement instruments were used like the *Standardized United States Census Questionnaire Survey of 2010* from which information could be compared for cross validity of the data collected by the hospital cancer registries. The questionnaires had a tested reliability and validity measures of Cronbach's alpha of 0.8

(Szklo, & Nieto, 2019). For the research study data triangulation was also used to increase the validity of the sociodemographic data.

Strengths and Limitations

The study investigated whether the association between breast cancer biological subtype and sociodemographic variables prevalent among young Black women contributed to the increased age-related race-specific mortality disparity trend for breast cancer in the United States. Our research was limited to premenopausal women aged 25–44 diagnosed with breast cancer between 2013 and 2017. The study characterized breast cancer epidemiology among young Black women by examining whether the mortality burden increased in TNBC biological subtypes when subpopulations were predisposed to unfavorable sociodemographic factors like socioeconomic disadvantages. Previous studies have highlighted the increased mortality rate among Black women with TNBC. However, this study is the first of its kind to examine age-related (25–44) race-specific mortality disparity trends among women diagnosed with TNBC biological subtype.

SEER 18 Registry and Research Plus database with extensive breast cancer epidemiology data by race was utilized. Additionally, the SEER program is the most extensive and comprehensive population-based cancer epidemiologic data source covering approximately 34.6% of the U.S. population (NCI, 2020). A proportional population representative sample was used to examine longitudinal trends of survival times among young women aged 25–44 years and the effects of sociodemographic factors on the relationship between tumor biology and survival times. The data spans from 2013-2018, a period sufficient to analyze the 5-year breast cancer survival trend.

Limitations to missing data on tumor characteristics, especially in the initial diagnosis of breast cancer among young Black women with limited access to hormonal receptor assays that are performed to inform clinicians of the type of receptors the breast cancer cells express. Multiple imputation methods were used to address issues of missing data for specific variables.

The production of disease is associated with socioeconomic and neighborhood determinants of health, perpetuated by preexisting structural barriers like lack of access to diagnostic tools for early detection of aggressive subtypes of breast cancer. Additionally, confounding factors like comorbidities in survival outcomes may not have been submitted to the registry and hence were not captured but these may have influenced the relationships under study.

Access to testing for hormonal receptor assays are vital in early diagnosis and treatment of breast cancer. The study would inform policy and health promotion intervention on factors that shape breast cancer health outcomes.

Other risk factors that may influence the relationship of sociodemographic factors and biological subtype in predicting survival outcomes among young Black women with specific biological subtypes of breast cancer may have been apparent. For example, the stage of breast cancer at diagnosis, type of treatment received, disease recurrence and comorbidities. These variables were not adjusted for in the Cox-proportional hazards model.

Summary

This chapter included an insight on the quantitative methods related to research design, population sample, sampling procedure, ethical considerations, research questions and hypotheses, data collection methods, the operationalization of variables, and the description of data analysis used to address the research objectives. To assess the role of tumor subtype on outcome disparities by race among young women with increased risk of breast cancer, I evaluated the effect of sociodemographic factors on breast cancer survival outcome using a longitudinal cohort study.

A quantitative retrospective longitudinal study design using secondary data from the *SEER 18 Registry and Research Plus databases*. The details of the study design were explained. Data were collected and recorded by a SEER Registrar who administered the survey and consent procedures to collect the data. The dependent variable and the independent variables of the study were drawn from the dataset. The differences between groups and the relationships between variables were modeled using Cox proportional hazards models. Kaplan Meier survival analysis methodology and log rank test were used to estimate survival differences between the two subpopulations (Whites and Blacks).

The main predictor variables considered were the biological subtypes of breast cancer, and sociodemographic factors used to test the study hypotheses and answer the three research questions posed for the study. The ethical considerations, assumptions, strengths, and limitations were also discussed. The results from this study were presented in Chapter 4.

Chapter 4: Results

The purpose of this study was to examine the associations between biological subtypes of breast cancer (TNBC and non-TNBC) and patient-level sociodemographic factors and how they influence survival outcomes in specific subpopulations. Understanding the role of these associations in shaping individual and population health outcomes is key to addressing the challenges of health disparities in mortality outcomes among young Black women with TNBC. The analysis was framed by the ecosocial theory conceptual model that provided multiple dimensions of the relationship between breast cancer biological subtypes and survival outcomes and the intersectionality of sociodemographic variables in influencing these health outcomes. In the study, I examined whether associations of sociodemographic factors may influence the excess mortality rate among young Black women (25–44) with TNBC. I hypothesized that sociodemographic variables confound the disproportionate poor survival outcomes among young Black women with TNBC.

Herein, I provide a survival analysis of young women with TNBC and non-TNBC breast cancer biological subtypes representative of the target U.S. population diagnosed between 2013–2018. Data for 34,007 cancer cases and deaths were extracted using SEER* Stat software (Version 8.3.9) from the SEER program Registry 18 database. The data accessed were nationally representative, and a stratified random sample of 3238 cases was obtained. The results of this analysis by the biological subtypes of breast cancer TNBC and non-TNBC among the study population will be used to address the following research questions:

Research Question 1: Do young Black women with TNBC biological subtype have poor survival outcome compared to other young Black women with the non-TNBC biological subtypes (Hormone Receptor (HR) +ve/HER2 +ve, HR +ve/HER -ve, HR -ve/ HER2 enriched) of breast cancer?

$H_0$1: There is no difference in survival outcome based on the biological subtype of breast cancer (TNBC vs. non-TNBC) among young Black women diagnosed with breast cancer.

H_a1: There is a difference in survival outcome based on the biological subtype (TNBC vs. non-TNBC) of breast cancer among young Black women diagnosed with breast cancer.

Research Question 2: Is there a difference in survival rate among young Black women with TNBC subtype and non-TNBC subtypes (Hormone Receptor (HR) +ve/HER2 +ve, HR +ve/HER -ve, HR -ve/ HER2 enriched) when adjusted for sociodemographic factors?

$H_0$2: There is no difference in survival rate among young Black women with TNBC subtype and non-TNBC biological subtypes when adjusted for sociodemographic factors.

H_a2: There is a difference in survival rate among young Black women with TNBC subtype and non-TNBC biological subtypes when adjusted for sociodemographic factors.

Research Question 3: Is there a difference in survival rate between young Black women and young White women with the same biological subtype-TNBC after adjusting for sociodemographic factors?

$H_0$3: There is no difference in survival rates between young Black women and young White women with the same biological subtype-TNBC after adjusting for sociodemographic factors.

H_a3: There is difference in survival times between young Black women and young White women with the same biological subtype-TNBC after adjusting for sociodemographic factors.

Data Collection

The SEER Program is under the NCI and supports cancer surveillance activities in the United States. All 50 states have laws requiring newly diagnosed cancers to be reported to a central registry. The SEER Program currently collects and publishes cancer incidence and survival data from population-based cancer registries covering approximately 34.6% of the U.S. population (CDC, 2020). In addition, surveillance epidemiologic data support research activities related to cancer. SEER Registry 18 database was used in the study.

The dataset was accessed on May 22, 2021, after approval from the Walden University IRB and NCI SEER data access committee. Data were extracted from the *SEER 18 registry Research Plus database* with patient data reported from 2013–2018. The study sample was obtained from SEER by selecting breast cancer cases diagnosed

between 2013 and 2018 among Black and White women ages 25–44 years. In total, 34,007 cases were obtained, with 5730 Black women and 28277 White women.

