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Geographical Proximity to Health Facilities and Breast Cancer Morbidity and Mortality Among Women in South Carolina's Best Chance Network

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GEOGRAPHICAL PROXIMITY TO HEALTH FACILITIES AND BREAST CANCER MORBIDITY AND MORTALITY AMONG WOMEN IN SOUTH CAROLINA'S BEST CHANCE NETWORK

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DEDICATION

To my wife and son, Bi Vang and Chadsen Khang.

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ABSTRACT

Death rates for breast cancer have steadily decreased in women due to early detection, such as mammography, and improved treatments. Despite the benefit of mammography, many women are not up-to-date on screening and do not receive timely follow-up after abnormal mammogram finding. Breast cancer is a major contributor to morbidity and mortality among women in South Carolina. To reduce the disproportionate burden of breast cancer and cervical cancer among women in South Carolina, the South Carolina Best Chance Network (BCN) was established to provide service delivery and ensures timely and complete diagnostic follow-up and treatment initiation for underserved women.

The purpose of this dissertation was to examine whether travel distance to the screening provider and mammography facility are associated with completion of abnormal mammography follow-up, breast cancer stage at diagnosis, and mortality among women in the BCN. Women enrolled in BCN between 1996 and 2009 were included in the study. Cox proportional hazard modeling was used to assess the relationship between travel distance and time to resolution. Multivariable logistic regression was used to assess the association between travel distance and breast cancer stage at diagnosis. Cox proportional hazard modeling and Kaplan-Meier survival methods were used to determine breast cancer-specific and all-cause survival probabilities.

Women who lived farther from their diagnosing mammography facility had longer day to resolution compared to those who lived the closest (p=0.05). African American women had significantly longer day to resolution compared to European American women. There was no association between travel distance to the screening provider, mammography facility and breast cancer stage at diagnosis. There was also no association between travel distance and breast cancer-specific and all-cause mortality.

Travel distance from patient's residence to the diagnosing mammography facility may have an impact on the completion of abnormal mammographic finding. However, living farther from the screening provider and mammography facility do not increase late-stage breast cancer at diagnosis and mortality among women in BCN. Support to the BCN program to expand services should be promoted to reduce the disparity in days to completion of abnormal mammographic finding. Capturing an accurate measurement of travel distance/time will help better understand whether location of the health facilities affects breast cancer outcome.

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LIST OF ABBREVIATIONS

AA .... African American

ACS .... American Cancer Society

BCN .... Best Chance Network

BIRADS .... Breast Imaging Reporting and Data System

BRCA .... Breast Cancer

BSE .... Breast Self-Examination

CBE .... Clinical Breast Exam

DCIS .... Ductal Carcinoma in Situ

EA .... European American

ER .... Estrogen Receptors

FDA .... Food and Drug Administration

GIS .... Geographic Information System

HR .... Hazard Ratio

HER2 .... Human Epidermal Growth Factor Receptor 2

LCIS .... Lobular Carcinoma in Situ

MHT .... Menopausal Hormone Therapy

MUA .... Medically Underserved Areas

NAACCR .... North American Association of Central Cancer Registries

NBCCEDP .... National Breast and Cervical Early Detection Program

OR .... Odds Ratio

PR .... Progesterone Receptor

SCCCR .... South Carolina Central Cancer Registry

SD.. Standard Deviation

SC DHEC.................. South Carolina's Department of Health and Environmental Control

SEER .... Surveillance, Epidemiology, and End Results

SES .... Socioeconomic Status

CHAPTER 1

INTRODUCTION

This chapter presents an overview of the problem; it begins with breast cancer statistics, mammography screening and utilization, follow-up after abnormal mammography, breast cancer stage at diagnosis, breast cancer problem in South Carolina, the National Breast and Cervical Cancer Early Detection Program (NBCCEDP), and an introduction to Geographic Information System (GIS). It continues with the purpose and specific aims, and the significant of the dissertation. Lastly, it ends with a summary of the chapter.

Statement of the Problem

Breast Cancer Statistics

Breast cancer is the most common type of cancer among women and ranks second as a cause of death from cancer in the United States (1). About 1 in 8 women born today will be diagnosed with breast cancer at some point during their lifetime (2). In 2012, the American Cancer Society estimates approximately 226,870 new cases and 39,920 deaths from breast cancer among women in the United States (1). From 2002-2006, the age-adjusted incidence of breast cancer was 121.8 per 100,000 women and the age-adjusted death rate was 24.5 per 100,000 women per year (3). Among women in the United States, the overall 5-year relative survival rate is ~90%, a significant improvement from 63% in the early 1960s (1).

Mammography Screening and Utilization

Death rates for breast cancer have steadily decreased in women due to earlier detection, such as mammography, and improved treatments (4-9). Mammography is the single most effective method of early detection for breast cancer. It can identify the cancer at an early stage, when treatment is more effective (1). The American Cancer Society screening guidelines recommend that average-risk women aged 40 and older receive mammography screening on an annual basis (1). About 38%-54% of women do not maintain annual adherence to screening mammograms (10, 11), and only 49% having received screening when using a biennial schedule (11). Annual mammography with adequate follow-up is estimated to result in reductions in mortality ranging from 25% to 44% (6, 7, 12-15). Mammography is a highly accurate screening tool, but like most medical tests, it does not have perfect sensitivity and specificity. Generally, reported positive predictive values ranges from 78% to 90% (1, 16, 17). One drawback of mammography is the false positive results. One large study found that over a 10-year period of annual mammogram screenings, the chance of having a false positive result was close to 50% (18).

Despite the benefit of mammography, many women are not up-to-date on screening (10, 11, 19, 20) and in fact, mammography uses have been declining in the past years (10, 21-23). This indicator of inadequate screening is associated with late stage breast cancer at diagnosis (24-26), which contributes largely to survival and mortality. Factors associated with mammography utilization have been scrutinized in numerous studies, which includes patients characteristics, socioeconomic status, insurance status, having a primary health care provider, recommendations for screening from primary

health care providers, lack of transportation/or time and distance, language barriers, concern about the effects of radiation, and fear of cancer (27-36).

Abnormal Mammography and Follow-up

Mammography screening for breast cancer reduces mortality from breast cancer when women receive timely follow-up and appropriate treatment (7, 15). Mammogram results are interpreted by radiologists using the American College of Radiologist Breast Imaging Reporting and Data System (BIRADS™) categories: 0 – “incomplete”; 1-“Negative”; 2-“Probably benign”; 3-“Suspicious”; 4-“Suspicious abnormality”; 5-Highly suspicious of malignancy”; and 6-“Known biopsy proven malignancy” (37). A category of 3, 4, and 5 will require additional diagnostic procedures to determine the presence or absence of the disease (37). About 9%-15% of women who receive mammography screening have abnormal finding that require further testing (38), and approximately 30%-50% never return for follow-up testing (39, 40). Incomplete screening and delayed abnormal follow-up can negate the potential benefits of identifying breast cancer at an early stage, where treatment is more effective and cure is more likely. Though many factors predicting incomplete and delayed abnormal breast cancer screening follow-up have been examined (26, 39-50), none has looked at distance to mammography facilities and completion of abnormal breast cancer screening follow-up.

Breast Cancer Stage of Diagnosis

Breast cancer stage at diagnosis is an important factor in survival and mortality. The 5-year relative survival rates among women whose breast cancer is diagnosed while in the regional stage are nearly four times greater than those of women whose cancer has

spread to distant (distant stage) lymph nodes or organs at the time of diagnosis (84% vs. 23%) (2). Studies consistently show that low-income, health insurance status, community poverty, and racial/ethnic minorities are more likely to be diagnosed with late-stage breast cancer (51-57). Over the past decades, researchers have also explored geographic proximity to health care or mammography locations and breast cancer stage at diagnosis (58-66), which has found to be an important predictor of breast cancer stage at diagnosis.

Breast Cancer in South Carolina

In 2012, the American Cancer Society estimated 3,570 women in the state of South Carolina were diagnosed with breast cancer and about 18% of the diagnosed women died of the disease (1). Breast cancer is the most common cancer diagnosed and is the second largest cause of cancer deaths among women in South Carolina (67). Statewide, the age-adjusted incidence of breast cancer from 2002-2006 have remained stable at around 119 per 100,000 women (1), with a higher age-adjusted incidence among European American women compared to African American women (127.6 and 111.3 per 100,000 women, respectively) (68). The burden of this disease is heavily on low income, uninsured African American (51, 69).

The National Breast and Cervical Cancer Early Detection Program (NBCCEDP) and South Carolina's Best Chance Network (BCN)

Minority, uninsured, and lower socioeconomic status women often do not have access to early detection (28, 36). These women are less likely to utilize mammography screening (28-32, 36), less likely to have timely and complete follow-up after an

abnormal mammography screening (39-41, 44), more likely to be diagnosed with advanced-stage breast cancer (51, 54, 56), and have poorer survival (51-53). To reduce the disproportionate burden of breast cancer and cervical cancer among these women, the U.S. Congress authorized the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) in 1990 (70). Since then, the program has established service delivery and ensures timely and complete diagnostic follow-up and treatment initiation for underserved women screened through the program.

South Carolina's NBCCEDP, also known as the Best Chance Network (BCN), is a network of public and private partnerships with more than 250 health care providers offering screening and follow-up services to disadvantaged women in the State. At close to 18% (71), South Carolina has one of the highest proportions of uninsured women in the nation, which majorities of these women are eligible to enroll in the program. The majority (60%) of the women in BCN are African American and reside in rural counties (72). The BCN offers an unique opportunity to explore the relationship between distance to the provider, mammography facilities, and breast cancer morbidity and mortality among women with equal access to screening services.

Geographical Information Systems (GIS)

Geographical Information System (GIS) is a system designed to input, store, edit, retrieve, analyze, and output geographic data information (73). It allows individuals to view, understand, question, interpret, and visualize data in various ways that reveal relationships, patterns, and trends in the forms of map, reports, and charts (74). The application of GIS has been used by health care researchers for decades and in recent

years, it has grown rapidly. GIS can be a useful tool to help understand the spatial organization of providers, mammography facilities, and its relationship to access and utilization, breast cancer stage at diagnosis, and mortality. Understanding the geographical and social connections between providers and the locations of mammography facilities is important for developing effective healthcare interventions to reduce breast cancer morbidity and mortality.

Purpose and Specific Aims

The purpose of this dissertation was to examine whether travel distance to the provider, diagnosing mammography facility, and closest mammography facility are associated with completion of abnormal mammography follow-up, breast cancer stage at diagnosis and mortality among women in South Carolina's National Breast and Cervical Cancer Early Detection Program (NBCCEDP), Best Chance Network (BCN).

Aim 1: Determine the relationship between geographic proximity to the provider, diagnosing mammography facility, and closest mammography facility and completion of abnormal mammography follow-up among women in the Best Chance Network (BCN).
R**esearch Question 1:** Are there associations between distance to the provider, diagnosing mammography facility, closest mammography facility, and completion of abnormal mammography follow-up among women in the BCN?

Aim 2: Evaluate the role of distance to the provider, diagnosing mammography facility, closest mammography, and breast cancer stage at diagnosis among women in the BCN.
Research Question 2: Does living further from the provider, diagnosing mammography facility, and closest mammography increase the risk of having advanced stage of breast

cancer at diagnosis among women in the BCN? Also, is there a difference by race/ethnicity?

Aim 3: Evaluate the role of distance to the screening provider, mammography facility, and mortality among women in the BCN.

Research Question 3: Does living further from the provider and closest mammography facility increase the risk of breast cancer mortality among women in the BCN? Also, is there a difference by race/ethnicity?

Significant of Research

Breast cancer is a major contributor to morbidity and mortality among women in South Carolina and nationally. Among other factors, timely follow-up of an abnormal mammogram and breast cancer stage at diagnosis contribute largely to breast cancer morbidity and mortality. This study examined some important predictors, distance to the provider, diagnosing mammography facility, closest mammography facility, and its relationship with completion of abnormal mammography follow-up and breast cancer stage at diagnosis and mortality among low socioeconomic status women in South Carolina. This study contributes to the understanding of population-level barriers to abnormal follow-up and breast cancer stage at diagnosis, which may guide policy development and the development of effective programs to reduce breast cancer morbidity and mortality. From a recent review of the literature, there has been no study examining distance to the provider, mammography facilities, and its effect on completion of abnormal follow-up and breast cancer stage at diagnosis and mortality among women

in South Carolina. This study adds to the breast cancer disparities research in South Carolina.

Summary

Among women in the United States, breast cancer is most common cancer and the second leading cause of death (1). The American Cancer Society estimated over 226,870 women were diagnosed with breast cancer in 2012, and about 18% of them died of the disease (1). Mammography is the single most effective screening tool for early detection of breast cancer. Mammography screening for breast cancer reduces mortality from breast cancer when women receive timely follow-up and appropriate treatment. With all the benefits of mammography, many women are not up-to-date on screening and not maintaining annual adherence to screening mammograms (10, 11, 19, 20).

Breast cancer stage at diagnosis is an important factor in survival and mortality. Studies consistently show that low-income, health insurance status, community poverty, and racial/ethnic minorities are more likely to be diagnosed with late-stage breast cancer (53-59); Women with these factors are also less likely to utilize mammography screening (28-32, 36), less likely to have timely and complete follow-up after an abnormal mammography screening (39-41, 44), and have poorer survival (51-53). Understanding the geographical and social connections between providers, mammography utilization, and the locations of mammography facilities are important for the development of effective healthcare interventions to reduce breast cancer morbidity and mortality. The objective of this dissertation was to examine whether travel distance to provider, diagnosing mammography facility, and closest mammography facility affect completion

of abnormal mammography follow-up, stage of breast cancer at diagnosis and mortality among women who have equal access to screening in South Carolina's Best Chance Network.

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CHAPTER 2

BACKGROUND & SIGNIFICANCE

This chapter presents a literature review of breast cancer, including Breast Cancer Incidence and Prevalence, Breast Cancer Risk Factors, Breast Cancer Morbidity and Mortality, and Breast Cancer Stage at Diagnosis. It follows with Mammography Screening Recommendations and Utilizations, Abnormal Mammography and Follow-up, Distance to Mammography Facilities and Breast Cancer Stages at Diagnosis, Breast Cancer Problem in South Carolina and the Best Chance Network (BCN), Geographic Information System and Measurement of Access to Health Care, and concludes with a summary of the chapter.

Breast Cancer Overview

Breast Cancer Incidence and Prevalence

Breast cancer is a type of cancer that starts in the breast where cells divide and grow without normal control. Among women in the United States, breast cancer is the most commonly diagnosed cancer and is the second cause of cancer-related mortality (1, 2). About 12.1% of women born today will be diagnosed with breast cancer in their lifetime (3). The American Cancer Society (ACS) estimated 226,870 women in the United States were diagnosed with breast cancer and 39,920 died of this cancer in 2012 (1). From 2002-2006, the age-adjusted incidence of breast cancer was 121.8 per 100,000 women and the age-adjusted death rate was 24.5 per 100,000 women per year (4).

The incidence of breast cancer has been unstable in the last decades; from 1975-1980, the incidence decreased by 0.5% per year; between 1980-1987, the incidence increased by 4.0% per year, between 1987-1994, it decreased by 0.1% per year, between 1994-1999, the incidence increased by 1.6% per year, and from 1999-2006, breast cancer incidence decreased by 2.0% per year (2). The rapid increase of breast cancer incidence between 1980 and 1987 is most likely attributed to widespread use of mammography screening and increased detection of breast cancers at an early stage. The decrease from 1999-2006 may reflect reductions in the use of menopausal hormone therapy (MHT), following the publication of results from the Women's Health Initiative in 2002, which found that women using estrogen plus progestin had a 24% increase risk for breast cancer (5-6).

Breast cancer risk factors

There are several factors that are linked to breast cancer risk. Some factors affect risk greater than others and some are modifiable, while others are not. Some of the risk factors reported by the American Cancer Society include age, overweight, use of estrogen and progestin, physical inactivity, consumption of alcoholic beverages, high breast density, reproductive factors (long menstrual history, having no child, and having first child after age 30), family history of breast cancer, inherited genetic mutations in the breast cancer susceptibility genes BRCA1 and BRCA2, socioeconomic status, and race/ethnicity (1).

The risk of developing breast cancer increases with age. From birth through age 39, the probability of developing breast cancer is 0.43% (1 in 233 women); 3.75% (1 in

27 women) for ages 40 to 49; 3.40% (1 in 29 women) for ages 60 to 69; and 6.50% (1 in 15 women) for ages 70 and older (1). Obesity has shown to affect breast cancer risk. However, the risk is different for pre- and postmenopausal women; before menopause, obese women have a lower risk of developing breast cancer compared to healthy weight women. After menopause, being overweight increases the risk of developing breast cancer by 30 to 60%. (7-10). Postmenopausal hormones use, such as estrogen plus progestin, increases the risk of developing and dying from breast cancer (5, 6, 11-14). Beral et al. (14) found that women who use estrogen plus progestin for more than five years double their risk of developing breast cancer.

Physical activity is an important contributor to health outcome. For breast cancer, regular activity may help lower the risk (15, 16). In fact, regular exercise can lower breast cancer risk by about 20% (16). Studies have also shown that physical activity increases survival among women with breast cancer (17-18). Alcohol consumption is also associated with higher risk of developing breast cancer. The risk increases with the amount of alcohol a woman drinks. One large study found that daily consumption of about 10g (1 drink) was associated with a 9% increase in risk of breast cancer (19). Increasing the alcohol consumption to ≥30g/day (3+ drinks) was associated with a 43% increase in risk (19).

Breast density is the proportions of fat and tissue in the breast. Women with high breast density (greater tissue compared to fat) are at a higher risk of developing breast cancer (20, 21). One study found that women with 75% or more mammographic density reading had an odds of 4.7 (95% CI: 3.0-7.4) times the odds of breast cancer compared to women with less than 10% mammographic density (21).