Stratified proportional random sampling was done to establish a representative sample of 3283 cases: 575 (17.5%) Black women and 2708 (82.5%) White women. One hundred ninety-seven (6%) of the cases had missing values for breast cancer subtype.

Analysis Results

Demographics

The sample obtained from the SEER Registry 18 was a nationally representative sample (N = 34,007), and a stratified random sample of 3238 cases were extracted. The sample consisted of 575 (17.5%) Black women and 2708 (82.5%) White women. The mean age for Black women was 38 (SD = 5), and White women had a mean age of 39 (SD = 5). Furthermore, the overall mean age was 38.82 (SD = *4.56*). Demographics of the study population are presented in Table 2.

Regarding breast cancer biological subtype distribution by race, 16.0% of the study population was diagnosed with TNBC biological subtype while 78.0% had non-TNBC (see Table 2).

At the end of my study, 86.8% of Black women were alive compared to 93.6% of White women. More Black women experienced the event of death than Whites, 13.2% versus 6.35% (see Table 2). Two thousand three hundred and eighty-eight (84.7%) of Whites earned more than $50,000 annually compared to 431 (15.3%) Black women. Of those who earned less than $49,999, 320 (69.0%) are White and 144 (31.0%) are Black.

Of the White women, 88.2% earned more than $50,000 annually, and 11.8% earned less than $49,999, whereas among the Blacks, 25% earned less than $49,999, and 75% earned more than $50,000.

The majority of the metro population was White, 2495 (82.3%) compared to Blacks, 538 (17.7%). I observed a similar trend in the non-metro area with, 37 (14.8%) Blacks and 213 (85.2%) Whites. Most Black women resided in the Metro areas 93.6% compared to those in non-metro (rural areas), who were 6.4% (see Table 2).

Table 2

Descriptive Characteristics of Cases by Race

Demographics	Total count (n = 3283) No. (%)	Race	
		Blacks No. (%)	Whites No. (%)
Race and ethnicity	3283 (100.0)	575 (17.5)	2708 (82.5)
Breast cancer biological subtype			
Triple-negative	526 (16.0)	145 (26.7)	399 (73.3)
Non-triple negative	2560 (78.0)	381 (15.0)	2161(85.0)
Missing data	197 (6.0)		
Median household income			
> $50,000	2819 (85.9)	431 (15.3)	2388 (84.7)
< $49,999	464 (14.1)	144 (31.0)	320 (69.0)
Geographical location			
Metro areas	3033 (92.4)	538 (17.7)	2495 (82.3)
Non-metro areas	250 (7.6)	37 (14.8)	213 (85.2)
Vital status			
Alive	3035 (92.4)	499 (16.4)	2536 (83.6)
Dead	248 (7.6)	76 (30.6)	172 (69.4)
Event of death by race		13.2%	6.35%
Overall mean survival time (months)			
TNBC		56.2	58.6
Non-TNBC		64.0	67.9
Missing data	197 (6%)		

The mean survival time (months) for TNBC was lower among Black women (*M* = 56.2, *SE* = 2.25, CI [51.80 ,60.62]) compared to White women in the same age group (*M* = 58.60, *SE* = 1.35, CI [55.96 ,61.25]). A similar trend was observed among women with non-TNBC by race, Black women had a lower mean survival time (*M* = 64, *SE* = 1.06, CI [61.92, 66.09]; see Table 3) versus White (*M* = 67.9, *SE* = 0.31, CI [67.28, 68.51]; see Table 3).

Table 3

Mean Survival Time in Months by Race and Breast Cancer Biological Subtype

		Mean (months)			
				95% Confidence interval	
Race	Breast cancer subtype	Estimate	Std. error	Lower bound	Upper bound
Black	Triple-Negative	56.21	2.25	51.804	60.624
	Non-TNBC	64.008	1.064	61.922	66.094
	Overall	61.821	1.007	59.847	63.796
White	Triple-Negative	58.603	1.351	55.955	61.252
	Non-TNBC	67.891	.314	67.276	68.506
	Overall	66.475	.344	65.800	67.150
Overall	Overall	65.656	.337	64.995	66.316

Table 4 below shows the coding that was used in the Cox proportional model.

Table 4

Categorical Variable Coding Used in the Cox Proportional Hazards Model

Variable (Categorical)		Frequency	(1)
Geographical location	1=Metro area	2852	0
	2=Non-metro area	234	1
Biological subtype (BCS)	0=non-TNBC	2542	0
	1=TNBC	544	1
Median household income	1=<49,999	434	0
	2=>=50,000	2652	1

Table 5

Results of the Log Rank Test

Variables		5-Year survival probability (months)	Results of the log rank test		
			$\chi 2$	*DF*	*p*-value
Race	Black White	0.79 0.88	30.777	1	.001*
Biological subtype (Overall)	TNBC n-TNBC	0.78 0.89	124.013	1	.001*
Biological subtype (Blacks)	TNBC n-TNBC	0.62 0.79	13.031	1	.001*
TNBC	Black White	0.63 0.78	13.507	1	.001*

* Significance at the .05 level.

Table 6

Cox Proportional Model for the Unadjusted Risk of Mortality by Biological Subtype Among Young Black Women

	Hazard ratio		95.0% CI for HR	
Variable	(HR)	*p*-value	Lower	Upper
Biological subtype	2.343	.001*	1.453	3.777

* Significance at the .05 level.

Table 7

Adjusted Cox Proportional for Mortality Risk Among Black Women After Adjusting for Covariates

	Hazard ratio		95.0% CI for HR	
Variables	(HR)	*p*-value	Lower	Upper
Median Income Level	1.307	.349	.746	2.289
Geographical Loc	.550	.148	.244	1.237
Age	.966	.185	.919	1.017
Biological subtype	2.220	.001*	1.373	3.589

*Significance at the .05 level

Table 8

Unadjusted Cox Proportional Model for Young Women with Breast Cancer

	Hazard Ratio		95.0% CI for HR	
Variable	(HR)	*p*-value	Lower	Upper
Biological subtype	3.988	.001*	3.064	5.190

*Significance at the .05 level.

Table 9

Cox Proportional Model for Young Women with Breast Cancer After Adjusting for Covariates

Variables	Hazard ratio (HR)	*p*-value	95.0% CI for HR	
			Lower	Upper
Biological subtype	3.613	.001*	2.758	4.731
Median Income	.851	.389	.591	1.228
Geographical Loc	.997	.992	.600	1.658
Age	.988	.375	.961	1.015
Race	.606	.001*	.451	.815

*Significance at the .05 level

Table 10

Adjusted Cox Proportional Model for the Interaction Between Geographical Location and Biological Subtype

Variables	Hazard ratio (HR)	*p*-value	95.0% CI for HR	
			Lower	Upper
Median Income	.813	.273	.561	1.177
Geographical Loc	.643	.199	.328	1.261
Biological subtype +Geographical Loc	3.990	.002*	1.653	9.631

*Significance at the .05 level, + indicates model interaction

Table 11

Adjusted Cox Proportional Model for the Interaction Between Median Household Income and Breast Cancer Biological Subtype

Variables	Hazard ratio (HR)	*p*-value	95.0% CI for HR	
			Lower	Upper
Median Income	.526	.001*	.357	.777
Geographical Loc	.998	.995	.599	1.664
Biological subtype+Median Income	3.920	.001*	2.907	5.285

*Significance at the .05 level, + indicates model interaction

Research Questions

Survival Analysis Among Young Black Women with TNBC and Non-TNBC Breast Cancer Biological Subtypes

Research Question 1

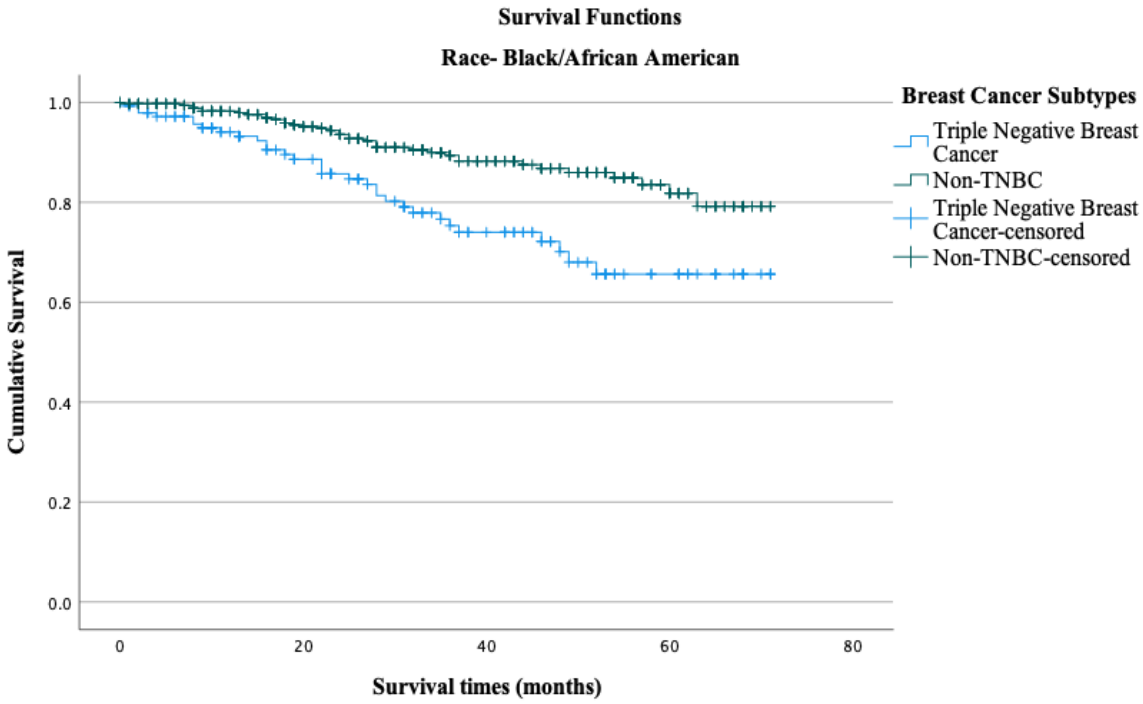
Do young Black women with TNBC biological subtype have a poor survival rate than young Black women with the non-TNBC biological subtypes of breast cancer?

According to the findings, we reject the null hypothesis that there was no difference in survival functions based on the biological subtype (χ^2 (1) = 13.031, $p < .05$; see Table 5). Table 5 presents the Kaplan Meier survival analysis of the biological subtypes of breast cancer (TNBC and non-TNBC) among young Black women. The findings are statistically significant that there is a difference in the survival functions based on biological subtype among young Black women. Young black women with TNBC have a lower probability of survival compared to those with non-TNBC biological subtypes (5-year overall probability of survival 0.62 vs 0.79; see Table 5).

Figure 2 presents the Kaplan Meier survival curves by breast cancer biological subtype among Black women and shows that Blacks with TNBC had a lower probability of survival than Blacks with non-TNBC. Therefore, the research hypothesis was accepted that there were differences in survival outcome based on biological subtype among young Black women with breast cancer.

Figure 2

Kaplan Meier's Survival Curves by Breast Cancer Biological Subtype Among Young Black Women



Survival Rate of TNBC and Non-TNBC Among Young Black Women Adjusting for the Sociodemographic Factors

Research Question 2

Is there a difference in survival rate among young black women with TNBC subtype and non-TNBC subtypes (Hormone Receptor (H.R.) +ve/HER2 +ve, H.R. +ve/HER -ve, H.R. -ve/ HER2 enriched) when adjusted for sociodemographic factors?

There was a statistically significant difference in hazard ratio among young Black women with TNBC compared to young Black women with non-TNBC adjusting for other covariates (HR = 2.220, 95% CI [1.373, 3.589], p = .001; see Table 7). The null hypothesis was rejected that there is no difference in survival function among young black women by biological subtype.

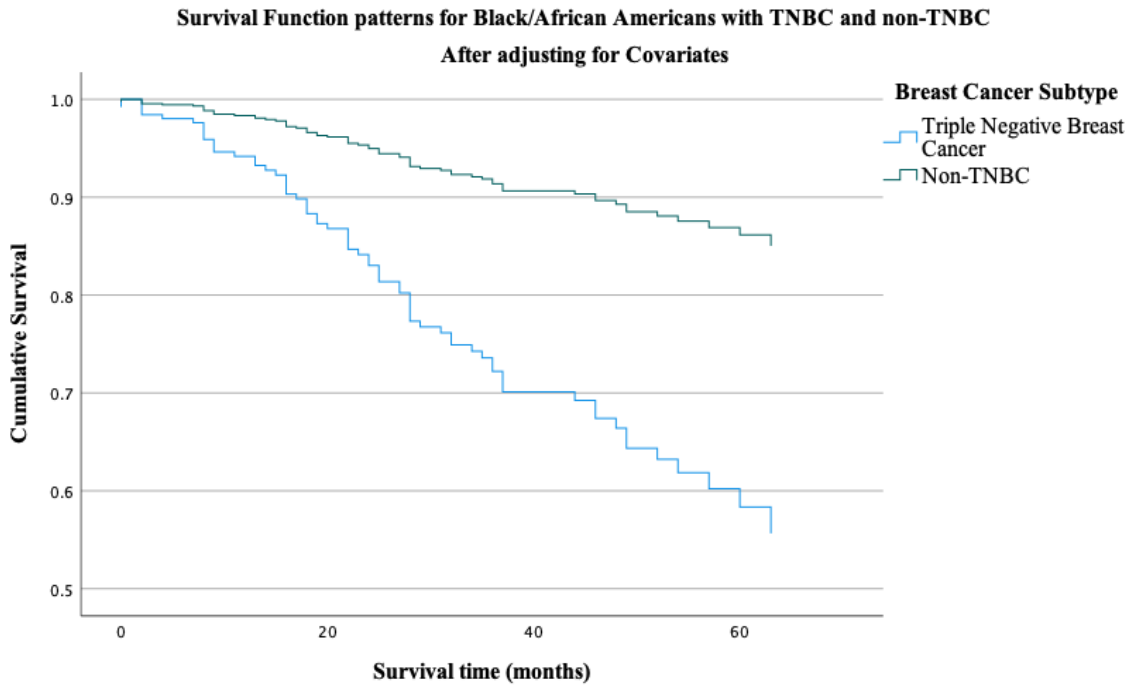
In the initial model, young Black women with TNBC were 2.343 more times likely to die compared to Black women with non-TNBC before adjusting for covariates (HR = 2.343, 95% CI [1.453, 3.777], p = .001; see Table 6) compared the adjusted model in which other covariates were considered, the hazard ratio decreased (HR = 2.220, 95% CI [1.373, 3.589], p = .001; see Table 7). After adjusting for covariates, the mortality risk of young Black women with TNBC was 2.2 more times compared to young Black women with non-TNBC

Figure 3 below shows the survival probability curves of Black women with TNBC and non-TNBC after adjusting for covariates in the Cox proportional hazards model. The figure shows that young Black women with TNBC had a lower probability of survival than young Black women with non-TNBC biological subtype when adjusted for

covariates- age, median household income, and Geographical location. The 5-year cumulative survival was 0.58 among young Black women with TNBC compared to 0.88 among the young Black women with non-TNBC (see Figure 3).