Reproductive factors are some of the strongest risk factors for breast cancer development and accounts for nearly 50% of all breast cancer cases (1). Studies have shown that reproductive factors, such as long menstrual history, having no child, and having first child after age 30, are all strong risk factors for breast cancer (22-24). Women who had their first child after age 30 were 1.27 times likely to develop ductal breast cancer, 1.79 times for lobular breast cancer, and 1.66 times more likely to develop tublar breast cancer compared to women who had their first child before age 20 (24). Inherited genetic mutations in the breast cancer susceptibility genes BRCA1 and BRCA2 can also increase a women's risk for breast cancer; however, these mutations are rare (1% of the population) and accounts for 5%-10% of breast cancer cases (1). Family history of breast cancer increases the risk of developing breast cancer as well. A woman who has one immediate relative (mother, sister or daughter) with breast cancer increases her risk by two times; and with more than one immediate relative with the cancer, it increase the risk to four times higher compared to those with no family history (25, 26).

Women with higher SES (high income and/or high education level) have higher risk of developing breast cancer (27). There are many factors that may contribute to this association. Women with higher SES are more likely to have child at a later age, have fewer children, and also are more likely to use postmenopausal hormones compared to lower SES women (28-29). On the other hand, women with higher SES are less likely to die from breast cancer. One study found that women with no education beyond high school were 1.39 times more likely to die from breast cancer compared to women who were college graduates (30). Among all race/ethnicity, European American women have the highest incidence of breast cancer. From 2004-2008, the incidence rate of breast

cancer among European American was 127.3 per 100,000 women compared to 199.9 per 100,000 women for African American (3). However, African American women are more likely to die from breast cancer compared to European American women.

Breast Cancer Mortality

In 2012, an estimate of 39,920 women died of breast cancer (1). Though it is the second leading cause of cancer mortality among women, death rates have steadily decreased in the past decades (1, 2). Women younger than 50 years of age had a larger decrease than women older than 50 years of age (3.2% vs. 2.0% per year, respectively) (1). Early detection and improved treatment have contributed largely to this decrease in breast cancer and mortality in recent years.

Although overall death rates for breast cancer have declined in the past decades, the mortality rates differ among racial/ethnic groups and age groups. From 2002-2006, African American had the highest breast cancer death rates (33.0 per 100,000 women) compared to European American (23.9 per 100,000 women) (2, 3). Breast cancer deaths among African American women have also been declining at a slower rate compared to European American women (31). In the 1980s, death rates were similar for both African American and European American women; however, since the early 2000s, African American women had a 39% higher mortality rate compared to European American women (31). This disparity may be due to breast cancer tumor characteristics seen in African American. Breast cancers diagnosed in African American women are more likely to have higher grade, advanced stage, and an aggressive subtype, which all contribute largely to this mortality disparity (32, 33). Difference in access to and utilization of early

detection and treatments may also explain why African American women have higher mortality compared to European American women (34-36).

Age is also an important factor in breast cancer development and mortality. Women younger than 40 years of age have more aggressive breast cancer subtype, which is associated with higher mortality compared to older women (37, 38). Premenopausal women are also more likely to have aggressive subtype and are more likely to die from breast cancer compared to postmenopausal women (39).

Among women in the United States, the overall 5-year relative survival rate is ~90% (1). Survival rates vary considerably among racial/ethnicity, age, tumor characteristics, and social factors. The overall 5-year relative survival rate is much lower for African American women compared to European American women; from 1999-2006, the 5-year relative survival rate for breast cancer among African American women was 78%, a 13% lower compared to European American women (1). This difference can be attributed to both later stage at diagnosis and poorer stage-specific survival among African American women. From 2003-2007, the median age of mortality from breast cancer was 68 years of age (3). Majority (57.5%) of breast cancer mortality occurred in women 65 years old and above (3).

Breast Cancer Stage at Diagnosis

Stage of breast cancer is based on the size of the tumor, whether it has invaded nearby tissues, and whether it has spread within the breast or to other parts of the body (40). Breast cancer is categorized into stage 0 through stage IV. Stage 0 is carcinoma in situ, where the cancer cells have not spread outside of the ducts or lobules. Stage 0 is

classified into two types: ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS). DCIS is the earliest form of cancer where cells are still within a duct and have not invaded into the surrounding fatty breast tissue. LCIS is when abnormal cells are found in the lobules of the breast. It is usually not considered a cancer; however, it increases the risk of developing breast cancer. Stage 1 is the early stage of invasive breast cancer. Cancer in stage 1 has not spread to surrounding lymph nodes or outside of the breast. Stage 2 breast cancer is also considered an early stage cancer. Depending on the tumor characteristics, it divided into two stages: stages 2A and 2B. Stage 3 breast cancer is a more advanced stage of breast cancer. Stage 3 cancer is divided into three categories: Stage 3A, stage 3B, and stage 3C. Stage 3A is when the tumor is larger than 5 centimeters in diameter and has spread to the axillary lymph nodes. Stage 3B tumor can be any size; however, it has spread to the axillary lymph nodes and possibly other lymph nodes in the body. Stage 3C is the more aggressive type, which is present in adjoining tissue such as muscles or skin. Stage 4 breast cancer is the most advanced and aggressive of all stages. In this stage, the cancer has spread to other organs or tissues of the body, and most often these are the bones, lungs, liver, and brain (40).

The 5-year relative survival rates among women whose breast cancer is diagnosed while in the early stages have higher survival compared to those diagnosed in later stages. Among women diagnosed with breast cancer in stage 0, the 5-year relative survival rate is approximately 93% (41). Stage 1 has a 5-year relative survival rate of 88%, stage 2A 81%, stage 2B 74%, stage IIIA 67%, stage IIIB 41%, stage IIIC 49%, and stage IV breast cancer has a 5-year relative survival rate of 15% (41). Breast cancer stage at diagnosis is an important factor in survival and mortality among women.

Studies consistently show that low-income, health insurance status, community poverty, and racial/ethnic minorities are more likely to be diagnosed with late-stage breast cancer and have poorer survival (42-48). Examining seven state registries, Byers et al. (43) found that among 4,844 women diagnosed with breast cancer, those living in the lowest SES areas had substantially increased risk of breast cancer mortality (HR= 1.59, 95% CI:1.35-1.87) compared to women not in the lowest SES area. After adjusting for age and race/ethnicity, the risk of mortality was still significantly higher for women living in low SES areas (HR=1.33, 95% CI: 1.11-1.58). Clegg et al. (47) found from 11 Surveillance, Epidemiology, and End Results (SEER) cancer registries that lower income women were statically significantly associated with an increased risk of being diagnosed with a late-stage breast cancer (p=0.02). The odds for late-stage breast cancer for the two lowest income categories were 2.3 and 1.8 times higher than those women in the highest income group, respectively (47). The author also found that non-Hispanic black females were 2.2 times more likely to be diagnosed with late-stage breast cancer compared to non-Hispanic white females. Smith et al. (42) examined women participating in the National Breast and Cervical Cancer Early Detection Program and found that African American women with late-stage breast cancer at diagnosis and negative ER/PR hormone receptor were at increased risk of mortality compared to European American women. Barry and Been (46) conducted a study examining residential characteristics and late-stage breast and cervical cancer among women in the SEER registries. They found that women in three major metropolitan SEER areas (Atlanta, Georgia; Detroit, Michigan; and San Francisco, California) that resided in economically and socially distressed or

medically underserved areas (MUAs) were more likely to have late-stage breast cancer at diagnosis compared to those women who were not in those areas.

Mammography Screening Recommendations and Utilizations

Regularly breast cancer screening is the best way for women to reduce their risk of dying from breast cancer. In fact, death rates for breast cancer have steadily decreased in women due to earlier detection, such as mammography, and improved treatments (4-9). Breast self-examination (BSE), clinical breast exam (CBE), and mammography are the most widely used methods for breast cancer screening.

Breast self-examination is done by a woman examining her own breasts to detect for possible lumps, changes in size or shape of the breast, or any abnormality of the breast. Clinical breast exam is examination by a health care provider, who uses his or her hands to feel for lumps or other changes in the women's breast. A mammogram is an x-ray screening of the breast. Inside tissues of the breast are examined for abnormal changes. Mammography is the single most effective method of early detection for breast cancer. It can identify the cancer at an early stage, when treatment is more effective (1, 49). The American Cancer Society screening guidelines recommend that average-risk women aged 40 and older receive mammography screening on an annual basis; have clinical breast exam about every 3 years for women in their 20s and 30s and every year after age 40; and an annual breast self-exam as an option for women starting in their 20s (1).

Annual mammography with adequate follow-up is estimated to result in reductions in mortality ranging from 25% to 44% (50-55). Mammography is a highly

accurate screening tool, but like most medical tests, it does not have perfect sensitivity and specificity. Generally, reported positive predictive values ranges from 78% to 90% (1, 56, 57). One drawback of mammography is the false positive results. Elmore et al. (58) conducted a 10-year retrospective cohort study of breast-cancer screening and found that over the 10-year period of annual mammogram screenings among 2,400 women, the chance of having a false positive result was close to 50%.

Despite the benefit of mammography, many women are not up-to-date on screening (59-61) and, in fact, mammography uses have been declining in the past years (59, 62-64). About 38%-54% of women do not maintain annual adherence to screening mammograms (59, 60), and only 49% having received screening when using a biennial schedule (60). Inadequate screening is associated with late stage breast cancer at diagnosis (65-68), which contributes largely to survival and mortality.

Hahn et al. (66) found that among 829 women who had no mammograms in the past 5 years had 1.95 times the risk of developing stage III/IV breast cancer compared to those who had more than 2 mammograms in the past 5 years. They also found that the risk was higher for African American women compared to European American women; African American women had an odds of 3.57 (95% CI=2.26-5.65) of having stage III/IV compared to European women. In a large prospective cohort of over 1 million women, Smith-Bindman el al. (68) found that among women who had at least one mammogram between 1996 and 2002, African American women had higher risk of developing advanced-stage breast cancer compared to European American women.

Factors Associated with Mammography Utilization

Factors associated with mammography utilization have been scrutinized in numerous studies, which includes patients characteristics, socioeconomic status, insurance status, having a primary health care provider, recommendations for screening from primary health care providers, lack of transportation/or time and distance, language barriers, concern about the effects of radiation, and fear of cancer (69-78). A systematic review of 221 studies by Schueler, Chu and Smith-Bindman (70) found that physician access barriers were associated with not obtaining mammography. Not having a physician-recommend mammography and having no primary care provider were found to be highly predictive factors for not obtaining mammography (OR: 0.16, 95% CI 0.08-0.33 and OR: 0.47, 95% CI 0.39-0.57, respectively). Barr et al. (74) also concluded that the number of primary care and gynecology physician visits was strongly associated with having a subsequent mammogram.

Participation of healthcare facilities in encouraging breast cancer screening can be an important factor in increasing breast cancer screening. Quinley et al. (77) compared mammography screenings among women attending health facilities that send annual mammography reminders to those women who attend health facilities that do not send reminders. They found that among women who attend facilities that send annual reminders, 74% of the women received a second mammogram within 18 months compared to 67% for women who did not receive reminders.

Abnormal Mammography and Follow-up

Mammogram results are interpreted by radiologists using the American College of Radiologist Breast Imaging Reporting and Data System (BIRADS^{TM}) categories: 0 – “incomplete”; 1-“Negative”; 2-“Probably benign”; 3-“Suspicious”; 4-“Suspicious abnormality”; 5-Highly suspicious of malignancy”; and 6-“Known biopsy proven malignancy” (79). A category of 3, 4, and 5 will require additional diagnostic procedures to determine the presence or absence of the disease (79). Table 2.1 shows the BIRADS^{TM} categories and recommendations for the categories.

Table 2.1. Breast Imaging Reporting and Database System (BI-RADS^{TM})

Category	Meaning	Follow-up Recommendations
0	Assessment is Incomplete, need additional imaging evaluation	Additional imaging are needed before a final assessment can be assigned
1	Negative	Routine annual screening mammography
2	Probably benign	Routine annual screening mammography
3	Suspicious	Initial short-term follow up (usually 6-month examination)
4	Suspicious abnormality	Biopsy should be considered
5	Highly suspicious of malignancy	Requires biopsy or surgical treatment
6	Known biopsy proven malignancy	Definitive therapy

About 9%-15% of women who receive mammography screening have abnormal finding that require further testing (80, 81), and approximately 30%-50% never return for follow-up testing (82, 83). The patient, provider, and system can all contribute to adequate follow-up. Many factors contributing to inadequate or incomplete follow-up

have been examined (67, 84-100). These factors include: fear (100), language barrier (82, 89), patient anxiety (85, 89, 93), age (90, 95, 96, 98, 99), cost (90, 93), lack of provider (100), having case management (88, 91, 92), ethnicity (84, 94-96, 99, 100), education (86, 96, 98), and income (97, 99).

Though these factors may contribute largely to inadequate to abnormal-follow-up, there are inconsistent findings. Kerner et al. (87) found no association between SES variables and timely follow-up on abnormal mammography. One study looking at women participating in the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) also found no association between completion of recommended workup and race (99). Nevertheless, incomplete screening and delayed abnormal follow-up can negate the potential benefits of identifying breast cancer at an early stage, where treatment is more effective and cure is more likely. Of the many factors predicting incomplete and delayed abnormal breast cancer screening follow-up that have been examined, none has looked at distance to providers, mammography facilities, and completion of abnormal breast cancer screening follow-up. This present study will examine this structural and environmental factor that could affect the delay and completion of abnormal mammography follow-up.

Distance to Mammography Facilities and Breast Cancer Stages at Diagnosis

Studies consistently show that low-income, health insurance status, community poverty, and racial/ethnic minorities are more likely to be diagnosed with late-stage breast cancer (42-47). A multilevel approach using spatial methods has been widely used in breast cancer research to understand some of the disparities in morbidity and mortality.

A common spatial method that has been examined is spatial accessibility to healthcare facilities. Accessibility, such as long travel distance, can discourage women to seek routine preventive care or screening. In the past decades, researchers have explored geographic proximity to health care or mammography locations and breast cancer stage at diagnosis (101-109). However, finding has been inconsistent between the studies. There are six studies that found no association between travel distance to mammography and breast cancer stage at diagnosis (101-106); however, three studies found that there is an association (107-109).

Tarvo et al. (101) found no association between breast cancer stages at diagnosis and patients' residential address to nearby mammography facilities in Chicago. In their study, breast cancer stage was categorized as in situ, local, and distant. They calculated distance using street network from the residential address of each cancer case to each mammography facility. Instead of using the closest mammography, the authors used the mean distance to the five closest mammography facilities. While the author tried to account for choice and constraints that may exist in mammography facility availability to individuals, they found no association between travel distance and breast cancer stages.

In Virginia, Schroen and Lohr (102) found no relevant relationship between travel distance to the nearest mammography facility and invasive tumor size. For the outcome, tumor size was used instead of cancer stages. Distance was calculated from patients' home location to the nearest mammography facility. After adjusting for age, race, income, they found no association between travel distance and late stage breast cancer at diagnosis.

Wang et al. (103) conducted a similar study in Illinois and found no statistically significant association between travel time to mammography facilities and stage of breast cancer at diagnosis. In this study, each cancer case was geocoded to the county and zip code of residence rather than patients' residential address. They defined late-stage breast cancer as diagnosis in stages 2 through 7. Though there was no association between travel time to mammography facilities and breast cancer stage at diagnosis, they did found an association between geographical access to primary care physician and late-stage breast cancer. The authors noted the no association finding may be due to the homogeneous population (close proximity) to mammography. The average estimated travel time was fairly short in Illinois, which may conclude that travel time to mammography might not be a major issue in the studied population. This study has two limitations. First, they did not have information on patients' mammography utilization and, therefore, could not calculate distance to the actual mammography that the patients actually use. Second, patients' residence was geocoded to zip code centroids, which may not be an accurate estimate of travel time.

Three of the more recent studies from 2010-2011 also found no association between travel distance and breast cancer stage at diagnosis. A study in 2010 by Celaya et al. (104) found that among women in New Hampshire, there was no association between late-stage breast cancer and travel time to the nearest mammography facility. In this study late stage breast cancer was categorized at stages 2 and 4. They calculated proximity using both travel time and travel distance using road network and still found no association. They also found that urban/rural residence was not associated with late stage breast cancer in their population of study.

Onega et al. (105) studied this association in Washington in 2011 and also reported no significant association between travel time and breast cancer stage. Women with breast cancer stage 1, 2A, and 2B were examined in their study. They examined two outcomes: stage of breast cancer (stage 2B as late stage) and tumor size (≥2cm as late stage). They used travel time (in minutes) instead of distance (in miles) like some of the previous studies. With different outcome and travel distance measurement, they still found no association between travel distance and breast cancer stage at diagnosis. One major limitation to this study was that patients were limited only to women with early-stage breast cancer (1, 2A, and 2B).

One of the more recent study by Henry et al. (106) used 10 population-based state cancer registries (Arkansas, California, Iowa, Idaho, Kentucky, North Carolina, New Hampshire, New Jersey, New York, and Oregon) to study whether there is an association between travel distance and breast cancer stage at diagnosis. From the 10 cancer registries, there were 161,619 women in the study. Tumors that were in situ or localized stages were considered “early stage” and regional or distant stages were considered “late stage”. This is the first study to measure both travel distance from the patients’ residence to the closest mammography facility and to their diagnosing facility. They found no association to the nearest mammography facility. However, when using distance to the diagnosing facility, they found weak evidence that shorter travel time was associated with late stage breast cancer at diagnosis; however, the direction of the effect was the opposite of what is expected. The odds of having late stage breast cancer at diagnosis was lower for women with longer travel time to their diagnosing facility. The odds of late stage breast cancer at diagnosis for women who lived 40-50 minutes from their diagnosing

facility was 0.83 times the odds for women who lived <10 minutes. The trend was similar as the distance from the diagnosing facility increased.