Figure 3

Cox Proportional Hazards Model for Survival Function by Biological Subtype Among Young Black Women



Survival Rate Among Young Black and White Women with TNBC Adjusting for the Sociodemographic Factors

Research Question 3

Is there a difference in survival rate between young Black women and young White women with the same biological subtype-TNBC after controlling for sociodemographic factors?

The hazard of death was 3.99 times among young Black women with TNBC compared to young White women before adjusting for covariates in the model (HR = 3.988, 95% CI [3.064, 5.190], p = .001; see Table 8). In the full model, the breast cancer biological subtype was statistically significant, adjusting for other covariates. The risk of death was 3.613 more times among young Black women with TNBC compared to young White women adjusting for other covariates (HR = 3.613, 95% CI [2.758, 4.731], p = .001; see Table 9). Race was also a significant predictor survival outcome among young women after adjusting for covariates (HR = 0.606, 95% CI [0.451, 0.815], p = .001; see Table 9). White women with TNBC had a 39.4% decrease in hazard of death compared to Black women with TNBC breast cancer, after adjusting for covariates.

The interaction between geographic location and breast cancer subtype was statistically significant (HR = 3.990, 95% CI [1.653, 9.631], p = .002; see Table 10). The interactions between geographical location and breast cancer biological subtype were associated with increased risk of mortality among women in non-metro areas with TNBC compared to women in metro areas with TNBC.

Median household income was a significant predictor of survival outcome (HR = 0.526, 95% CI [0.357, 0.777], p = .001; see Table 11). An increase median household income was associated with a 47.3% reduction in the risk of mortality among young White women with TNBC compared to young Black women with TNBC. There was also a significant interaction between median household income and breast cancer biological subtype (HR = 3.92, 95% CI [2.907, 5.285], p = .001; see Table 11). Median household income and breast cancer biological subtype were predictors of survival outcome among

women with breast cancer. Therefore, the results were statistically significant to reject the null hypothesis that there is no difference in the probability of survival among young white women with TNBC and young Black women with TNBC after adjusting for other covariates (HR = 3.613, 95% CI [2.758, 4.731], p = .001; see Table 9).

The log-rank test also showed a statistically significant difference in survival functions among young Black and White women with TNBC biological subtype (χ^2 (1) =13.507, p = .001; see Table 5). The 5-year probability of survival among young women with TNBC was lower among Blacks compared to Whites (0.63 versus 0.78; see Table 5). The research hypothesis was accepted.

Figure 4 presents the Kaplan Meier survival curve of TNBC biological subtype among Whites and Black women ages 25–44 and shows that young Black women with TNBC had a lower probability of survival compared to young White women with TNBC biological subtype.

Figure 4

Kaplan Meier's Survival Curves for TNBC Biological Subtype by Race Among Young Women with Breast Cancer

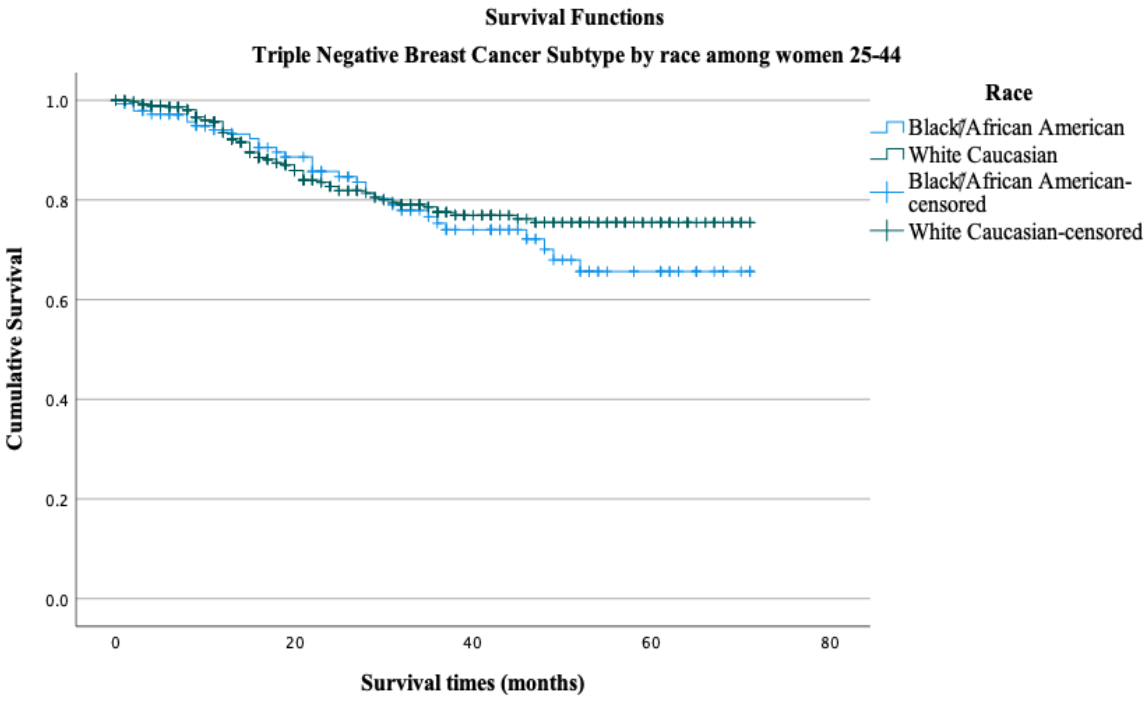
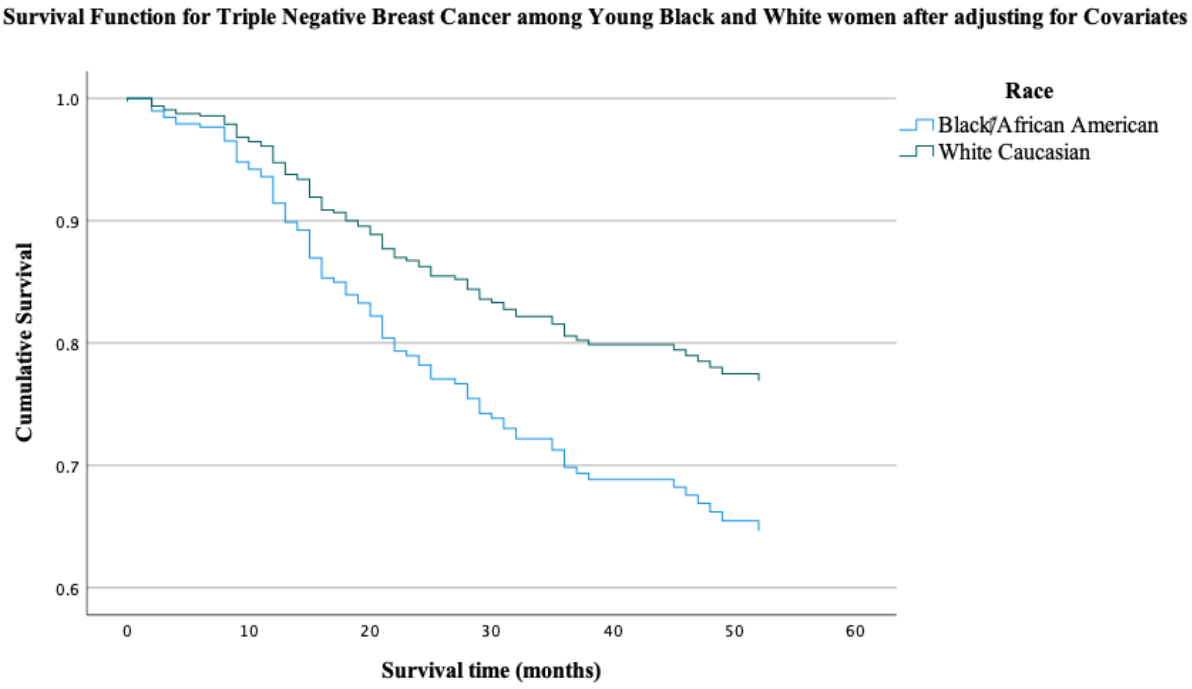


Figure 5 shows the survival function curves for TNBC biological subtype by race; the trend shows that young Black women with TNBC have a lower probability of survival compared to young White women with TNBC after adjusting for covariates (HR = 3.613, 95% CI [2.758, 4.731], p = .001; see Table 9*)*.A similar trend was displayed graphically in Figure 5 below that shows that young Black women with TNBC suffer worse adverse outcome compared to young White women with the same TNBC biological subtype. Hence regardless of the biological characteristics of the tumor, survival outcome by race is statistically significant. After adjusting for the covariates of geographical location and median household income levels.

Figure 5

Survival Function of TNBC Biological Subtype Among Young Black and White Women After Adjusting for Covariates



Testing Assumptions

Kaplan Meier's survival analysis method assumes that the event status consists of two mutually exclusive events (Rulli et al., 2018). The dependent variable of event status was mutually exclusive because the outcome was either censored or the event of death occurred. The pattern of censorship per group was also similar as tested in SPSS. The percentage of censored events was close, with 87% among young Black women to 93.8% among young White women. The overall censored events were 92.7%. The assumption of a similar amount and pattern of censorship per group was met.

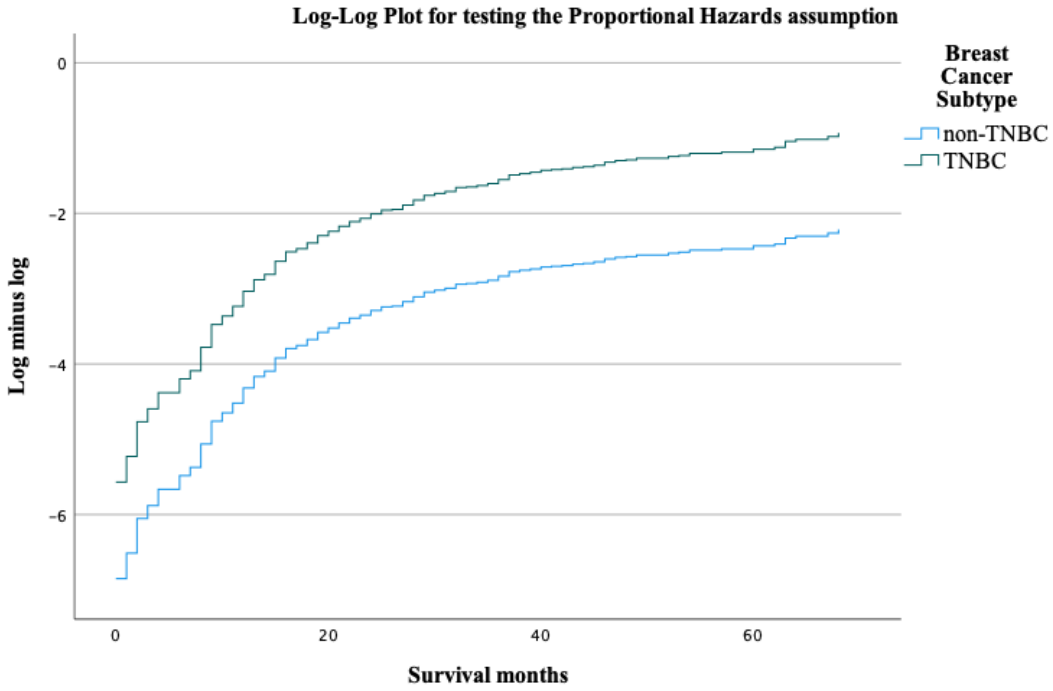
The Log-rank test was used to evaluate whether the differences in Kaplan Meier's survival curves were statistically significant. The Cox proportional hazards survival

analysis was used to detect and estimate the effect of predictor variables- race, income levels, breast cancer biological subtype, age, and geographical location on survival among the study population. The measure of association estimated by the Cox proportional hazards model was the hazard ratio (HR) with the likelihood chi-square statistic calculated by comparing the deviance (-2 Log Likelihood) of the null model with the model being used to predict the effect of the covariates. The model used was statistically significant from the null model ($\chi 2(1) = 13.507$, $p = .001$; see Table 5). The individual contribution of covariates to the model were assessed for statistical significance test given with each coefficient in the main output shown in Table 9.

Thus, the predictor variables had a multiplicative or proportional effect on the predicted hazard. The estimated coefficients in the Cox proportional hazards regression model, *b*, represented the change in the expected log of the hazard ratio relative to a one-unit change in the predictor variable, holding all other predictors constant. The assumption of proportional hazards was tested using cLog-Log Plot in SPSS. Figure 6 below shows the graphical test for the assumption of hazard proportionality. The survival curves of the breast cancer biological type (Independent variable) do not cross over from early period observations and remain parallel after that. The plot suggests that the model used does not violate the proportional hazards assumption.

Figure 6

Log-Log Plot to Test the Assumption of Proportional Hazards in the Cox Model



Summary

In Chapter 4, the study results were presented in which the three research hypotheses were accepted as statistically significant associations were observed. Black women with TNBC had a decreased survival outcome compared to those Black women diagnosed with non-TNBC. Similar findings were observed when the model was adjusted for covariates. Young Black women with the TNBC biological subtype had an increased risk of death than young White women after adjusting for age, race, median household income levels, and geographical location. The results showed a statistically significant difference in the survival function among women with breast cancer between 25–44 by race and the breast cancer biological subtype. The results showed that despite a lower

proportion of Black women with TNBC, the probability of survival over 5 years was low. The findings are consistent with previously published studies. The results also showed a statistically significant interaction between median household income, geographical location, and breast cancer biological subtype. Chapter 5 interprets the findings, limitations of the study, social change implications, and recommendations for further research studies.

Chapter 5: Discussion, Conclusions, and Recommendations

Disparities in breast cancer health outcomes among young Black women represent a significant and urgent public health concern in the United States. A large body of research on disparities in breast cancer mortality outcomes suggests a strong relationship between breast cancer biological subtype and sociodemographic factors. The purpose of this retrospective cohort study was to examine the associations between biological subtypes of breast cancer (TNBC and non-TNBC) and patient-level sociodemographic factors and how they influence survival outcomes in specific subpopulations using the SEER *Registry 18 Research Plus* database. According to literature, breast cancer biological subtypes and sociodemographic variables are important prognostic indicators of survival outcome among breast cancer patients (Doepker et al., 2018; Vidal et al., 2017; Warner et al., 2015; Yersal & Barutca, 2014). However, their role in predicting survival outcomes among certain subpopulations and age groups has not been fully explored. Therefore, this study contributes to the literature by enhancing our knowledge to understand disparities in breast cancer outcomes and how to address them better.