The first study to find an association between travel distance and breast cancer stage at diagnosis was conducted in Los Angeles by Gumpertz et al. (107). In this study, stage of breast cancer was categorized as “advanced disease” if the stage of breast cancer at diagnosis is regional with tumor diameter < 10 cm or as distant with any tumor size. They used Euclidean (straight line) distance from the patients’ census tract centroid to the nearest mammography facility. Distance was broken down into two categories: 10km vs. 1km. After adjusted for neighborhood characteristics and tumor biology, distance from the census tract centroid to the nearest mammography facility was a significant predictor of advanced stage of breast cancer; however, this association was only found for Hispanic and White women. This study used census tract centroids to calculate the distance to the mammography facility, which may not be an accurate measurement of travel distance. They also did not use road network, therefore, distance calculated may be under estimated.

Another study that found an association between travel distance and breast cancer stage was done in Kentucky by Huang et al. (108) in 2009. Tumors that were in situ, or stage 1 or 2 were considered “early stage,” and tumors stage 3 or 4 were considered “advanced stage.” They calculated travel distances from patients’ zip code centroid to the nearest mammogram facility along the road network. Adjusting for various characteristics, they found that women living 15+ miles from the nearest mammography was 1.48 times more likely to have advanced stage of breast cancer at diagnosis compared to women who lived less than 15 miles. There are two limitations to this study.

First, this study assumes that women had access to mammogram centers closest to their homes, which may not always be true due to other circumstances. The other is using zip code centroids as patients' place of residence; this may not accurately measure true residence, which may affect true distance calculation from home to nearest mammography facility.

The last and more recent study by Dai (109) in 2010 found that there is an association between travel distance and late-stage breast cancer at diagnosis in Detroit. In this study, early stage breast cancer was defined as "in situ" and "localized," and late stage was defined as "regional" and "distant." The author used zip code centroids of patients' residence to calculate the distance to the nearest mammography and primary care facilities. Controlling for socioeconomic factors at ZIP code level, the author found that women living in areas with greater black segregation and poorer mammography access significantly increases the risk of late stage breast cancer at diagnosis. Compared to Wang et a. (103) who found association between primary care access and late-stage breast cancer, this study found no association between this relationship. Like previous studies, a limitation of this study is the use of ZIP code of residence at diagnosis and not using network road to calculate the distance.

All of these studies, except one (106), had no information on patients' mammography utilization. Using the nearest mammography facility may not represent patient utilization. A patient may not utilize the nearest facility due to personal and neighborhood characteristics, such as hours of operation, insurance requirement, and location to work. Relying on the closest mammography facility may underestimate the

true travel distance between patients' residence and actual mammography usage if the closest facility is not the one being utilized.

When mammographic facilities are not conveniently located, women may not have regular mammograms, which may result in diagnosis of breast cancer at later stage. Geographic proximity is an important factor in determining breast cancer stage at diagnosis; however, studies have found inconsistent association between this relationship. From the above studies, there were differences and similarity in the methodology used in examining breast cancer stage and travel distance to mammography facility. Even though, some studies used the more precise measurement of distance (patients' residence at diagnosis and road network), they still found no association between breast cancer stage at diagnosis and travel distance. Others used zip code centroids to calculate the distance travel and found association between this relationship. The inconsistent results in the literature highlight the need for further research to determine whether women living further from mammography facilities are at an increased risk of having late stage breast cancer at diagnosis. This dissertation examines this relationship in South Carolina among women participating in the National Breast and Cervical Cancer Early Detection Program (NBCCEDP).

Breast Cancer Problem in South Carolina and the Best Chance Network (BCN)

South Carolina is a relatively rural state with approximately 30% African American (110). The poverty rate in South Carolina from 2008-2009 is about 20%, with African American having the higher rate compared to European American (35% vs. 13%, respectively) (110). At close to 18% (111), South Carolina has one of the highest

proportions of uninsured women in the nation, which is a strong predictor of breast cancer mortality and morbidity (27, 28, 30, 47). Along with the appalling statistics of the state, South Carolina has some of the highest cancer statistics in the nation, especially breast cancer morbidity and mortality (112, 113).

In 2012, the American Cancer Society estimated 3,570 women in the state of South Carolina were diagnosed with breast cancer and about 660 women died of the disease (1). Breast cancer is most common cancer diagnosed and is the second largest cause of cancer deaths among women in South Carolina (112). Statewide, the age-adjusted incidence of breast cancer from 2002-2006 have remained stable at around 119 per 100,000 women (1), with a higher age-adjusted incidence among European American women compared to African American women (127.6 and 111.3 per 100,000 women, respectively) (114). The burden of this disease weighs heavily on low income, uninsured African American (42, 99).

To reduce the disproportionate burden of breast cancer and cervical cancer among women, the U.S. Congress authorized the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) in 1990 (115). Since then, the program has established service delivery and ensures timely and complete diagnostic follow-up and treatment initiation for underserved women screened through the program.

South Carolina's NBCCEDP, also known as the Best Chance Network (BCN), is a network of public and private partnerships with more than 250 health care providers offering screening and follow-up services to disadvantaged women in the State. South Carolina has one of the highest proportions of uninsured women in the nation, of which

majority of these women are eligible to enroll in the program. The majority (60%) of women in BCN are African American and reside in rural counties (111). The BCN offers an unique opportunity to explore the relationship between distance to the provider, mammography facilities, and breast cancer morbidity and mortality among women in South Carolina.

Geographic Information System and Measurement of Access to Health Care

Geographical Information System (GIS) is a system designed to input, store, edit, retrieve, analyze, and output geographic data information (116). It allows individuals to view, understand, question, interpret, and visualize data in various ways that reveal relationships, patterns, and trends in the forms of map, reports, and charts (117). The application of GIS has been used by health care researchers for decades and in recent years, it has grown rapidly. The capability of GIS has made it possible for health care researchers to spatially understand health issues such as health care distribution, access and utilization, disease risks related to environmental exposures, and morbidity and mortality, social demographic data, and morbidity and mortality (118-120).

In terms of health care accessibility, there are several measurements of accessibility. Distance to the nearest provider is one of the most commonly used measures of spatial accessibility in health care research. This is done by calculating the distance between patients' residence or centroid of a ZIP code and census tract to the nearest health care provider. There are three commonly used methods to measure this distance: i) Euclidean or straight line distance; ii) travel distance along a road network;

and iii) travel time along a road network (both taking account of traffic and not taking account of traffic) (121, 122).

The Euclidean distance measures straight-line distance from two points of interests. These points can be points, lines or polygons (121). This method has its advantage and disadvantage. The key advantage of using this method is that it is easy to calculate. The disadvantage is that it does not take into account the transportation network or topography of an area that might lengthen the distance traveled from one point to the other.

Travel distance along a road network or street distance is based on the network of streets that would be traveled from one location to another (122). This method offers a more accurate measure of the actual path between two points; therefore, it provides a more realistic measure of actual distance traveled than the Euclidean method. Travel time or driving time is similar to travel distance between two points, but is based on driving time on a road network. This process utilizes information about road length and average travel speeds along street segments (122).

In geographical access to health services, travel distance and travel time along the road network are recognized as the more appropriate measures of the travel effort actually experiences than the Eulicudean distance, which does not take into account of physical barriers (e.g. rivers or hills) and patchy road network (123). In fact, Shalid et al. (124) found that Euclidean distance tends to underestimate road distance and travel time when measuring the distance between patients' residence and health care facility.

Using GIS to estimate actual travel time by patients has shown good correlations. Haynes et al. (125) conducted a validation study comparing GIS estimates of travel distance with the actual times reported by 475 cancer patients who had travelled by car to attend clinics. The correlation between reported times and estimated travel times was 0.87, which is a moderately strong association. They also found that straight line distance and reported travel was moderately strong correlation ($r=0.85$, $p<0.001$).

GIS can be a useful tool to help understand the spatial organization of mammography facilities and its relationship to access and utilization of mammography, breast cancer stage at diagnosis, and mortality. Understanding the geographical and social connections between mammography utilization and the locations of mammography facilities are important for developing effective healthcare interventions to reduce breast cancer morbidity and mortality.

Summary

Among women in the United States, breast cancer is the most commonly diagnosed cancer and is the second cause of cancer-related mortality. In 2012, 226,870 women in the United States were diagnosed with breast cancer and 39,920 died as a result of this cancer. From 1999 to 2006, breast cancer rates had decreased by 2.0% per year, which may be due to the reduction in use of menopausal hormone therapy. There are several factors that are linked to breast cancer risk. Some factors affect risk greater than others and some are modifiable, while others are not.

Comparing to European American women, African American women had the highest breast cancer death rates (33.0 per 100,000 vs. 23.9 per 100,000). This disparity

may due to the breast cancer characteristics diagnosed among African American women. Breast cancer stage at diagnosis is an important factor in survival and mortality. The 5-year relative survival rates among women whose breast cancer is diagnosed while in the early stages have higher survival compared to those diagnosed in later stages. Regular breast cancer screening is the best way for women to reduce their risk of dying from breast cancer. In fact, annual mammography with adequate follow-up is estimated to result in reductions in mortality ranging from 25% to 44%.

Mammogram results are interpreted by radiologists using the American College of Radiologist Breast Imaging Reporting and Data System (BIRADS™). A category of 3, 4, and 5 will require additional diagnostic procedures to determine the presence or absence of the disease. About 9%-15% of women who receive mammography screening have abnormal finding that require further testing. The patient, provider, and system can all contribute to adequate follow-up.

Travel barriers, such as long travel distance, can discourage women to seek routine preventive care or screening. A common measurement of spatial accessibility is travel distance or travel time from a residential place to the closest facility. Geographic proximity may be an important factor in determining breast cancer stage at diagnosis; however, studies have found inconsistent association between this relationship. The inconsistent results in the literature highlight the need for further research.

South Carolina has some of the highest cancer statistics in the nation, especially breast cancer morbidity and mortality. South Carolina also has one of the highest proportions of uninsured women in the nation. South Carolina's NBCCEDP, also known

as the Best Chance Network (BCN), is a network of public and private partnerships with health care providers offering screening and follow-up services to disadvantaged women in the State. The BCN offers an unique opportunity to explore the relationship between distance to provider, mammography facilities, and breast cancer morbidity and mortality among women in South Carolina.

There are three commonly used methods to measure travel distance between two points of interest: i) Euclidean or straight line distance; ii) travel distance along a road network; and iii) travel time along a road network. GIS can be a useful tool to help understand the spatial organization of mammography facilities and its relationship to access and utilization of mammography, breast cancer stage at diagnosis, and mortality.

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CHAPTER 3

METHODOLOGY

This chapter describes the data source and methods that was used to conduct the study. The chapter begins with the study design and then goes on to describing the data source, participant inclusion criteria, outcome of interest, main exposure and covariates, and data analysis for each of the specific aims. Lastly, it ends with a summary of the chapter.

Study Design

This study was a retrospective cohort study that covers a period of 14 years between 1996 and 2009. The purpose was to investigate travel distances (to the screening provider, diagnosing mammography facility, and closest mammography facility) and completion of abnormal mammography follow-up, breast cancer stage at diagnosis, and mortality among women participating in the Best Chance Network. The present study used secondary data, collected for billing and national surveillance purposes, and no primary data collection among participants was required. Of note, all analytic work requiring the use of protected health information (e.g. distance calculation) was completed on-site at the South Carolina's Department of Health and Environmental Control (SC DHEC). Only a de-identified dataset was released from DHEC for analysis. Neither the PI nor any other investigators were able to view identifiable or restricted data.

Data Source and Data Analysis for Aims 1, 2 and 3

Aim 1: Determine the relationship between geographic proximity to the screening provider, closest mammography facility, diagnosing mammography facility, and completion of abnormal mammography follow-up among women in the Best Chance Network (BCN).

R**esearch Question 1: Are there associations between travel distance to the screening provider, closest mammography facility, diagnosing mammography facility, and completion of abnormal mammography follow-up among women in the BCN?**

For aim 1, the dataset source came from the South Carolina Best Chance Network. The program is part of the National Breast and Cervical Cancer Early Detection Program (NBCCEDP), which began in 1990 (1). It is a network of public and private partnerships with more than 250 health care providers offering service delivery and ensures timely and complete diagnostic follow-up and treatment initiation for underserved women screened through the program. Over the past five years (2005-2010) the program had served over 36,500 women in the State (2).

Mammogram results are interpreted by radiologists using the American College of Radiologist Breast Imaging Reporting and Data System (BIRADS^{TM}) categories: 0 – "incomplete"; 1-"Negative"; 2-"Probably benign"; 3-"Suspicious"; 4-"Suspicious abnormality"; 5-Highly suspicious of malignancy"; and 6-"Known biopsy proven malignancy" (3). A category of 4 and 5 will require additional diagnostic procedures to determine the presence or absence of the disease. All participants with abnormal mammography are provided with case management services, which work with the

participant to help her receive follow-up diagnostic services within 60 days. In the last five years (July 2005-June 2010), the Best Chance Network performed over 40,100 mammography screening and 5,241 of them were abnormal or incomplete results (2).

Inclusion Criteria for Aim 1

Women included in the dataset include:

- Enrolled in BCN between 1996 and 2009
- Having an abnormal mammogram, a BIRADS category of 4 or 5
- Having diagnostic work-up planned for breast cancer
- Having status and date of final diagnosis record
- Known screening provider
- Residence address is not a PO Box address

Aim 1 Outcome of Interest

The dependent variable for aim 1 was time-to-resolution or completion of abnormal mammogram follow-up. The measure of time was the number of days between the first mammogram and the date that the follow-up status was finalized (work-up completed, refused, or lost-to-follow up). A completed work-up is designated when the diagnostic testing is complete and a final diagnosis has been made (benign or malignant breast cancer). Refused work-up indicates a woman had her diagnostic work-up performed by another provider. A loss-to-follow up status indicates that the woman died, moved before her work-up started, or BCN could not make contact with the patient.

Aim 1 Main Exposure and Covariates

There were three main exposure variables for aim 1: There were three main exposure variables of interest: travel distance to the screening provider, travel distance to the diagnosing mammogram facility, and travel distance to the nearest mammography facility. All three distance calculations were calculated along a road network from patients' residence to the facility of interest. Confounders and effect modifiers included age, race, previous mammogram, yearly family income, and insurance status at time of visit with the BCN.

Data Analysis

GIS Approach

Mammography facilities, screening providers, and patients' residence were geocoded to the exact street address of location. The geocoded addresses (latitudes and longitudes) were used to calculate the three distances (in miles) between residence and the diagnosing mammography facility, screening provider, and the nearest mammography facility. All geocoding of addresses was done using ArcGIS (ESRI, Redlands, CA). Distance calculations were performed by using the Network Analyst tool function in ArcGIS. Once the distance variables were calculated, a de-identified dataset was exported to SAS for analyses. All GIS analyses of this study were done on-site at SC DHEC.

Statistical Methods

Descriptive statistics were calculated for all characteristic variables. Chi-square test and t-test were used to examine the bivariate associations between demographic and race variables. The median days and distances from the abnormal mammogram to diagnostic resolution were assessed with Kaplan-Meier survival method. Wilcoxon test of equality over strata was used to test for statistical significant between the distances.

Cox proportional hazard modeling was used to assess the relationship between work-up completion and travel distance to the screening provider and mammography facility. Women whose final status was recorded as refused or loss-to-follow up were considered censored observations. The proportional hazards assumption was examined through the logarithm of negative logarithm of survival probability with logarithm of time and the Schoenfeld residuals were further evaluated to confirm that there were no violations of the assumption. All analyses were performed using SAS version 9.3 (Cary, NC). A two-sided alpha level of 0.05 was used to determine significant for all tests.

Aim 2: 1) Investigate whether travel distance to the screening provider and mammography facility are associated with breast cancer stage at diagnosis among women participating in South Carolina's BCN, 2) examine whether there are racial disparities in the distribution of breast cancer stage at diagnosis among BCN participants, and 3) examine whether there are any differences in the distribution of breast cancer stage at diagnosis among BCN participants and non-BCN participants?

Research Question 2: Does living further from the screening provider, diagnosing mammography facility, and diagnosing mammography facility increase the risk of being diagnosed with a more advanced stage of breast cancer at diagnosis among women in the BCN? Also, is there a difference by race/ethnicity? Are there significant differences in the distribution of breast cancer stage at diagnosis among BCN and non-BCN women in the State of South Carolina?

The South Carolina Central Cancer Registry is a population-based data system that collects cancer statistics in the state of South Carolina. From the last audit, the registry has a completeness rate of 96.9% and an accuracy rate of 96.4%, both of which exceeded the national standard of 95%. SCCCR also maintains a "Gold Certification" from the North American Association of Central Cancer Registries (NAACCR) (4). Thus, the data are of high quality, validity, and completeness. For aim 2, the dataset source came from both the BCN and SCCCR. SCCCR did the data linkage to the BCN data. This data linkage allowed the identification of BCN breast cancer cases in SCCCR, the screening providers, and the diagnosing mammography facility. To compare breast cancer stage at diagnosis between BCN and non-BCN women, we identified non-BCN women with breast cancer from SCCCR between 1996 and 2009.

Inclusion Criteria for Aim 2

Women included in the dataset include:

- Is a first primary breast cancer case in SCCCR between 1996 and 2009
- Enrolled in BCN between 1996 and 2009
- Known breast cancer stage at diagnosis

- Known screening provider
- Residence address is not a PO Box address

Aim 2 Outcome of Interest

The outcome of interest was breast cancer stage at diagnosis. Using the Surveillance Epidemiology and End Results (SEER) Summary Staging guide, breast cancer stages were dichotomized into ‘early stage’ and ‘late stage’; *In situ* and localized (confined to primary site) stages were considered ‘early stage’ and regional (spread to regional lymph nodes) or distant (cancer has metastasized) stages were categorized as ‘late stage’.

Aim 2 Main Exposure and Covariates

As with aim 1, there were three main exposures: distance travel to the screening provider, distance travel to the diagnosing mammography facility, and distance travel to the nearest mammography facility. Confounders and effect modifiers included age, race, income at time of enrollment, insurance status at time visit with the BCN, and marital status. Race was categorized as EA and AA. Income at time of enrollment was categorized into three groups: <$10000, $10000-$19999, and >$20000. Health insurance status was categorized as Yes and No. Marital status was categorized into five groups: single, married, separated/divorced, widowed, and unknown.