Krieger (2011) emphasized that understanding disease characteristics in the population involved conceptualizing disease biomarkers in relation to the changing magnitudes of health inequities in the population. The present study, to my knowledge, is the first of its kind to examine the relationships between these biological subtypes of breast cancer and the sociodemographic factors in breast cancer mortality outcome disparities in the specific age group of 25–44 years. The study used a nationally

representative sample of young women who were followed longitudinally. The data consisted of a large, diverse sample that provided an opportunity to measure the associations between sociodemographic factors and breast cancer biological subtype within the age group of 25–44 years, whose effects may have been masked in previous studies.

In this chapter, I will discuss key findings, directions for future research, and implications for public policy and public health interventions.

Key Findings and Interpretations

The key findings of the study are presented according to the research questions that were studied.

Research Question 1

Do young Black women with TNBC biological type have a poor survival rate compared to other young Black women with the non-TNBC biological subtypes (Hormone Receptor (H.R.) +ve/HER2 +ve, H.R. +ve/HER -ve, H.R. -ve/ HER2 enriched) of breast cancer?

The results suggest that survival functions among young Blacks with different breast cancer biological subtypes were statistically significant ($p < .001$). The Kaplan Meier survival analysis, young Black women with the TNBC subtype had a significantly lower overall survival than young Black women with non-TNBC. The results suggest that breast cancer biological subtype is a significant predictor of survival outcome among Black women with breast cancer. The findings are consistent with previous studies that showed a higher risk of breast cancer recurrence and death among women with TNBC

(Biswas et al., 2016; Ding et al., 2019; Doepker et al., 2018; Partridge et al., 2016; Saini et al., 2019; Vidal et al., 2017). Race level differences in mortality outcome based on biological subtypes of breast cancer provide an insight into whether biologic characteristics may vary with age. Younger women are more likely to experience aggressive disease than older women (Parise & Caggiano, 2018; Partridge et al., 2016). Yuan et al. (2021) similarly found that aggressive forms of TNBC in postmenopausal women were attributed to metabolic risk components present at diagnosis. However, those metabolic risk factors contributing to the excess mortality among young Black women were not ascertained in my study. Studies involving metabolic disease risk in younger women may be crucial to understand these health disparities further.

Determining breast cancer biological subtype survival outcome by race facilitates our understanding of the role of biology in health outcome disparities. The findings also confirm the primary relationship of the modified ecosocial conceptual model used in the study that links the TNBC biological subtype to excess morbidity and mortality in vulnerable subpopulations.

Research Question 2

> Is there a difference in survival rate among young Black women with TNBC subtype and non-TNBC subtypes (Hormone Receptor (H.R.) +ve/HER2 +ve, H.R. +ve/HER -ve, H.R. -ve/ HER2 enriched) when adjusted for sociodemographic factors?

There were statistically significant differences in survival function between young Black women with TNBC and non-TNBC after adjusting for sociodemographic factors-

median household income and geographical locations ($p < .05$). The 5-year survival probability of young Black women with TNBC was .59 compared to .88 with non-TNBC. Therefore, breast cancer biological subtype was a significant predictor of survival probability after adjusting for the covariates-geographical location and median household income levels.

There was also a statistically significant interaction between geographic location and breast cancer subtype in predicting survival outcome in young Black women with TNBC and non-TNBC. Interaction between breast cancer subtype and median household income was also statistically significant. The study adduced that median household income and geographical location interactions confounded the relationship between breast cancer subtype and survival outcome. The hazard ratio increased compared when the variables were not adjusted for. The findings are consistent with previous studies that showed evidence of neighborhood factors like geographical location in increasing poor survival outcomes among breast cancer women (Dietze et al., 2015; Prakash et al., 2020; Reeder-Hayes & Anderson, 2017). TNBC in Black women may interact with sociodemographic factors and contribute to the excess mortality burden among women with TNBC versus non-TNBC subgroup. There was no statistically significant association between age and TNBC ($p > .05$). However, Doepker et al. (2018) found that tumor characteristics of race, age, and tumor stage were a significant prognostic indicator of TNBC. The prognosis of TNBC in the younger cohort was not dependent on age, implying that other pathological characteristics like early metastasis may explain the poor overall survival among those with TNBC. Similarly, Kumar and Aggarwal (2016) found

that TNBC was associated with the Black race, younger age, higher grade, mitotic index, and more advanced stage at diagnosis, explaining the excess mortality burden. However, their findings contrast with Yuan et al. (2021), who found that more metabolic risk factors with old age explain the poor overall survival among post-menopausal women. The findings reinforce our argument that biological characteristics of breast cancer are associated with the excess mortality rate among TNBC subgroups is dependent on interactions of biology and sociodemographic factors.

The statistically significant findings of interactions between median household income, geographical location, and breast cancer biological subtype ($p < .05$) may explain how social disadvantages influence morbidity and mortality among young Black women with TNBC. From our findings, geographical location and median household income levels confounded the relationship between the biological subtype of breast cancer and overall survival.

Research Question 3

Is there a difference in survival rate between young Black women and young White women with the same biological subtype-TNBC after controlling for sociodemographic factors?

There was a statistically significant difference in survival outcomes among young Black women with TNBC compared to young White women with TNBC after adjusting for the covariates- geographical location and median household income levels ($p < .001$). Young Black women experienced poor survival outcomes compared to White women. Among young women with TNBC, Black women experience a disproportionate mortality

burden despite adjusting for sociodemographic factors. The findings are consistent with previous studies that examined the associations between race and biological subtypes of breast cancer (Brenner et al., 2016; Matt et al., 2015; Parise & Caggiano, 2018; Prakash et al., 2020; Walsh et al., 2019). Although the proportion of young Black women in the present study who had TNBC was lower than White women with TNBC, race was a statistically significant predictor of overall survival among women with TNBC ($p < .05$).

Similarly, Doepker et al. (2018) and Walsh et al. (2019) found that black women with TNBC had 5- and 10-year overall survival that was significantly worse compared to white women. However, in the Doepker et al.'s study, the median age of the participants was 62.4 years compared to my study in which the mean age was 38 years. Younger Black women with TNBC biological subtype had poor overall survival compared to White women with TNBC after adjusting for other covariates.

The present study reported a disproportionately poor survival rate among young Black women compared to White women, with significant associations of TNBC biological subtype, median household income, and geographical location among young Black women. Doepker et al. (2018) also found that Black women tend to present with more advanced disease and adverse prognostic factors like early metastasis, comorbidities (obesity and diabetes) that influence survival outcomes compared to White women. Moreover, in my study, after adjusting for these factors, breast cancer biological subtype was still a significant predictor of overall survival in young Black women versus White women (63% vs. 79%; $p < .05$).