Data Analysis

GIS Approach and Statistics Methods

As with aim one, distance calculations and goecoding were done on-site at SC DHEC. A de-identified dataset was exported to SAS for analyses. Descriptive statistics were performed for all characteristic variables. Chi-square test and t-test were used to test for differences between demographic and race variables. Chi-square was also used to compare breast cancer stage at diagnosis between BCN and non-BCN women. Multivariable logistic regression was used to assess the association between travel distance (to the screening provider, diagnosing mammography facility, and closest mammography facility) and stage of breast cancer at diagnosis. To assess whether travel distance was influenced by race, an interaction term was created between travel distance and race in each of the model (travel distance to screening provider-race, travel distance to diagnosing mammography facility-race, and travel distance to closest mammography facility-race). All distances to the health facilities were broken into < 5 miles, 5-<10 miles, 10-<15 miles, and 15+ miles for statistical analysis. All analyses were performed using SAS version 9.3 (Cary, NC). A two-sided alpha level of 0.05 was used to determine significance for all tests.

Aim 3: Evaluate the role of distance to the screening provider, nearest mammography facility, and mortality among women in the BCN.

Research Question 3: Does living further from the screening provider and closest mammography facility increase the risk of breast cancer mortality? Also, is there a difference by race/ethnicity?

For aim 3, the dataset source was the same dataset as in aim 2 (linkage between SCCCR and BCN).

Inclusion Criteria for Aim 3

Women included in the dataset include:

- Is a first primary breast cancer case in SCCCR between 1996 and 2009
- Known year of diagnosis
- Known screening provider
- Enrolled in BCN between 1996 and 2009
- Residence address is not a PO Box address

Aim 3 Outcome of Interest

The outcome of interest was breast cancer-specific and all-cause mortality. To determine breast cancer-specific mortality, we looked at the “Sequence Number” and the “Cause of Death” from the cancer registry data. If the “Sequence Number” was “00”, meaning that the subject had one malignant primary in her lifetime, and the “Cause of Death” was “Cancer”, then the death was related to breast cancer. If the subject died of any cause of death, including breast cancer, then the death was considered all-cause mortality.

Aim 3 Main Exposure and Covariates

For aim 3, there were three main exposures: distance travel to the screening provider, distance travel to the nearest mammography facility, and distance travel to the diagnosing mammography facility. Patients’ characteristics were obtained from the BCN

and SCCCR, which included age, race, breast cancer stage, estrogen receptor status, marital status, health insurance, income, and first course of treatment. Breast cancer stage at diagnosis was categorized as *in-situ*, localized, regional, and distant. Estrogen receptor (ER) status was categorized as positive, negative, and borderline. Income at time of enrollment was categorized into three groups: <$10000, $10000-$19999, and >$20000. Health insurance status was categorized as Yes or No. Marital status was categorized into married or not married. Cancer treatments were categorized as surgery, radiation, chemotherapy, hormonal therapy, and none.

Data Analysis

GIS Approach and Statistics Methods

As with aims 1 and 2, geocoding and distance calculations were done on-site at SC DHEC and only a de-identified dataset was given to the researcher for analyses. Descriptive statistics were calculated for all characteristics variables. Chi-square tests and t-tests were used to examine the associations between characteristics variables and race. Survival probabilities for breast cancer-specific and all-cause mortality were examined using Kaplan-Meier survival method. Cox proportional hazard modeling was used to assess the relationship between mortality and travel distance to the screening referral provider, diagnosing mammography facility, and closest mammography facility. To assess whether travel distance was influenced by race, we created an interaction term between travel distance and race in each of the Cox proportional hazard model (travel distance to screening provider-race, travel distance to diagnosing mammography facility-

race, and travel distance to closest mammography facility-race). Due to low sample size, all distances were categorized into <10 miles and 10+ miles for analysis.

Individuals not found to be deceased at the end of the time period, December 31, 2009, were considered to be alive at the time of censoring. For breast cancer specific mortality, non-cancer cause of death and cancer death other than breast cancer were also considered censored. The proportional hazards assumption was examined through the logarithm of negative logarithm of survival probability with logarithm of time and the Schoenfeld residuals were further evaluated to confirm that there were no violations of the assumption. Missing data were excluded from analyses. All analyses were done using SAS statistical software version 9.3 (Cary, NC). All statistical tests were 2-sided with a P-value of ≤ 0.05 used to determine statistical significance.

Summary

This study used 14 years of data (1996-2009) to investigate the relationship between three types of travel distances (to the screening provider, diagnosing mammography facility, and closest mammography) and completion of abnormal mammography follow-up, breast cancer stage at diagnosis, and mortality among women participating in South Carolina's Best Chance Network. Data source for aim one came from BCN and for aims two and three, the data source came from a linkage between SCCCR and BCN. Geocoding and distance calculations were performed on-site at the SC DHEC. Only a de-identified dataset was released from DHEC for analyses. All data analyses were performed using SAS v. 9.3.

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CHAPTER 4

TRAVEL DISTANCE TO SCREENING FACILITIES AND COMPLETION OF ABNORMAL MAMMOGRAPHY FOLLOW-UP AMONG DISADVANTAGED WOMEN[1]

[1] Khang, L., S.A. Adams, S.E. Steck, J. Zhang, S. Xirasagar, D. Lydiard. To be submitted to *Cancer Epidemiology Biomarkers and Prevention* or *Breast Cancer Research.*

Abstract

Introduction: Breast cancer is the most common cancer diagnosed and is the second leading cause of cancer deaths among women in South Carolina. Annual mammography, with timely and complete follow-up of abnormal mammogram, improves breast cancer prognosis and survival. Though many studies have examined factors in predicting incomplete and delay in abnormal mammogram follow-up, none has used geospatial methods to examine these factors. Consequently, the purpose of this study was to examine the relationship between travel distance to the screening provider, mammography facility, and completion of abnormal mammogram follow-up among disadvantaged women in South Carolina. **Methods:** Women participating in South Carolina's Best Chance Network between 1996 and 2009 with abnormal mammogram (BI-RADS category of 4 or 5) were included in the study. Racial differences in characteristics and completion of abnormal mammogram follow-up were tested using chi-square and t-tests. Kaplan-Meier survival method was used to compute time to completion of abnormal mammogram follow-up and Cox proportional hazard modeling was used to assess the relationship between work-up completion and travel distance to screening provider and mammography facility. **Results:** Among 1,388 women with mammography abnormalities, more than 95% achieved completion in follow-up. There was no significant association between race and overall completion of abnormal mammogram work-up. However, there was significant difference in time to completion of abnormal mammogram work-up and race; African American women had longer time to completion compared to European American women. Accounting for race, age, previous mammograms, income, and insurance status, women who lived closest to their

diagnosing mammography facility were more likely to complete their work-up compared to those who lived the farthest (HR=1.41; 95% CI=1.00-1.80). **Conclusion:** There is no racial disparity in the overall completion of abnormal mammogram follow-up among women in the Best Chance Network. However, distance to the diagnosing mammography facility plays a role on the completion of abnormal mammogram work-up and days to completion of the work-up, which was longer for African American women.

Introduction

Breast cancer is the most commonly diagnosed cancer and is the second cause of cancer-related mortality among women in the United States (1). Mammography is the single most effective method of early detection of breast cancer; it can identify the cancer at an early stage, when treatment is more effective (2). The American Cancer Society screening guidelines recommend that average-risk women aged 40 and older receive mammography screening on an annual basis (1). Annual mammography with adequate follow-up is estimated to result in reductions in mortality ranging from 25% to 44% (3-7). Despite the benefit of mammography, many women are not up-to-date on screening (8-10) and about 38%-54% do not maintain annual adherence to screening mammograms (8, 9). Inadequate screening and follow-up are associated with late stage breast cancer at diagnosis (10-14), which lead to poor survival.

About 9%-15% of women who receive mammography screening have an abnormal finding that require further testing (15, 16), and approximately 30%-50% will delay follow-up testing (17, 18). Women who delay follow-up testing increase the risk of having larger tumor size, late-stage breast cancer at diagnosis, and poorer prognosis.

Factors contributing to inadequate or incomplete abnormal mammogram follow-up include: fear (19), language barrier (20), race/ethnicity (21-25), lack of provider (25), income level (24, 26), and education (27).

South Carolina is a relatively rural state with approximately 30% African American representation (28). The poverty rate in South Carolina from 2008-2009 is about 20%, with African Americans having a higher rate compared to European Americans (35% vs. 13%, respectively) (28). At close to 18% (29), South Carolina has one of the highest proportions of uninsured women in the nation. Breast cancer is the 3rd most common cancer diagnosed and is the second leading cause of cancer deaths among women in South Carolina (30).

To reduce the disproportionate burden of breast cancer and ensure adequate follow-up from abnormal mammograms among disadvantaged women in South Carolina, the Best Chance Network (BCN), which is the state program of the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) was established in 1991. The program has established service delivery and ensures timely and complete diagnostic follow-up and treatment initiation for underserved women screened through the program. Though many studies have examined factors in predicting incomplete and delay in abnormal mammogram follow-up (19-27), none have used geospatial methods to examine factors related to distance to screening facilities. The purpose of this study was to examine the relationship between travel distance to the screening provider, diagnosing mammography facility, closest mammography facility, and completion of abnormal mammogram follow-up among women participating in the Best Chance Network.

Methods

Study Setting/Participants

Study participants were women from the Best Chance Network of South Carolina. The program provides free mammograms, clinical breast exams, Pap tests, pelvic exams, diagnostic procedures, case management, community education on breast/cervical cancer and early detection for underserved women aged 47-64 years, who are at or below 200% of the Federal trade poverty level, and those who lack insurance or have insurance that only covers hospital care. BCN is a network that consists of public and private partnerships between federally-funded primary care centers, private physicians, laboratories, university sponsored clinics, free clinics, regional medical centers, and radiology facilities. In the last five years (January 2007-December 2011), the BCN has performed 24,917 mammograms to eligible women in the state (31). .

Mammogram results are interpreted by radiologists using the American College of Radiologist Breast Imaging Reporting and Data System (BIRADS^{TM}) categories: 0 – "incomplete"; 1-"Negative"; 2-"Probably benign"; 3-"Suspicious"; 4-"Suspicious abnormality"; 5-Highly suspicious of malignancy"; and 6-"Known biopsy proven malignancy" (32). A category of 4 and 5 requires additional diagnostic procedures to determine the presence or absence of the disease. All participants with abnormal mammography are provided with case management services, which work with the participant to help her receive follow-up diagnostic services within 60 days.

Subjects were included in the analyses if they were enrolled in BCN between 1996 and 2009 and had an abnormal mammogram BI-RADS reading (BI-RADS category

of 4 or 5). Only women with race/ethnicity categorized as African American (AA) and European American (EA) were included in the sample because other individual racial or ethnic groups (n=31) did not have sufficient numbers to make meaningful contributions to the analysis. A total of 1,392 BCN participants were obtained from BCN.

The study was approved by the South Carolina's Department of Health and Environmental Control (SC-DHEC) and was exempted from approval from the Institutional Review Board of the University of South Carolina Office of Research.

Measures

The outcome of interest was time-to-resolution or completion of abnormal mammogram follow-up. The measure of time was the number of days between the first mammogram and the date that the follow-up status was finalized (work-up completed, refused, or lost-to-follow up). A completed work-up is designated when the diagnostic testing is complete and a final diagnosis has been made (benign or malignant breast cancer). Refused work-up indicates a woman had her diagnostic work-up performed by another provider. A loss-to-follow up status indicates that the woman died, moved before her work-up started, or BCN could not make contact with the patient.

There were three main exposure variables of interest: travel distance to the screening provider, travel distance to the diagnosing mammogram facility, and travel distance to the nearest mammography facility. The travel distances were calculated in miles and along the road network based on point location of residence to the facilities using ArcGIS 9.3 (Redland, CA) Network Analyst. Geocoding of residence and facilities were done using the Method and Tiers method (33) developed by the SC-DHEC.

Patients' addresses, screening providers' addresses, and diagnosing mammography facilities' addresses were obtained from BCN. The closest mammography facilities were identified from a regularly updated list of Food and Drug Administration (FDA) accredited facilities (34). Of the 1,392 subjects, we excluded 4 subjects because they were out of state. We also excluded all patients and screening providers with missing addresses, addresses that were PO Boxes and those that were matched to the 5-digit zip code only. There were 1,073 subjects left with matchable addresses. There were 218 screening providers; however, we were able to geocode only 137 facilities due to missing addresses and PO Boxes. There were 500 patients with a diagnosing mammography facility designated. Due to change in data collection, a portion of the records only captured the provider where the initial referral or screening mammography was performed. Thus, we were unable to perform geospatial analyses using diagnosing facility for these individuals. There were a total of 111 certified mammography facilities, identified from the FDA list, in South Carolina that were used as the closest mammography facilities. All distances to the screening provider, diagnosing mammography facilities, and closest mammography facilities were broken into < 5 miles, 5-<10 miles, 10-<15 miles, and 15 + miles. Demographic characteristics obtained from BCN for analyses included age, race, previous mammogram, yearly family income, and insurance status at time of visit with the BCN.

Statistical Analysis

Descriptive statistics were calculated for all characteristic variables. Chi-square test and t-test were used to examine the bivariate associations between demographic and

race variables. The median days and distances from the abnormal mammogram to diagnostic resolution were assessed with Kaplan-Meier survival method. Wilcoxon test of equality over strata was used to test for statistical significant between the distances.

Cox proportional hazard modeling was used to assess the relationship between work-up completion and travel distance to the screening provider and mammography facility. Women whose final status was recorded as refused or loss-to-follow up were considered censored observations. The proportional hazards assumption was examined through the logarithm of negative logarithm of survival probability with logarithm of time and the Schoenfeld residuals were further evaluated to confirm that there were no violations of the assumption. All analyses were performed using SAS version 9.3 (Cary, NC). A two-sided alpha level of 0.05 was used to determine significant for all tests.

Results

A total of 1,073 women were identified through the BCN. The mean age for AA and EA women was 54.4 (SD=7.01) and 53.8 (SD=7.79), respectively. There was no statistically significant difference in the mean age between the two race groups ($p=0.15$). EA women had higher income than AA women ($p<0.01$). There was statistically significant difference for travel distance to the screening provider among AA and EA women, with EA women having longer travel distance ($p<0.01$). For both groups of women, more than 95% had completed follow-up of abnormal mammogram. There was no statistically significant difference in insurance status, previous mammograms, and BI-RADs reading among the groups of women. The study population characteristics are displayed in Table 4.1.

The median day to resolution with travel distances are displayed in Table 4.2. The median day to resolution for travel distance to the screening provider, diagnosing mammography facility, and closest mammography facility were within 3 days of each other (22 days, 23 days, and 25 days, respectively). There was no significant difference between the travel distance to the screening provider and time to resolution. However, there was significant difference between travel distance to the diagnosing mammography facility and time to resolution. Women who lived farther from their diagnosing mammography facility had longer median day to resolution. Figures 4.1-4.3 present the estimated Kaplan Meier survival curves for travel distance to the health facilities and time to resolution.

The median days to resolution, stratified by race, are displayed in Table 4.3. For travel distance to the screening provider, diagnosing mammography facility, and closest mammography facility, AA women had significantly longer days to resolution compared to EA women. The largest difference in time to resolution was in travel distance to the diagnosing mammography facility (28 days for AA women vs. 22 days for EA women). Figures 4.4-4.6 present the estimated Kaplan Meier survival curves for travel distance to the health facilities and time to resolution, by race.

Table 4.4 presents the Cox proportional hazard analysis by travel distance to each of the facilities. Accounting for race, age, previous mammograms, income, and insurance status, women who lived closest (< 5 miles) to the diagnosing mammography facility were more likely to complete their work-up compared to those who lived the farthest (15 + miles) (HR=1.41; 95% CI=1.00-1.80). Though the interaction between travel distance

and race was not statistically significant, we further analyzed by race because it was integral to our post-hoc hypothesis. When stratified by race, AA women who lived the closest to their diagnosing mammography facility were 1.39 times more likely to complete the recommended work-up compared to AA women who lived the farthest from their diagnosing mammography (Table 4.5).

Discussion

To our knowledge this is the first study to use geospatial method to examined travel distance and completion of abnormal mammography follow-up among a population of women with homogeneous socioeconomic status. In this analysis of women participating in South Carolina's Best Chance Network, we found that geographical location of the health facility plays a role in the completion of work-up following an abnormal mammographic finding. Women who lived the closest to their diagnosing mammography facility were more likely to have a completed abnormal mammogram follow-up compared to those who lived the farthest. Similar to other studies, we found race was not significantly associated with overall completion of mammographic work-up (22, 24, 35-36). However, in all travel distances, AA women had longer days to completion of abnormal mammogram work-up compared to EA women. Among travel distance to the diagnosing and closest mammography facilities, women who lived the farthest had longer median days to resolution compared to those who lived the closest.

We performed a sensitivity analysis using travel distance to the diagnosing mammography and compared with travel distance to the closet mammography facility. Interestingly, we observed no association between completion of abnormal mammogram

follow-up and travel distance to the closest mammography facility, but we did observe an association with travel distance to the diagnosing mammography facility. Women were more likely to have their abnormal mammogram follow-up completed if they were living closest to their diagnosing mammography facility. There may be reasons why we see this unparalleled result. As of 2011, there were 111 certified mammography facilities (excluding mobile facilities) in South Carolina. We used this updated list of certified mammography facilities to calculate distance to the closest mammography facility. Several of these facilities may have been added in recent years and calculating the distance between these facilities and the patient's residence may not be the actual closest mammography facility utilized. By using this list, we are assuming that women received service at a facility closest to home and that all facilities were in existence at the beginning of the study (1996). Selection of a facility for service depends on many criteria and may not always be the closest to home. Hence, inaccuracy of travel distance to the closest mammography center can occur. This sensitivity analysis showed that by using the closest mammography facility instead of the actual utilized mammography facility, we may bias our findings toward to null.