The potential interactions are essential to understanding the disproportionate poor survival rates of young Black women with TNBC. The modifiable lifestyle factors like income and access to care have been associated with reduced risk of morbidity and mortality in breast cancer patients (Parise & Caggiano, 2018; Walsh et al., 2019). Based on my findings, survival outcomes among young Black women with TNBC may be affected by income levels and geographical location. Young Black women with TNBC in metro areas earning higher income have better survival outcomes than those earning less income in non-metro areas. These findings are consistent with studies that showed a disproportionate mortality burden among Black women with TNBC with socioeconomic adversities (Prakash et al., 2020; Warner et al., 2015). Prakash et al. (2020) and Warner et al. (2015) examined biologic and nonbiologic risk factors in breast cancer disease and found that the biological risk factors directly linked to TNBC in Black women may potentially interact with nonbiologic factors to promote a higher prevalence of TNBC, which is associated with a more aggressive biology, and poor survival. However, in contrast to the Prakash et al.'s and Warner et al.'s studies, I explored the biologic and nonbiologic (sociodemographic variables) interactions in younger women 25–44 years.

The effect of age on the survival of women with early breast cancer seems to vary by breast cancer subtype (Partridge et al., 2016). Hence my findings support that early diagnosis through improved access to care and empowerment through socioeconomic opportunities, like educational advancement, high-quality employment, and equitable access to healthcare and cancer preventive programs, will improve the survival outcome among young Black women with TNBC disease.

Findings in Relation to the Modified Ecosocial Theory Conceptual Model

In the ecosocial theory modified conceptual model I theorized that sociodemographic factors confound the association between the breast cancer biological subtype and survival outcome. The interaction analyses using the Cox proportional hazard model showed that sociodemographic factors such as geographical location and median household income level were significant contributors to racial differences in survival outcome as the hazard of death increased significantly in the interaction model (HR = 3.990, 95% CI [1.65, 9.631], $p < .05$) versus the adjusted model (HR = 3.613, 95% CI [2.758, 4.731], $p < .05$). Race-specific survival outcome disparities persisted after accounting for the sociodemographic factors of geographical location and median household income levels. Therefore, young Black women with TNBC were more likely to suffer significant adverse outcomes when faced with socioeconomic disadvantages compared to young White women with similar TNBC biological subtype. The findings are consistent with the modified ecosocial theory modified conceptual model that sociodemographic factors are mediators/confounders of the observed racial disparities in breast cancer survival among women with similar breast cancer biological subtype.

Whereas observed differences in breast cancer biological subtypes contribute to breast cancer mortality disparity, my study highlights those interactions between breast cancer biological subtype and sociodemographic factors such as median household income levels and geographical location also play a significant role in the observed racial differences in breast cancer mortality. The results support the ecosocial theoretical conceptual model that these observed interactions between sociodemographic factors and

breast cancer biological subtype are potential drivers of unequal TNBC survival outcome trend observed between young Black women and young White women.

The observed interactions between geographical location, median household income and biological subtype were statistically significant consistent with the modified ecosocial theory conceptual model. The sociodemographic variables confound the association between breast cancer biological subtype and survival outcomes.

Assumptions and Limitations

This study sought to determine if sociodemographic factors confound the association between breast cancer biological subtype and survival rate among young Black women. In the limitations of the quantitative study, firstly, the results could only demonstrate associations and not causation. The study did not determine the causality of any identified associations but provided a basis for further research based on these findings. Secondly, the SEERs database uses self-report questionnaires with responses collected at the hospital or health center level. Whereas the survey instruments have reliable internal validity, respondents may have had a recall and social desirability bias. Data triangulation using the *Research Plus* database to validate information was used to reduce the threat of self-reporting bias. Thirdly, Medical surveillance bias may have existed. Medical surveillance bias would occur when one group of subjects is followed up more closely than the others (White patients vs. Black patients) at the hospital level (Szklo, & Nieto, 2019). The rigor of statistical analysis undertaken is assumed to have controlled for any profound effect. Fourthly, the determination of breast cancer biological subtypes-ER, P.R., and HER2 were performed by a wide variety of laboratories without

testing inter-rater reliability (Parise, & Caggiano, 2018). Threats to reliability could influence the generalizability of our findings. However, the robust statistical methods used may have controlled for any random or systematic errors in the observations attributed to differences in testing breast cancer molecular subtypes. Finally, the study did not measure variables like the stage of breast cancer at diagnosis, type of treatment received, disease recurrence, and comorbidities that may have had an overall effect on the predictive models of the association between sociodemographic and breast cancer biological subtype in disease outcome. Additionally, the database had missing information. However, the exclusion of these participants had minimal effect on the statistical power of the study.

Although there are study limitations, the longitudinal study design approach had a clear advantage in examining the variability of the repeated measures over time. However, limitations in the initial diagnosis of breast cancer among young Black women may have been apparent. The limited access to hormonal receptor assays performed to inform clinicians of the type of receptors the breast cancer cells express may have led to the exclusion of some young Black women from the study. Overall, the findings of the study are generalizable. The study sample was obtained by probability sampling and is representative of the general population.

Social Change

The research findings contribute to the scholarship of breast cancer burden and improve our knowledge about health disparities and their effects on cancer treatment outcomes among subpopulations. The cumulative effects of proximate social

determinants of health like socioeconomic opportunities, educational advancement, health literacy, neighborhood factors, access to safe water and clean air resources, racism, have an influence on the distal race specific biological differences. The interactions of these sociodemographic factors with specific breast cancer biological subtypes contribute to the disparities in survival outcomes.

The research highlights the multilevel socioecological effects that contribute to the disproportionate burden of disease in some subpopulations and demonstrates the need to increase access to specialized genomic sampling tests that identify aggressive forms of breast cancer disease among young Black women. Mortality rates and risks arising from the late-stage diagnosis of breast cancer disease are significantly greater among Black women compared to White women (Ademuyiwa et al., 2017; DeSantis et al., 2016). Limited access to preventive services like breast cancer screening and genomic sampling tests is evident in minority communities (DeSantis et al., 2016). The study provides empirical evidence to inform policymakers, and public health practitioners of the need for increased access to genetic screening (biological) tests to address breast cancer mortality disparity. Empowering young Black women to participate in breast cancer preventive programs driven by evidence-based research can achieve positive social change.

Directions for Future Research

Breast cancer is a leading cause of premature mortality among U.S. women (Ademuyiwa et al., 2017; CDC, 2020; Coughlin, 2019). Early detection is associated with reduced breast cancer morbidity and mortality (; CDC, 2020; Satoh & Sato, 2021). More research needs to be conducted on the role of biological differences, stage of breast

cancer, type of clinical intervention, disease recurrence, and the role of comorbidities in breast cancer survival outcomes that drive health disparities. Research is pertinent to understanding the in-depth mechanisms of disease processes and how they influence survival outcome models. Studies should examine the role of precision medicine in tackling breast cancer outcome disparities.

Prior studies have led to identifying molecular heterogeneity in breast cancer disease associated with different mechanisms of disease origin (Sachdev et al., 2019). Hence developing targeted therapies will require understanding the gene-expression signatures and biological characteristics of TNBC among black women. This will require more black women to be involved in breast cancer research to conduct gene-expression studies and understand the differential effects of treatment exposure.

Understandably, new paradigms in cancer therapy approaches are shifting from grouping heterogeneous patient populations for therapeutic interventions (without addressing the inherent differences in these subpopulations) to precision medicine that considers the molecular and biological specificities of the patient and their tumors that will influence the treatment outcomes. Subpopulations like young Black women with breast cancer appear to be defined by specific molecular characteristics for which individualized medicine may improve outcomes.