There are several limitations to this investigation that are worth noting. First, the BCN program collects minimal data elements; therefore, we did not have information on the patient-provider relationship, or patients' behaviors and beliefs about breast cancer screening. This information would be useful in determining the reasons for some of our findings. Misclassification for the variable 'status of mammogram at final diagnosis' can bias our finding. When grouping 'refused' and 'loss to follow-up' into incomplete work-up, we may have introduced misclassification bias if the factors associated with them are

different from each other. Nevertheless, our analyses (data not shown) showed that there were no significant differences between the mean travel distance between those in the 'refused' and 'loss to follow-up' groups. Exclusion of women for various reasons can also bias our findings. In this investigation, 315 women were excluded due to PO Box addresses or not geocodeable to the exact street level. If the characteristics of these women differ from those with geocodeable addresses, our results may be biased. We found no significant differences between insurance status, BI-RADS reading, and the status of mammography at final diagnosis among the geocodeable and non-geocodeable groups; hence, excluding women with non-geocodeable addresses is unlikely to bias our estimates.

Our main exposure was travel distance. Though women in the study were geocoded to the exact street address, the geocoded address may not be the actual location of residence. This can happen due to new developments, rural areas or streets that are not captured by the geocoding map. Therefore, when calculating the distance from residence to the providers and mammography facilities, we may be under or over-estimating the true distance of travel. How much this biases our findings is unknown.

Though we used road network to measure the distance from patient's residence to the screening provider and mammography facility, we had no information on other factors that can affect utilization such as car ownership or reliability of public transportation. The type of transportation a patient uses can affect whether a patient will go to the health center or not. It has been shown that transportation is an important factor and is associated with mammography receipt (37).

The major strength of this analysis is that we derived travel distance from the exact street address of a patient's residence to the screening provider and mammography facility. This method gives us a more precise measurement of travel distance compared to other method that has been used in computing travel distance, which uses the five-zip code centroid.

In addition, we were able to compute distance to the diagnosing mammography facility. Healthcare can sometime be a choice and patient may not always utilize the closest health facility due to various reasons. By using the actual diagnosing mammography facility to compute the distance from the patient's residence, we have a good estimate of the actual travel distance. From our analysis, we found an association between travel distance to diagnosing mammography facility and completion of abnormal mammogram follow-up, but not for the closest mammography facility.

In conclusion, we found no racial disparity in the overall completion of abnormal mammogram work-up among AA and EA women participating in the BCN program and approximately 86% of the women had their work-up completed within 60 days. This suggests that the program is meeting established program standards of timeliness and completeness of follow-up for women with abnormal mammographic finding. However, we did found that geographical location of the diagnosing mammography facility plays a role in the days to completion of work-up. Women living closest to their diagnosing mammography facility were more likely to complete the work-up and have shorter days to completion compared to those who lived the farthest. In addition, we found evidence of racial disparity in the time to completion of abnormal mammogram work-up; AA

women had longer days to completion compared with EA women. These finding reveals that geographic accessibility to mammography facility may have an impact on completion of abnormal mammogram work-up and days to completion of the work-up. Intervention strategies and additional support to the BCN program to expand services should be investigated to reduce the disparity in days to completion of abnormal mammographic finding among racial ethnic groups. Further research that examines factors which affect geographic access, such as ownership of reliable transportation and access to public transportation, may further our understanding.

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Table 4.1. Demographic Characteristics of the Study Population, by Race*

Characteristics	Black (n=591) n (%) n (mean±SD)	White (n=482) n (%) n (mean±SD)	p-value
Age			
<40 years	7 (1.2%)	13 (2.7%)	0.19
40-49 years	149 (25.2%)	135 (28.0%)	
50-64 years	416 (70.4%)	320 (66.4%)	
65 + years	19 (3.2%)	14 (2.9%)	
Previous Mammography			
Yes	258 (43.7%)	220 (45.8%)	0.79
No	254 (43.1%)	199 (41.5%)	
Unknown	78 (13.2%)	61 (12.7%)	
BI-RADS			
BI-RADS 5 (highly suggestive malignancy)	133 (22.5%)	107 (22.2%)	0.91
BI-RADS 4 (suspicious abnormality)	458 (77.5%)	375 (77.8%)	
Insurance			
Yes	56 (9.5%)	43 (9.0%)	0.52
No	535 (90.5%)	438 (90.9%)	
Income			
<$10,000	428 (72.4%)	284 (58.9%)	**<0.01**
$10,000-$19,999	145 (24.5%)	166 (34.4%)	
>$20,000	18 (3.1%)	32 (6.6%)	
Travel Distance			
Provider	371 (10.0±10.5)	313 (13.6±16.5)	**<0.01**
Diagnosing mammography facility	292 (15.1±15.2)	208 (16.2±17.3)	0.43
Nearest mammography facility	591 (7.9±6.9)	482 (7.9±5.9)	0.95
Status of Mammography at Final Diagnosis			
Work-up complete	562 (95.1%)	462 (95.9%)	0.55
Work-up not complete	29 (4.9%)	20 (4.2%)	

* Values may not add up to 1073 due to missing

Table 4.2. Median days to Diagnostic Resolution among Women in BCN with Abnormal Mammogram*, by Travel Distance

Distance	**n**	**Median Days to Resolution (Range)****	**P-value*****
Distance to Provider			
< 5 miles	212	22 (18-26)	0.99
5 - < 10 miles	151	21 (19-27)	
10 - < 15 miles	108	22 (20-28)	
15 + miles	173	23 (19-27)	
Total	*644*	*22 (21-24)*	
Distance to Diagnosing Mammography			
< 5 miles	120	22 (19-25)	**0.05**
5 - < 10 miles	103	21 (18-29)	
10 - < 15 miles	66	26 (20-33)	
15 + miles	182	29 (24-35)	
Total	*471*	*23 (21-27)*	
Distance to Closest Mammography			
< 5 miles	464	26 (23-28)	0.87
5 - < 10 miles	250	23 (21-28)	
10 - < 15 miles	139	24 (19-29)	
15 + miles	161	*27 (21-29)*	
Total	*1,014*	*25 (23-27)*	

*Bi-RADS results of 4 (suspicious abnormality) or 5 (highly suggestive of malignancy)

** Median days are from Kaplan-Meier estimates

*** Wilcoxon Test of Equality over Strata

Table 4.3. Median days to Diagnostic Resolution among Women in BCN with Abnormal Mammogram*, by Travel Distance and Race

	Black			White			
Distance	**n**	**Median Days to Resolution (Range)****	**p-value*****	**n**	**Median Days to Resolution (Range)****	**p-value*****	**p-value******
Distance to Provider							
< 5 miles	147	23 (18-31)	0.79	65	21 (14-25)	0.79	**<0.01**
5 - < 10 miles	79	25 (19-29)		72	20.5 (14-23)		
10 - < 15 miles	55	22 (19-29)		53	23 (18-31)		
15 + miles	75	28 (21-37)		98	20.5 (16-24)		
Total	*356*	*24 (21-28)*		288	21 (18-23)		
Distance to Diagnosing Mammography							
< 5 miles	89	22 (19-29)	0.09	31	21 (11-29)	0.36	**<0.01**
5 - < 10 miles	50	27 (15-31)		53	21 (18-29)		
10 - < 15 miles	37	32 (21-40)		29	20 (13-26)		
15 + miles	108	30 (25-40)		74	27 (20-35)		
Total	*284*	*28 (24-31)*		187	22 (20-26)		
Distance to Closest Mammography							
< 5 miles	287	25 (22-31)	0.79	177	26 (21-28)	0.56	**<0.01**
5 - < 10 miles	110	29 (21-37)		140	21 (18-23)		
10 - < 15 miles	73	26 (20-33)		66	19 (14-33)		
15 + miles	98	28 (22-35)		63	20 (14-27)		
Total	*568*	*27 (24-29)*		446	22 (21-25)		

*Bi-RADS results of 4 (suspicious abnormality) or 5 (highly suggestive of malignancy)

** Median days are from Kaplan-Meier estimates

*** Wilcoxon Test of Equality over Strata

**** Kaplan-Meier curves comparison of the number of days to resolution among black and white (Log-rank test)

Table 4.4. Crude and Adjusted Hazard Ratio of Completion of Abnormal Mammography Work-up

Distance	Incomplete Work-up (n)	Complete Work-up (n)	Crude Hazard Ratio (CI)	Adjusted Hazard Ratio (CI)*
Distance to Provider				
< 5 miles	14	209	0.94 (0.76-1.15)	1.04 (0.84-1.29)
5 - < 10 miles	4	161	1.04 (0.83-1.30)	1.05 (0.84-1.31)
10 - < 15 miles	5	109	1.06 (0.83-1.36)	1.08 (0.84-1.38)
15 + miles	5	177	1.00	1.00
Distance to Diagnosing Mammography				
< 5 miles	8	119	**1.32 (1.04-1.67)**	**1.41 (1.00-1.80)**
5 - < 10 miles	6	106	**1.33 (1.04-1.70)**	**1.33 (1.03-1.72)**
10 - < 15 miles	3	66	1.06 (0.80-1.42)	1.09 (0.81-1.45)
15 + miles	6	186	1.00	1.00
Distance to Closest Mammography				
< 5 miles	24	466	1.03 (0.86-1.23)	1.03 (0.86-1.23)
5 - < 10 miles	10	253	1.12 (0.92-1.37)	1.06 (0.87-1.30)
10 - < 15 miles	10	137	0.97-0.77-1.22)	0.87 (0.69-1.10)
15 + miles	4	168	1.00	1.00

*Adjusted for race, age, previous mammogram, income, insurance, and screening provider

CI=95% confidence limit

Table 4.5. Adjusted Hazard Ratio of Completion of Abnormal Mammography Work-up, by Race

	Black				White			
Travel Distance	**Incomplete Work-up (n)**	**Complete Work-up (n)**	**Crude HR (CI)**	**Adjusted HR (CI)**	**Incomplete Work-up (n)**	**Complete Work-up (n)**	**Crude HR (CI)**	**Adjusted HR (CI)**
Distance to Provider								
< 5 miles	12	140	0.94 (0.70-1.25)	1.03 (0.77-1.39)	2	69	1.18 (0.56-1.63)	1.19 (0.85-1.66)
5 - < 10 miles	2	80	1.08 (0.79-1.50)	1.13 (0.82-1.57)	2	81	1.04 (0.77-1.42)	0.94 (0.69-1.29)
10 - < 15 miles	2	56	1.27 (0.89-1.81)	1.29 (0.90-1.85)	3	53	0.91 (0.65-1.29)	0.89 (0.63-1.26)
15 + miles	3	76	1.00	1.00	2	101	1.00	1.00
Distance to Diagnosing Mammography								
< 5 miles	7	86	**1.40 (1.04-1.87)**	**1.39 (1.03-1.88)**	1	33	1.34 (0.87-2.05)	**1.58 (1.01-2.48)**
5 - < 10 miles	3	48	**1.42 (1.00-2.01)**	1.39 (0.97-1.99)	3	58	1.16 (0.82-1.66)	1.32 (0.91-1.92)
10 - < 15 miles	2	37	1.01 (0.69-1.48)	0.97 (0.65-1.44)	1	29	1.13 (0.73-1.76)	1.28 (0.81-2.02)
15 + miles	4	105	1.00	1.00	2	81	1.00	1.00
Distance to Closest Mammography								
< 5 miles	17	281	1.06 (0.84-1.34)	1.06 (0.84-1.34)	7	185	0.95 (0.71-1.27)	0.97 (0.72-1.31)
5 - < 10 miles	5	109	1.05 (0.80-1.39)	0.99 (0.75-1.32)	5	144	1.09 (0.81-1.48)	1.09 (0.80-1.48)
10 - < 15 miles	5	70	0.99 (0.73-1.36)	0.91 (0.66-1.25)	5	67	0.90 (0.63-1.29)	0.83 (0.57-1.20)
15 + miles	2	102	1.00	1.00	3	66	1.00	1.00

*Adjusted for race, age, previous mammogram, income, insurance, and screening provider

HR=Hazard ratio; CI=95% confidence interval

P-value interaction: Distance to provider*race = 0.20; p-value interaction: Distance to diagnosing mammography*race = 0.79; p-value interaction to diagnosing mammography*race = 0.80

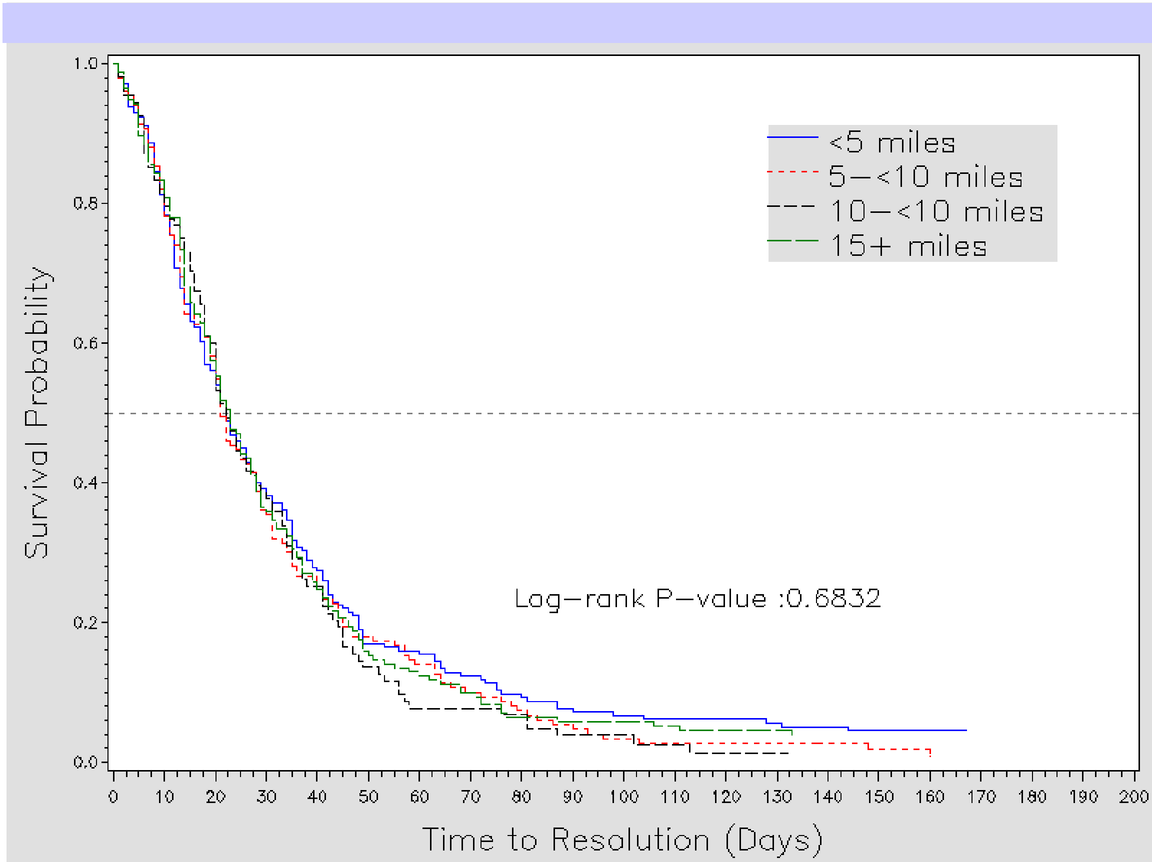

Figure 4.1: Days to Diagnostic Resolution, by Travel Distance to the Screening Provider

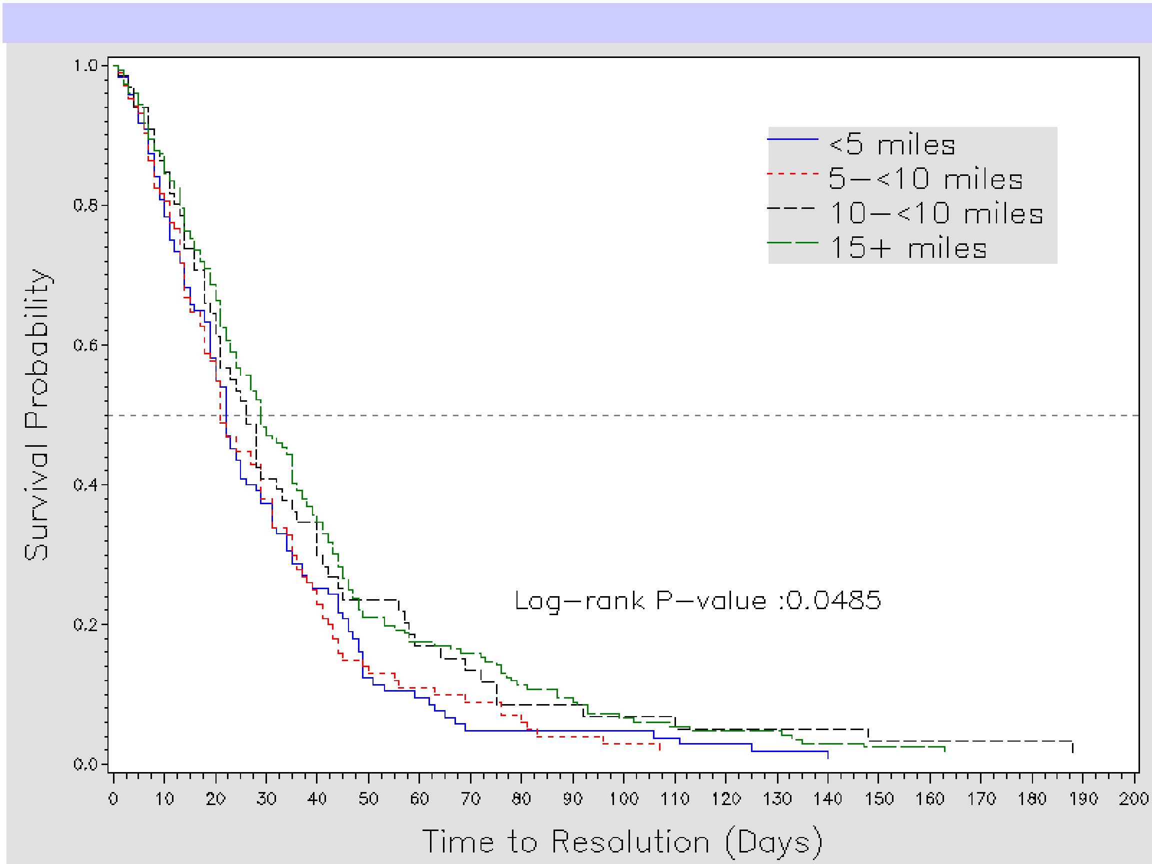

Figure 4.2: Days to Diagnostic Resolution, by Travel Distance to the Diagnosing Mammography Facility

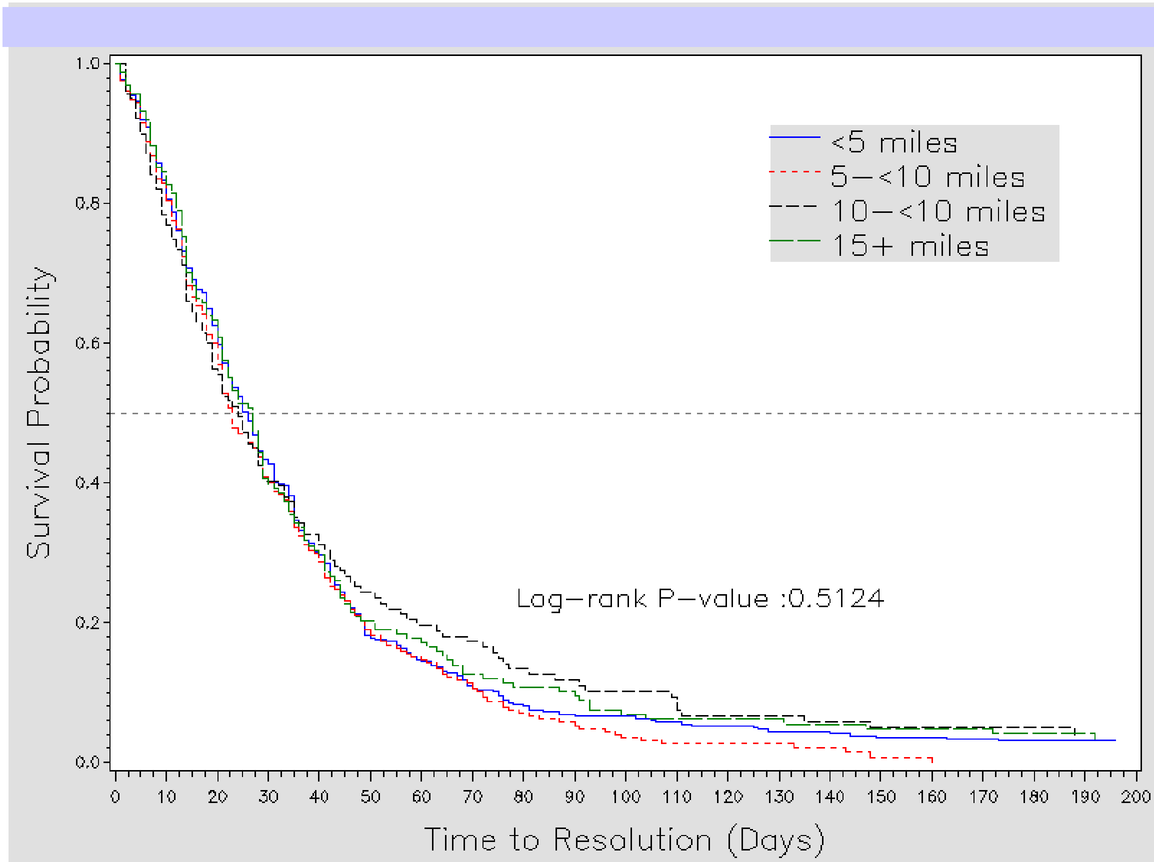

Figure 4.3: Days to Diagnostic Resolution, by Travel Distance to the Closest Mammography Facility

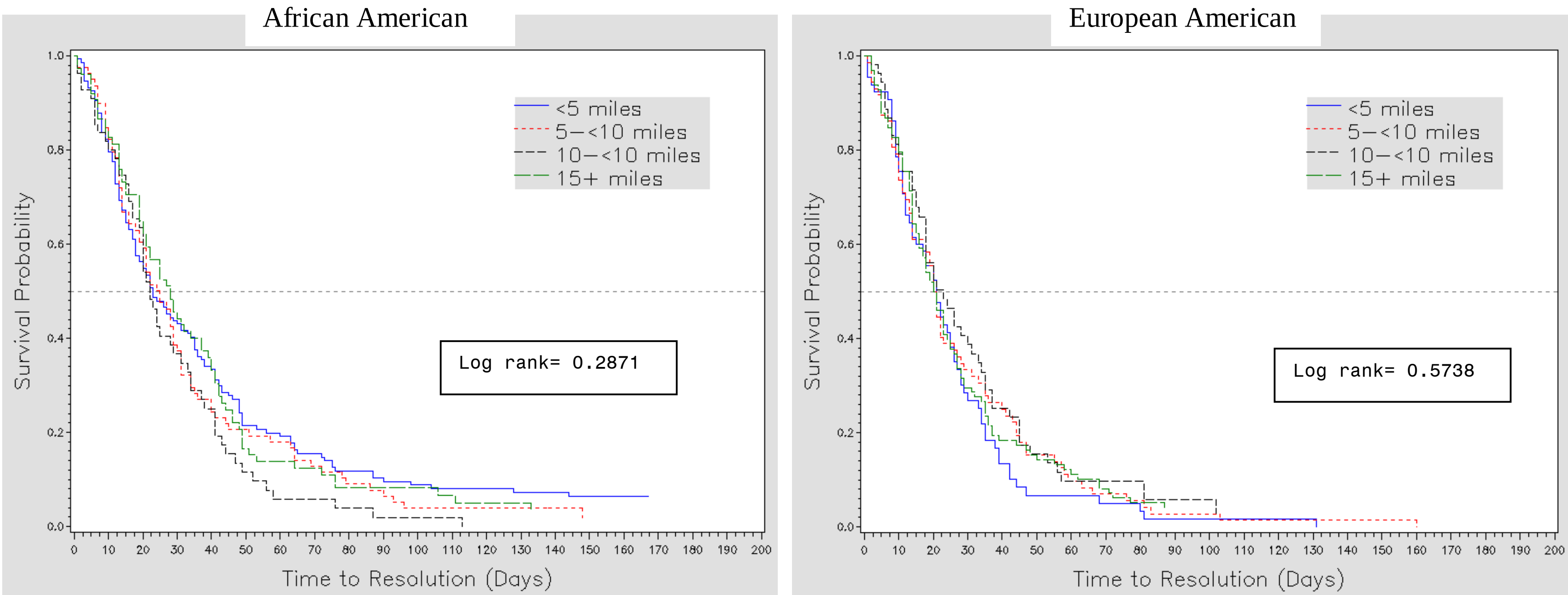

Figure 4.4: Days to Diagnostic Resolution, by Travel Distance to the Screening Provider and Race

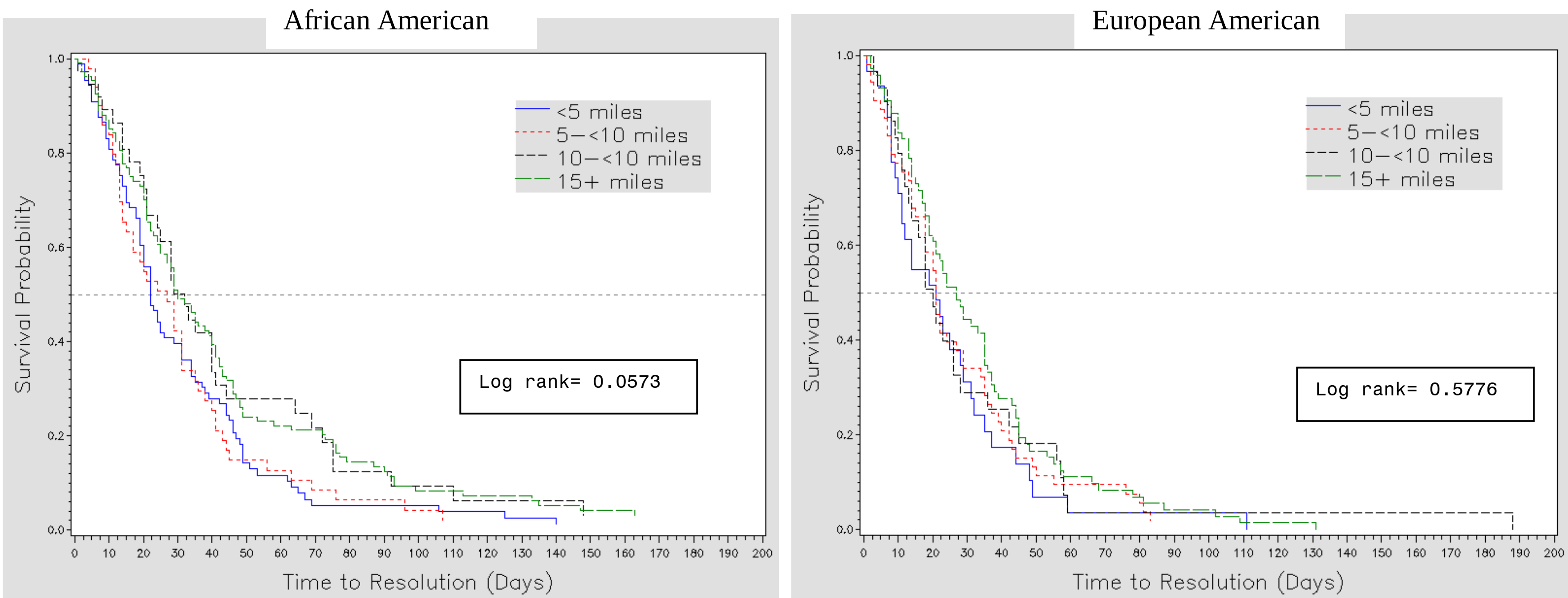

Figure 4.5: Days to Diagnostic Resolution, by Travel Distance to the Diagnosing Mammography Facility and Race

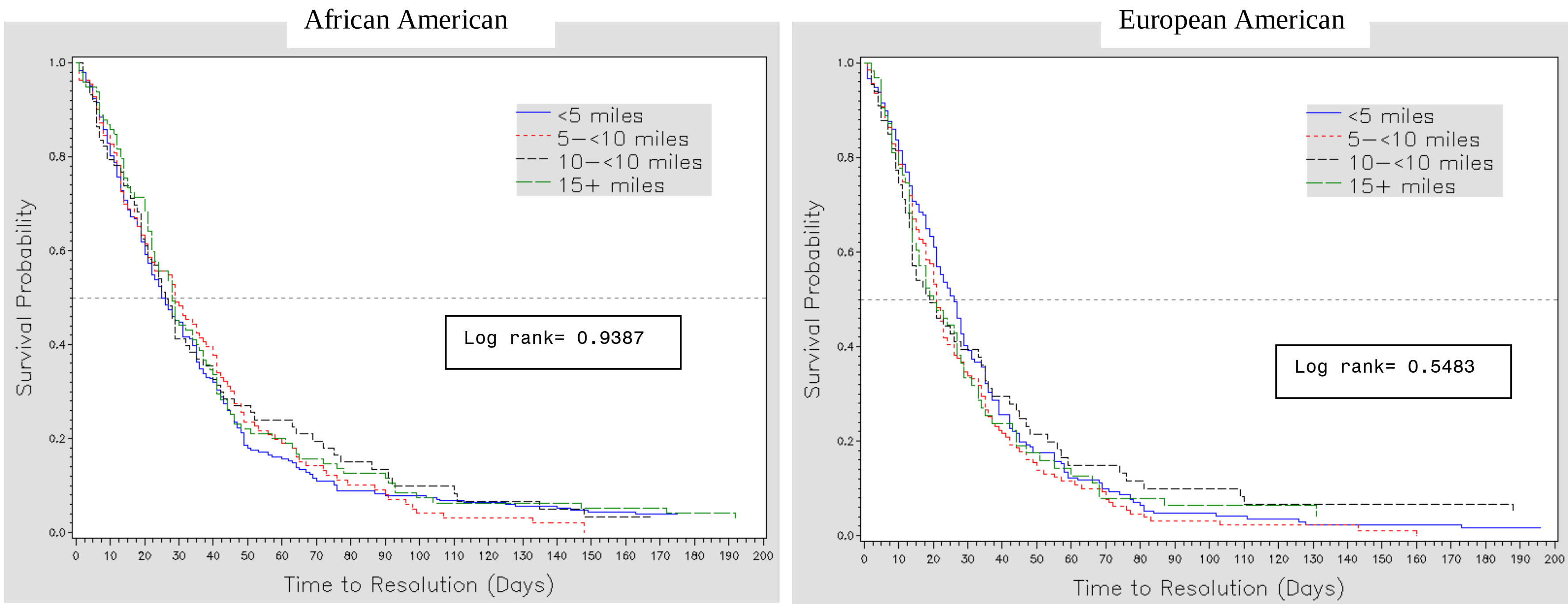

Figure 4.6: Days to Diagnostic Resolution, by Travel Distance to the Closest Mammography Facility and Race

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CHAPTER 5

TRAVEL DISTANCE TO SCREENING FACILITIES AND BREAST CANCER STAGE AT DIAGNOSIS AMONG DISADVANTAGED WOMEN[2]

[2] Khang, L., S.A. Adams, S.E. Steck, J. Zhang, S. Xirasagar, D. Lydiard. To be submitted to *Cancer Epidemiology Biomarkers and Prevention* or *Breast Cancer Research.*

Abstract

Introduction: South Carolina has some of the largest health disparities in the nation. Breast cancer is the most common cancer diagnosed and is the second largest cause of cancer deaths among women in the state. Breast cancer stage at diagnosis is an important predictor of survival and mortality. In the past decades, researchers have explored geographic proximity to health care or mammography locations and breast cancer stage at diagnosis. However, findings have been inconsistent between the studies. The purpose of this study was to examine 1) whether travel distance to the screening provider and mammography facility are associated with stage of breast cancer at diagnosis among disadvantaged women who have screening available at no cost, 2) whether there are racial disparities in breast cancer stage at diagnosis among women in South Carolina's Best Chance Network (BCN), and 3) whether there are any differences in the distribution of breast cancer stage at diagnosis among BCN participants and non-BCN participants. **Methods:** Women participating in South Carolina's BCN between 1996 and 2009 with a first primary breast cancer and linked to the South Carolina Central Cancer Registry were included in the study. Racial differences in demographic characteristics and breast cancer stage at diagnosis were tested using chi-square and t-tests. Multivariable logistic regression was used to assess the association between travel distance and breast cancer stage at diagnosis. **Results:** Among 681 women with breast cancer, there was no statistically significant difference in the distribution of cancer stages by race ($p=0.45$). There was no strong evidence that longer travel distance to the screening provider and mammography facility was associated with late stage breast cancer at diagnosis among women in BCN. Women in BCN had fewer *in situ* and localized breast cancers compared

to non-BCN women **Conclusion:** There is no association between travel distance to the screening provider and mammography facility among economically homogenous women who have screening available at no cost.

Introduction

Among women in the United States, breast cancer is the most commonly diagnosed cancer and is the second leading cause of cancer-related mortality (1). Using mammography for breast cancer screening is the single most effective method of early detection for breast cancer. Mammography can identify the cancer at an early stage, when survival rates are at their highest. Beginning at age 40, the American Cancer Society (ACS) recommends screening mammography on an annual basis for average-risk women (1). However, about 38-54% of women do not maintain annual adherence to screening mammograms (2, 3).

Breast cancer stage at diagnosis is an important determinant of survival and mortality (4). Women with breast cancer diagnosed at advanced stage have limited treatment options and poorer survival compared to women with early stage breast cancer. The 5-year relative survival rates among women whose breast cancer is diagnosed while in the regional stage are nearly four times greater than those of women whose cancer has spread to distant (distant stage) lymph nodes or organs at the time of diagnosis (84% vs. 23%) (4). Studies consistently show that women with low-income, women having no insurance or being under-insured, and racial/ethnic minorities are more likely to be diagnosed with late-stage breast cancer (5-11).

Spatial methods have been widely used in breast cancer research to understand some of the disparities in breast cancer morbidity and mortality (12-20). A common spatial method that has been examined is spatial accessibility to healthcare facilities. Accessibility, such as long travel distance, can discourage women to seek routine preventive care or screening. In the past decades, researchers have explored geographic proximity to health care or mammography locations and breast cancer stage at diagnosis (12-20). However, findings have been inconsistent between the studies. The inconsistent results in the literature highlight the need for further research.

South Carolina has some of the largest health disparities in the nation (1). Breast cancer is the most common cancer diagnosed and is the second largest cause of cancer deaths among women in South Carolina (21). Statewide, the age-adjusted incidence of breast cancer from 2004-2008 have remained stable at around 119 per 100,000 women (1), with a higher age-adjusted incidence among European American (EA) women compared to African American (AA) women (127.6 and 111.3 per 100,000 women, respectively) (22), yet higher mortality among AA women compared to EA women (21).

To reduce the disproportionate burden of breast cancer death among disadvantaged women in South Carolina, the Best Chance Network (BCN), which is the state program of the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) was established in 1991. South Carolina has one of the highest proportions of uninsured women in the nation, of which majority of these women are eligible to enroll in the program. The majority (60%) of women in BCN are AA and reside in rural counties (23). The BCN offers a unique opportunity to explore the relationship between

travel distance to health facilities and breast cancer stage at diagnosis among disadvantaged women who have screening available at no cost. Consequently, the purpose of this study was to 1) investigate whether travel distance to the screening provider and mammography facility are associated with breast cancer stage at diagnosis among women participating in South Carolina's BCN, 2) examine whether there are racial disparities in the distribution of breast cancer stage at diagnosis among BCN participants, and 3) examine whether there are any differences in the distribution of breast cancer stage at diagnosis among BCN participants and non-BCN participants?