Implications of Public Health Policy

The study found statistically significant interactions between biological and sociodemographic factors, associations that contribute to the excess burden of mortality among young Black women with breast cancer. The findings provide compelling

empirical evidence to inform policymakers and public health practitioners of the need for increased access to early-specialized breast cancer screening among vulnerable subpopulations. The United States Preventive Services Taskforce (USPTFS) has no recommendations for breast cancer screening among women less than 40 years of age. Whereas the benefits of comprehensive breast cancer screening may not outweigh the effects of increased radioactive exposure at a younger age in the general population of screening recipients, there is compelling empirical evidence that uniform definitions and standards of at-risk populations are needed to address potential gaps in breast screening practices.

The CDC defines cancer health disparities as observed differences in cancer measures such as incidence, prevalence, mortality, morbidity, survival rate, screening rates, and the defined stage at diagnosis that occurs in specific population groups (CDC, 2020; U.S. Health and Human Services, 2021). In the study, we investigated the extent of these survival disparities in the specific subpopulation of young Black women (25–44 years) and whether the association between breast tumor biological subtype and sociodemographic factors contributes to the excess disease burden. The findings are significant in understanding better therapeutic approaches in vulnerable subpopulations that address clinical-level outcomes. Targeted interventions like precision medicine are based on understanding the inherent biological propensities of these breast cancer subtypes.

Additionally, appropriate public health screening strategies should address the disproportionate exclusion of women facing an increased risk of being diagnosed with

biologically more aggressive tumors (TNBC), especially among young Black women. Clinical providers are faced with challenges of cultural and language barriers that may influence breast screening decisions. Therefore, and primary care settings should be aware of these vulnerable subpopulations. Breast cancer screening provides better public health surveillance of breast cancer prevalence and will help to improve health outcomes. Developing evidence-based, culturally competent public health interventions to reduce the increased TNBC breast cancer biological subtype among vulnerable populations is essential. Timely screening, early diagnosis, and treatment will prove crucial in addressing the disproportionate gaps in care among these vulnerable women.

Conclusion

This study examined the associations of biological and sociodemographic risk factors to survival outcomes among vulnerable subpopulations of young Black women 25–44 years of age. TNBC biological subtype is associated with a worse prognosis in young Black women compared to young White women. The study found statistically significant associations between sociodemographic factors and breast cancer biological subtype as significant prognostic indicators of breast cancer disease in young women. Young black women with TNBC biological subtype were more likely to die than young White women after adjusting for covariates. This could be due to lack of access to care, socioeconomic disadvantages, presentation with more advanced disease at health facilities, neighborhood factors, and differences in breast cancer biology. The study highlights these growing trends of disparities in health outcomes among breast cancer

patients. The risk factors associated with racial and ethnic biological differences in breast cancer remain largely unknown.

Most of the epidemiologic literature has concentrated on environment and lifestyle as agencies of disease. However, it places less importance on the broader determinants of health that can be changed through social action. Further, biological factors may confound disease risk factors in some subpopulations, contributing to health inequity. Public health scholars ought to be aware of these existential factors born out of the life course paradigm and that they may have an implication on health outcomes.

Our bodies biologically express economic and social inequality experiences, from intrauterine life to death, thereby producing social disparities in health across a broad spectrum of diseases. Biological expression of social inequality occurs in our bodies and contributes to the web of multi-causality of diseases (Krieger 2012; Krieger, 2001). Blacks are disproportionately affected by socioeconomic disadvantages that translate into physical conditions like obesity, diabetes, and other chronic diseases (Tremmel et al., 2017). Most of these conditions are risk factors for cancer development (Deshmukh et al., 2017). From our study, socioeconomic status (SES) remains a consistent and reliable predictor of a vast array of outcomes across the life span, including physical and psychological health. Thus, improving SES is relevant to all behavioral and social science realms, including research, practice, education, and advocacy to ensure equity in health outcomes.

Evidence from this study reinforces findings from previous studies that showed increased adverse survival outcomes for Black women with the TNBC biological

subtype. Based on the findings, the study highlights the nested hierarchies that influence disease outcomes among Black women with breast cancer. The cumulative effects of exposure to socioeconomic disadvantages are also known to influence physiological processes (biology) through phenomena like allostatic overload (Deshmukh et al., 2017; Parente & Palermo, 2013). Understanding the role of these processes in driving inequities in disease outcomes is vital to addressing disparities in health outcomes. The findings provide a basis for further research on the role of biophysiological processes in driving health disparities.

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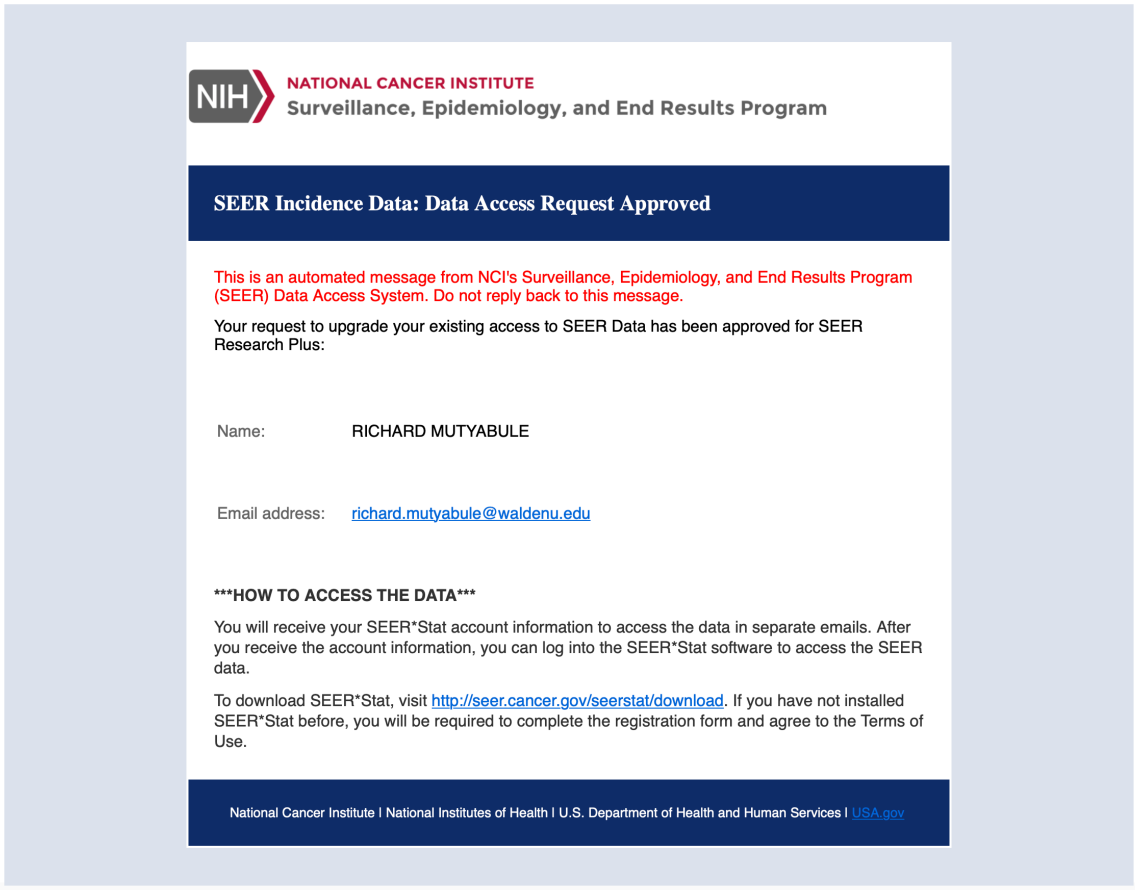
Appendix: SEER Data Access Approval



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