Methods

Study Setting/Participants

Study participants were women enrolled in the BCN of South Carolina, who developed breast cancer between 1996 and 2009. These women were linked to the South Carolina Central Cancer Registry (SCCCR) using probabilistic matching techniques with Link Plus software. The cut-off value used for our probabilistic matching was 1. Data from the BCN and SCCCR were linked by first name, last name, middle name (if provided), date of birth, address, and social security number (SSN).

The SCCCR is a population-based data system that collects cancer statistics in the state of South Carolina. From the last audit, the registry has a completeness rate of 96.9% and an accuracy rate of 96.4%, both of which exceeded the national standard of 95%. SCCCR also maintains a "Gold Certification" from the North American Association of Central Cancer Registries (NAACCR) (24). Thus, the data are of high quality, validity, and completeness.

There were 707 women with first primary breast cancer from BCN that were matched to the SCCCR. Only women with race/ethnicity categorized as AA and EA were included in the sample because other individual racial or ethnic groups (n=17) did not have sufficient numbers to make meaningful contributions to the analysis. We also excluded 9 women with unknown breast cancer stage at diagnosis. A total of 681 women were included in the study. To compare breast cancer stage at diagnosis between BCN and non-BCN women, we identified 46,126 non-BCN women with breast cancer from SCCCR between 1996 and 2009.

The study was approved by the South Carolina's Department of Health and Environmental Control (SC-DHEC), South Carolina Central Cancer Registry, and was exempted from approval from the Institutional Review Board of the University of South Carolina Office of Research.

Measures

The outcome of interest was breast cancer stage at diagnosis. Using the Surveillance Epidemiology and End Results (SEER) Summary Staging guide (25), breast cancer stages were dichotomized into 'early stage' and 'late stage'; *In situ* and localized (confined to primary site) stages were considered 'early stage' and regional (spread to regional lymph nodes) or distant (cancer has metastasized) stages were categorized as 'late stage'. Demographic characteristics obtained from BCN and SCCR for analyses included age, race, income at time of enrollment, insurance status at time visit with the BCN, and marital status. Race was categorized as EA and AA. Income at time of enrollment was categorized into three groups: <$10000, $10000-$19999, and >$20000.

Health insurance status was categorized as Yes and No. Marital status was categorized into five groups: single, married, separated/divorced, widowed, and unknown.

Three measures of geographic accessibility to health centers were calculated (travel distance to the screening provider, travel distance to the diagnosing mammography facility, and travel distance to the nearest mammography facility). The travel distances were calculated in miles and along the road network based on point location of residence (at the time of diagnosis) to the facilities using ArcGIS 9.3 (Redland, CA) Network Analyst. The Method and Tiers method (26), developed by the SC-DHEC, was used to geocode residential addresses and health facilities. All addresses, including patients, screening providers, and diagnosing mammography facilities were obtained from BCN. We excluded all addresses that were missing, were PO Boxes and those that were matched to the 5-digit zip code only. Of the 681 subjects women that matched to the SCCCR, we were able to geocode all of their addresses. There were 218 screening providers identified from BCN; however, we were able to geocode only 137 facilities due to missing addresses and PO Boxes. Due to change in data collection over the years, a portion of the records only captured the provider where the initial referral or screening mammography was performed. Thus, we were able to identify 314 patients with a diagnosing mammography facility designated.

Mammography facilities identified from a regularly updated list of Food and Drug Administration (FDA) accredited facilities (27) were geocoded and used as the closest mammography facilities.

Statistical Analysis

Descriptive statistics were performed for all characteristic variables. Chi-square test and t-test were used to test for differences between demographic and race variables. Chi-square was also used to compare breast cancer stage at diagnosis between BCN and non-BCN women. Multivariable logistic regression was used to assess the association between travel distance (to the screening provider, diagnosing mammography facility, and closest mammography facility) and stage of breast cancer at diagnosis. To assess whether travel distance was influenced by race, we created an interaction term between travel distance and race in each of the model (travel distance to screening provider-race, travel distance to diagnosing mammography facility-race, and travel distance to closest mammography facility-race). All distances to the health facilities were broken into < 5 miles, 5-<10 miles, 10-<15 miles, and 15+ miles for statistical analysis. All analyses were performed using SAS version 9.3 (Cary, NC). A two-sided alpha level of 0.05 was used to determine significance for all tests.

Results

There were a total of 681 women with first primary breast cancer diagnosed in the study. The majority (~54%) of the women were AA. The mean age for AA and EA women was 55.6 (SD=6.4) and 55.3 (SD=6.6), respectively. The distribution of cancer stage at diagnosis among all women was *in situ* (16.3%), localized (44.6%), regional (35.1%), and distant (4.0%). There was no statistically significant difference in the distribution of cancer stage at diagnosis by race (p=0.45). Interestingly, EA women had significantly longer travel distance to the screening provider and diagnosing

mammography facility ($p<0.01$ and $p=0.05$, respectively) compared to AA women. However, there was no difference in travel distance to the closest mammography facility between AA and EA. The study population characteristics are displayed in Table 5.1.

Table 5.2 displays the breast cancer stage at diagnosis among BCN women and non-BCN women in the state of South Carolina. Women in BCN had fewer *in situ* and localized breast cancer stages at diagnosis compared to non-BCN women. There was no statistically significant difference by race in the distribution of cancer stage at diagnosis among BCN women. However, there was a statistically significant difference between breast cancer stage at diagnosis and race among non-BCN women, with AA women having higher percentage of regional and distant breast cancer at diagnosis compared to EA women.

Table 5.3 presents the crude and adjusted odds ratios predicting late stage breast cancer at diagnosis. In both crude and adjusted analyses, we found no significant relation between travel distance to the screening provider, closest mammography facility and breast cancer stage at diagnosis. However, in the adjusted model, women living 5-<10 miles from their diagnosing mammography facility were 2.25 times more likely to be diagnosed with late stage breast cancer compared to women living < 5miles from their diagnosing facility. When stratified by race, there were no associations between travel distance to the screening provider, diagnosing mammography facility, closest mammography facility, and breast cancer stage at diagnosis (Table 5.4).

Discussion

The main purpose of this investigation was to examine whether travel distance to the screening provider and mammography facility were associated with stage of breast cancer at diagnosis. To our knowledge this is the first study to use geospatial methods to examine this relationship among disadvantaged women who have screening available at no cost. In this analysis of women participating in South Carolina's BCN, we found no convincing evidence that longer travel distance to the screening provider, diagnosing mammography facility, and closest mammography facility were associated with late stage breast cancer at diagnosis.

Our findings, though not what might be expected, are in agreement with some other studies that found no association between travel time and breast cancer stage at diagnosis (12-17). The lack of an association in the present study may reflect the BCN context. BCN is a network of public and private partnerships with more than 250 health care providers offering screening and follow-up services to disadvantaged women in the state. South Carolina is a relatively rural state and one might expect longer travel distance to health facilities among its residents. However, with an extensive BCN network providing service throughout the state, we found the mean travel distance to the screening provider is 10.9 miles (SD=10.5), diagnosing mammography facility is 14.6 miles (SD=15.8), and closest mammography facility is 8.1 miles (SD=6.5). One study found that among individuals living in rural Upper Great Plains states of Montana, North Dakota, South Dakota, and Wyoming had an average travel distance of 17 miles to health care services (28). With much shorter travel distance to screening providers and

mammography facilities, travel distance may not be a major issue in our population. It could also be that the program, with its financial access, is providing adequate service for those with geographic distance challenges.

One important aspect of our study was that we were able to compare breast cancer stage at diagnosis among BCN women to non-BCN women in the State of South Carolina. Though BCN women had slightly greater number of late stage breast cancers compared to non-BCN women, we found no evidence of racial disparity in breast cancer stage at diagnosis among women in BCN. This is evidence that the program is meeting established program standards of reducing health disparities among racial/ethnic groups.

The results of this study should be interpreted with consideration of several limitations. First, BCN and SCCCR collect minimal data elements; therefore, we did not have information on important factors that may contribute to stage of diagnosis, such as family history, body mass index, and other comorbidities. Though we used road network to measure the distance from patient's residence to the screening provider and mammography facility, we had no information on the mode of transportation. The type of transportation a patient uses can affect whether a patient will seek health care or not. It has been shown that transportation is an important factor in screening for breast cancer (29). A study in rural North Carolina found that individuals who had a driver's license had twice as many health care visits compared to those who did not (30). Though women in our study were successfully geocoded to the exact street address, the geocoded address may not be the actual location of residence. This can happen due to new developments, rural areas or streets that are not captured by the geocoding data. We expect this will be

improved as geocoding expands. Another limitation is that we excluded many of the women with non-geocodeable address. These women may reside in more rural areas and may have long travel distance to the health facilities or vice versa. How much this bias our finding is unknown.

There are many strengths to this investigation. The major strength is that we were able to calculate travel distance from the exact street address of the women's residence to the screening facilities. This method allowed us to depict a more accurate measurement of travel distance. Though we found no relationship between travel distance to the health facilities and breast cancer stage at diagnosis, we were able to calculate travel distance to the diagnosing mammography facility. Women may not utilize the nearest facility due to personal and neighborhood characteristics, such as hours of operation, conveniently located, and location to work. Relying on the closest mammography facility may underestimate the true travel distance between patients' residence and actual mammography usage if the closest facility is not the one being utilized. Another strength of our investigation is that when we investigate the association between travel distance to the health facilities and breast cancer stages at diagnosis, we were able to focused on a homogenous socioeconomic status women who have screening available at no cost. This allowed us in the design phase to eliminate some factors (e.g. income, health insurance status, and having a provider) which may impact breast cancer stage at diagnosis.

Previous research in this area has produced mixed results. The reasons for these contradictory findings are unclear, but study locations (metropolitan vs. non-

metropolitan) and geography may play a role. Research methodology can also explain the contrary findings. There were differences in the methodology used in examining breast cancer stage and travel distance to mammography facility among previous studies (12-20). Tarvo *et al.* used the mean distance to the closest five mammography facilities and found no association between travel distance and breast cancer stage at diagnosis (12). The study in Washington by Onega *et al.* measured travel time instead of travel distance and also found no relationship (16). Two studies used patient's zip code centroid to calculated distance to the nearest mammography facility and found that women who lived further from the mammography facility were more likely to be diagnosed with late stage breast cancer (19, 20).

In summary, we found no convincing evidence that longer travel distance to the screening provider and mammography facility was associated with late stage breast cancer at diagnosis among women participating in South Carolina's BCN. Though women in BCN have significantly higher proportion of late stage of breast cancer at diagnosis compared to non-BCN women, there was no racial disparity in the distribution of breast cancer stage at diagnosis among BCN women. Accurately capturing accessibility to health centers, including geography and transportation method, should be prioritized in future research.

Table 5.1. Demographic Characteristics of the Study Population, by Race*

Characteristics	African American (n=365) n (%) n (mean±SD)	European American (n=316) n (%) n (mean±SD)	p-value
Age	337 (55.6±6.4)	295 (55.3±6.6)	0.58
Breast Cancer Stage at Diagnosis			
In situ	67 (18.4%)	44 (13.9%)	0.45
Localized	160 (43.8%)	144 (45.6%)	
Regional	125 (34.3%)	114 (36.1%)	
Distant	13 (3.6%)	14 (4.4%)	
Marital Status			
Single	91 (25.9%)	39 (13.0%)	**<0.01**
Married	97 (27.6%)	116 (38.5%)	
Separated/Divorced	70 (19.9%)	72 (23.9%)	
Widowed	52 (14.8%)	41 (13.6%)	
Unknown	41 (11.7%)	33 (11.0%)	
Previous Mammography			
Yes	149 (40.9%)	145 (46.0%)	0.34
No	148 (40.7%)	122 (38.7%)	
Unknown	67 (18.4%)	48 (15.2%)	
Insurance			
Yes	87 (23.85%)	76 (24.1%)	0.93
No	278 (76.2%)	239 (75.9%)	
Income			
<$10,000	250 (68.5%)	189 (59.8%)	**0.03**
$10,000-$19,999	101 (27.7%)	104 (32.9%)	
>$20,000	14 (3.8%)	23 (7.3%)	
Travel Distance			
Provider	245 (9.3±9.6)	230 (12.6±12.0)	**<0.01**
Diagnosing mammography facility	176 (13.0±14.1)	138 (16.6±17.5)	**0.05**
Nearest mammography facility	365 (8.2±7.1)	316 (8.0±5.8)	0.64

* Values may not add up to 681 due to missing

Table 5.2. Breast Cancer Stage Among BCN Women Compared to Women in the State of South Carolina, 1996-2009

	BCN Women				Non-BCN Women						
Breast Cancer Stage	**Total**	**AA**	**EA**	**p^a**	**Total**	**AA**	**EA**	**p^b**	**p^c**	**p^d**	**p^e**
In situ	111 (16.3%)	67 (18.4%)	44 (13.9%)	0.45	8,131 (17.6%)	1,846 (17.6%)	6,187 (17.6%)	<0.01	<0.01	0.19	<0.01
Localized	304 (44.6%)	160 (43.8%)	144 (45.6%)		23,954 (51.9%)	4,660 (44.4%)	19,041 (54.2%)				
Regional	239 (35.1%)	125 (34.3%)	114 (36.1%)		12,172 (26.4%)	3,354 (31.9%)	8,695 (24.8%)				
Distant	27 (4.0%)	13 (3.6%)	14 (4.4%)		1,869 (4.1%)	650 (6.2%)	1,202 (3.4%)				

[a] P-value-comparison between AA and EA among BCN women
[b] P-value-comparison between AA and EA among non-BCN women
[c] P-value-comparison between BCN total women to non-BCN total women
[d] P-value-comparison between BCN AA women to non-BCN AA women
[e] P-value-comparison between BCN EA women to non-BCN EA women

Table 5.3. Crude and Adjusted Odds Ratios Predicting Late Stage Breast Cancer at Diagnosis among Women in BCN, 1996-2009

Distance	Early Stage Breast Cancer (n)	Late Stage Breast Cancer (n)	Crude Odds Ratio (CI)	Adjusted Odds Ratio (CI)*
Distance to Provider				
< 5 miles	102	62	Referent	Referent
5 - < 10 miles	71	41	0.95 (0.58-1.56)	1.04 (0.60-1.79)
10 - < 15 miles	48	31	1.06 (0.61-1.84)	1.14 (0.61-2.13)
15 + miles	71	49	1.14 (0.70-1.84)	1.27 (0.74-2.18)
Distance to Diagnosing Mammography				
< 5 miles	59	30	Referent	Referent
5 - < 10 miles	35	24	1.35 (0.68-2.66)	1.30 (0.62-2.73)
10 - < 15 miles	28	27	1.90 (0.95-3.77)	**2.25 (1.04-4.83)**
15 + miles	73	38	1.02 (0.57-1.85)	1.13 (0.59-2.14)
Distance to Closest Mammography				
< 5 miles	187	112	Referent	Referent
5 - < 10 miles	105	60	0.95 (0.64-1.42)	0.91 (0.59-1.40)
10 - < 15 miles	63	44	1.17 (0.74-1.83)	1.13 (0.68-1.88)
15 + miles	60	50	1.39 (0.89-2.17)	1.50 (0.94-2.41)

* Adjusted for age at diagnosis, race, income, insurance status, and marital status
CI=Confidence interval

Table 5.4. Crude and Adjusted Odds Ratios Predicting Late Stage Breast Cancer at Diagnosis among Women in BCN, by Race

	Black				White			
Travel Distance	**Early Stage Cancer (n)**	**Late Stage Cancer (n)**	**Crude OR(CI)**	**Adjusted OR (CI)***	**Early Stage Cancer (n)**	**Late State Cancer (n)**	**Crude OR (CI)**	**Adjusted OR (CI)***
Distance to Provider								
< 5 miles	66	42	Referent	Referent	36	20	Referent	Referent
5 - < 10 miles	31	23	1.17 (0.60-2.26)	1.28 (0.61-2.70)	40	18	0.81 (0.37-1.77)	0.70 (0.30-1.64)
10 - < 15 miles	24	11	0.72 (0.32-1.62)	0.55 (0.20-1.49)	24	20	1.50 (0.67-3.36)	1.69 (0.69-4.11)
15 + miles	31	17	0.86 (0.43-1.75)	1.23 (0.57-2.66)	40	32	1.44 (0.70-2.95)	1.24 (0.55-2.79)
Distance to Diagnosing Mammography								
< 5 miles	42	20	Referent	Referent	17	10	Referent	Referent
5 - < 10 miles	16	12	1.58 (0.63-3.95)	1.34 (0.48-3.79)	19	12	1.07 (0.37-3.11)	0.72 (0.21-2.45)
10 - < 15 miles	17	15	1.85 (0.77-4.45)	2.09 (0.75-5.84)	11	12	1.85 (0.59-5.75)	1.52 (0.42-5.49)
15 + miles	32	22	1.44 (0.68-3.09)	1.35 (0.58-3.17)	41	16	0.66 (0.25-1.75)	0.61 (0.21-1.78)
Distance to Closest Mammography								
< 5 miles	108	65	Referent	Referent	79	47	Referent	Referent
5 - < 10 miles	53	18	0.56 (0.31-1.05)	0.60 (0.31-1.18)	52	42	1.36 (0.79-2.34)	1.16 (0.64-2.11)
10 - < 15 miles	33	23	1.16 (0.63-2.14)	1.07 (0.53-2.16)	30	21	1.18 (0.61-2.29)	1.08 (0.51-2.26)
15 + miles	33	32	1.61 (0.91-2.87)	1.72 (0.92-3.21)	27	18	1.12 (0.56-2.25)	1.02 (0.60-2.63)

* Adjusted for age at diagnosis, race, income, insurance status, and marital status

OR= Odds ratio; CI=Confidence interval

P-value interaction: Distance to provider*race = 0.23; p-value interaction: Distance to diagnosing mammography*race = 0.56; p-value interaction: Distance to closest mammography*race = 0.09

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CHAPTER 6

TRAVEL DISTANCE TO SCREENING REFERRAL PROVIDER, MAMMOGRAPHY FACILITY, AND BREAST CANCER MORTALITY AMONG WOMEN IN A STATE BREAST CANCER SCREENING PROGRAM[3]

[3] Khang, L., S.A. Adams, S.E. Steck, J. Zhang, S. Xirasagar, D. Lydiard. To be submitted to *Cancer Epidemiology Biomarkers and Prevention* or *Breast Cancer Research.*

Abstract

Introduction: The death rates from breast cancer have declined in the past decades; however, disparities between racial/ethnic groups remain. South Carolina has some of the largest health disparities in the nation, particularly breast cancer morbidity and mortality. The Best Chance Network was established to reduce the burden of breast cancer among disadvantaged women in the state. Although much has been done to identify factors related to breast cancer mortality, little has been done to examine the influence of geographic accessibility to health facilities and breast cancer mortality. The purpose of this study was to investigate whether travel distance to the screening referral provider and mammography facility are associated with breast cancer-specific and all-cause mortality among women participating in South Carolina's Best Chance Network. We also sought to contrast and compare by race breast cancer-specific and all-cause survival among BCN participants. **Methods:** Women in South Carolina's Best Chance Network, who developed breast cancer between 1996 and 2009 and self-identified as either African American (AA) or European American(EA) (n=690), were included in the study. Chi-square and t-tests were used to determine racial differences in characteristics among the women. Kaplan-Meier survival methods were used to determine the breast cancer-specific and all-cause survival probabilities. Cox proportional hazard modeling was used to assess the relationship between travel distance and mortality (breast cancer-specific and all-cause mortality). **Results:** There were no statistically significant differences in breast cancer-specific and all-cause survival proportions between AAs compared to EAs. Women with 10+ miles of travel distance to the diagnosing mammography facility had ~ 2 fold excess risk of death from breast cancer (HR, 2.32; 95% CI, 1.12-4.80). However,

the association was no longer statistically significant after adjustment for various prognostics characteristics. In the adjusted model, there was no association between travel distance to the health centers and mortality (breast cancer-specific and all-cause mortality) among EA and AA women. **Conclusion:** We found no racial disparity in breast cancer-specific and all-cause survival among economically disadvantaged women participating in BCN. There is little evidence that geographic accessibility to these health facilities influence breast cancer-specific and all-cause mortality among women in a homogenous socioeconomic status.

Introduction

In 2012, the American Cancer Society estimates approximately 226,870 new cases and 39,920 deaths from breast cancer among women in the United States (1). Although the overall death rates for breast cancer have declined in the past decades, the mortality rates differ among racial/ethnic and age groups (1, 2). Even though European American (EA) women have higher breast cancer rates, African American (AA) women are more likely to die from the cancer (2).

Breast cancer is the second largest cause of cancer deaths among women in South Carolina (3). The age-adjusted mortality rate in South Carolina from 2004-2008 have remained stable at ~ 24.3 per 100,000 women (1), with AA women having higher age-adjusted mortality rate compared to EA women (31.2 and 22.2 per 100,000 women, respectively) (2). To reduce breast cancer disparities in South Carolina, the Best Chance Network (BCN), which is the state program of the National Breast and Cervical Early Detection Program (NBCCEDP), was established in 1991. The program provides free

mammograms, clinical breast exams, Pap tests, pelvic exams, diagnostic procedures, case management, community education on breast/cervical cancer and early detection for underserved women aged 47-64 years, who are at or below 200% of the Federal trade poverty level, and those who lack insurance or have insurance that only covers hospital care.

Studies have shown that breast cancer stage at diagnosis (4), age (5), race (2, 4), socioeconomic status (6), lifestyle (7-9), tumor characteristics (10-11), and reproductive factors (12-14) are associated with breast cancer mortality and survival. There have been several studies that examined travel distance to the mammography facility and breast cancer stage at diagnosis (15-23); however, little has been done to examine geographic accessibility to the screening referral provider, mammography facility, and its association with breast cancer mortality. Consequently, the objective of this study was to 1) investigate whether travel distance to the screening referral provider and mammography facility are associated with breast cancer-specific and all-cause mortality among women participating in South Carolina's BCN, and 2) to contrast and compare by race breast cancer-specific and all-cause survival among BCN participants . These women are homogeneous in terms of their socioeconomic status and they all have access to free screening, which will allow us to look at the independent effects of distance and cancer mortality.

Methods

Study Setting/Participants

The setting of this study was the Best Chance Network of South Carolina. The program is a network consisting of public and private partnerships between health clinics and radiology facilities to provide free mammograms, clinical breast exams, Pap tests, pelvic exams, diagnostic procedures, case management, community education on breast/cervical cancer and early detection for disadvantaged women (below 200% of the Federal trade poverty level and those who lack insurance coverage) in the state. From the BCN, women with breast cancer confirmed and linked to the South Carolina Cancer Registry (SCCCR) between 1996 and 2009 were included in the current analyses. Demographic information from women with breast cancer in BCN were linked to the SCCCR using probabilistic matching techniques by first name, last name, middle name (if provided), date of birth, address, and social security number (SSN). The cut-off score of 1 was used in Link Plus for the probabilistic matching.

From 1996 to 2009, there were 707 women with a first primary breast cancer diagnosed from BCN that were matched to the SCCCR. Due to the small sample of other ethnic groups (n=17), only women with race/ethnicity African American (AA) and European American (EA) were included in the study, leaving a total sample of 690 women for inclusion in the study. The study was approved by the South Carolina's Department of Health and Environmental Control (SC-DHEC), South Carolina Central Cancer Registry, and was exempted from approval from the Institutional Review Board of the University of South Carolina Office of Research.

Distance variables

Three travel distance variables were calculated: travel distance to the screening referral provider, travel distance to the diagnosing mammography facility, and travel distance to the nearest mammography facility. ArcGIS 9.3 (Redland, CA) Network Analyst was used to calculate the travel distance in miles along the road network based on point location of residence to the facilities. Patients' addresses, screening referral providers' addresses, and diagnosing mammography facilities' addresses were obtained from BCN. The closest mammography facilities were identified from the Food and Drug Administration's (FDA) list of accredited facilities (24). All addresses were geocoded using the Method and Tiers method (25) developed by the SC-DHEC Informatics Division.

Residential addresses among all 690 women were successfully geocoded to the exact street address. For all of the 690 women, we were able to calculate distance to the closest mammography facilities. Only 481 women had a screening referral provider's address and 319 women had a diagnosing mammography facility recorded. Hence, we were only able to calculate travel distance to the screening referral provider and diagnosing mammography facility for these women.

Outcomes

The outcome of interest was breast cancer-specific and all-cause mortality. To determine breast cancer-specific mortality, we looked at the "Sequence Number" and the "Cause of Death" from the cancer registry data. If the "Sequence Number" was "00", meaning that the subject had one malignant primary in her lifetime, and the "Cause of

Death" was "Cancer", then the death was related to breast cancer. If the subject died of any cause of death, including breast cancer, then the death was considered all-cause mortality.

Covariates

Patients' characteristics were obtained from the BCN and SCCCR, which included age, race, breast cancer stage, estrogen receptor status, marital status, health insurance, income, and first course of treatment. Breast cancer stage at diagnosis was categorized as *in-situ*, localized, regional, and distant. Estrogen receptor (ER) status was categorized as positive, negative, and borderline. Income at time of enrollment was categorized into three groups: <$10000, $10000-$19999, and >$20000. Health insurance status was categorized as Yes or No. Marital status was categorized into married or not married. Cancer treatments were categorized as surgery, radiation, chemotherapy, hormonal therapy, and none.

Statistical Analysis

Descriptive statistics were calculated for all characteristics variables. Chi-square tests and t-tests were used to examine the associations between characteristics variables and race. Survival probabilities for breast cancer-specific and all-cause mortality were examined using Kaplan-Meier survival method. Cox proportional hazard modeling was used to assess the relationship between mortality and travel distance to the screening referral provider, diagnosing mammography facility, and closest mammography facility. To assess whether travel distance was influenced by race, we created an interaction term between travel distance and race in each of the Cox proportional hazard model (travel

distance to screening provider-race, travel distance to diagnosing mammography facility-race, and travel distance to closest mammography facility-race). Travel distance was broken into <5 miles, 5-<10 miles, 10-<15 miles, and 15+ miles. However, due to low sample size in some categories, distances were grouped into <10 miles and 10+ miles for analysis.

Individuals not found to be deceased at the end of the time period, December 31, 2009, were considered to be alive at the time of censoring. For breast cancer specific mortality, non-cancer cause of death and cancer death other than breast cancer were also considered censored. The proportional hazards assumption was examined through the logarithm of negative logarithm of survival probability with logarithm of time and the Schoenfeld residuals were further evaluated to confirm that there were no violations of the assumption. Missing data were excluded from analyses. All analyses were done using SAS statistical software version 9.3 (Cary, NC). All statistical tests were 2-sided with a P-value of ≤ 0.05 used to determine statistical significance.

Results

Our study samples consisted of slightly more AA women compared to EA women (53.6% vs 46.4%, respectively). The mean age of the women was ~ 55 years old (standard deviation [SD] =6.7). The average travel distance to the screening provider, diagnosing mammography facility, and closest mammography facility were 10.8 miles (SD=10.9 miles), 14.4 miles (SD=15.7 miles), and 8.1 miles (SD=6.5 miles), respectively. EA women had significantly longer travel distance to the screening provider and diagnosing mammography facility compared to AA women. There were 90 breast

cancer specific deaths and 133 all-cause deaths. Table 6.1 presents the study population characteristics by race.

Figure 6.1 and 6.2 display the survival proportions for breast cancer-specific and all-cause among AA and EA women. There were no significant racial differences in the overall 5-year survival proportions for breast cancer-specific (~87% for EA women and ~85% for AA women, P = 0.64) and all-cause mortality (~81% for EA women and ~80% for AA women, P = 0.90).

Table 6.2 presents the results of the Cox proportional hazards models for breast cancer-specific and all-cause mortality. There was no association between travel distance to the screening referral provider, diagnosing mammography facility, closest mammography facility and all-cause mortality. Women with 10+ miles of travel distance to the diagnosing mammography facility had ~ 2.3-fold excess risk of death from breast cancer compared to those with < 10 miles of travel distance (hazard ratio [HR], 2.32; 95% confidence interval [CI], 1.12-4.80). However, after adjustment for age, race, ER status, marital status, income, insurance status, breast cancer stage at diagnosis, and treatment, the association was no longer statistically significant. Women with 10+ miles of travel distance to the closest mammography facility also had excess risk of death from breast cancer compared to those with < 10 miles of travel distance to the closest mammography facility (HR, 1.83; 95% CI, 1.21-2.77). The association was also not significant after adjustment for covariates.

Table 6.3 presents the Cox proportional hazard analyses for breast cancer-specific mortality by race. After adjustment for age, ER status, marital status, income, insurance

status, breast cancer at diagnosis, and treatment, there was no association between travel distance to the health centers and mortality (breast cancer-specific and all-cause mortality) among both race groups. However, in the crude model for breast cancer-specific, both AA and EA women who lived 10+ miles from the closest mammography facility had an increased risk of death from breast cancer compared to those who lived < 10 miles (HR=1.75 [95% CI=1.00-3.05 and HR=1.93 [95% CI=1.04- 3.60], respectively).

The Cox proportional hazard analyses for all-cause mortality, by race, are displayed in table 6.4. There was no association between travel distance to the screening referral provider, diagnosing mammography facility, closest mammography facility and all-cause mortality among EA and AA women.

Discussion

The purpose of this study was to assess whether travel distance to the screening referral provider, diagnosing mammography facility, and closest mammography facility are associated with breast cancer mortality and all-cause mortality among women in the BCN of South Carolina. The overall breast cancer-specific 5-year survival rate among women in BCN was ~86%. We found no significant racial differences in the overall 5-year survival rate for breast cancer-specific and all-cause mortality among EA and AA women. Interestingly, the breast cancer-specific survival rate among AA women (~85%) was much higher than the United States national average of ~77% (2).

We found no evidence that longer travel distance to the screening referral provider, diagnosing mammography facility, and closest mammography was associated with all-cause mortality. In our crude analysis for breast cancer-specific mortality,

women who lived 10+ miles from their diagnosing mammography facility and closest mammography facility had increased risk of breast cancer mortality compared to those who lived < 10 miles from the facility. However, the association diminished once we controlled for other characteristics. The null finding was similar to a study in Northern England, which found no association between travel time to the general practitioners and breast cancer survival (26). This study looked at approximately 28,000 breast cancer cases from the Northern and Yorkshire Cancer Registry & Information Service (NYCRIS) and found that patients living further from the general practitioner were not associated with breast cancer survival. However, they found an inverse association with travel time to the hospital and breast cancer survival; women living further from the hospital had a better chance of breast cancer survival compared to those living the closest. Though the population of this study may not be comparable to those in the BCN, similar findings were observed.

The findings from this study are subject to several limitations. One limitation of this study is that we had limited data on potentially important covariates. BCN and SCCCR collect minimal data for reporting purpose and we have no information on some of the important factors (e.g. family history, body mass index, lifestyle, and other comorbidities) that contribute largely to breast cancer mortality and survival. We also have limited data on tumor characteristics, such as Her-2/neu expression and progesterone receptor status, which also affect breast cancer mortality. Another limitation is that we have no information on the mode of transportation that the women use to get services from these facilities. Studies have shown that the type of transportation can affect health care visits (27, 28). Though all addresses were successfully geocoded, the

geocoded address may not be the actual location of residence. This can happen due to new developments, rural areas or streets that are not stored in the geocoding map. Due to the demographic of our sample, which are mostly low income and uninsured women, the findings may not be generalizeable to other populations.

Our study also has several strengths. To our knowledge, this is first study to investigate whether travel distance influence breast cancer-specific and all-cause mortality among disadvantaged women in a funded program, which aims at improving breast and cervical health disparities. Another strength of this study was that we were able to compute travel distance from the exact street address of the women's residence to the health facilities, which is a more accurate measurement of travel distance compared to using straight line or eulicudean distance. An additional strength was we were able to estimate travel distance based on the actual use of the mammography facility by using patient's diagnosing mammography facility and residence at time of diagnosis.

We found no racial disparities in breast cancer-specific and all-cause mortality among women in BCN. The findings in this study may be unique, because our population was from a program that was established to provide adequate screening and follow-up among women who enter the program; therefore, we see no racial disparities. These findings may reveal that the program is meeting established program standards of reducing health disparities among racial/ethnic groups.

There was no association between travel distance to the screening referral provider, diagnosing mammography facility, closest mammography facility and all-cause or breast cancer mortality after adjustment for several covariates. Though not what

expected, we were not surprised with these null findings because our previous study (not yet published) did not find any convincing evidence that travel distance to the screening referral provider and mammography facility was associated with breast cancer stage of diagnosis. If we had found that travel distance to these facilities was associated with breast cancer stages at diagnosis, then we would have expected to find an association.

In conclusion, these findings suggest that geographic accessibility to these health facilities (screening referral provider, diagnosing mammography facility, and closest mammography facility) may not be a mediator to breast cancer mortality and survival among women in programs like BCN. Further research should be conducted of similar programs like BCN and in other parts of the country to confirm these findings. The geography from where our population came from was relatively rural and may not be generalized. Future research that examines factors which may affect geographic accessibility, such as mode of transportation, should also be investigated.

Table 6.1. Demographic Characteristics of the Study Population, by Race*

Characteristics	Black (n=370) n (mean±SD)	White (n=320) n (mean±SD)	p-value
Age	370 (55.6±6.7)	320 (55.4±6.6)	0.75
Travel Distance			
Provider	248 (9.3±9.6)	233 (12.5±12.0)	**<0.01**
Diagnosing mammography facility	179 (12.6±14.1)	140 (16.4±17.5)	**0.05**
Nearest mammography facility	370 (2.46±1.19)	320 (2.54±1.03)	0.36
	n (%)	**n (%)**	
All Cause of Deaths			
Dead	70 (18.9%)	63 (19.7%)	0.80
Alive	300 (81.1%)	247 (80.3%)	
Breast Cancer Deaths			
Dead	50 (13.5%)	40 (12.5%)	0.69
Alive	320 (86.5%)	280 (87.5%)	
Breast Cancer Stage at Diagnosis			
In situ	67 (18.4%)	44 (13.9%)	0.45
Localized	160 (43.9%)	144 (45.6%)	
Regional	125 (34.3%)	114 (36.1%)	
Distant	13 (3.6%)	14 (4.4%)	
Behavior of Cancer			
In-situ	67 (18.1%)	44 (13.8%)	0.12
Invasive	303 (81.9%)	276 (86.3%)	
Estrogen Receptor Status			
Positive	115 (60.5%)	115 (74.2%)	**<0.01**
Negative	75 (39.5%)	38 (24.5%)	
Borderline	0 (0.0%)	2 (1.3%)	
Marital Status			
Unmarried (single/separated/divorced)	214 (68.2%)	153 (56.7%)	**<0.01**
Married	100 (31.8%)	117 (43.3%)	
Insurance			
Yes	87 (23.5%)	77 (24.1%)	0.85
No	283 (76.5%)	242 (75.9%)	
Income			
<$10,000	254 (68.7%)	190 (59.4%)	**0.02**
$10,000-$19,999	102 (27.6%)	107 (33.4%)	
>$20,000	14 (3.8%)	23 (7.2%)	
Treatment			
Surgery only	91 (43.1%)	73 (42.9%)	**0.02**
Surgery, radiation	36 (17.1%)	35 (20.6%)	
Surgery, radiation, chemotherapy	50 (23.7%)	21 (12.4%)	
Surgery, radiation, chemotherapy, hormone	18 (8.5%)	26 (15.3%)	
Hormone only	0 (0.0%)	2 (1.2%)	
None	16 (7.6%)	13 (7.7%)	

* Missing were excluded; number may not add up to total

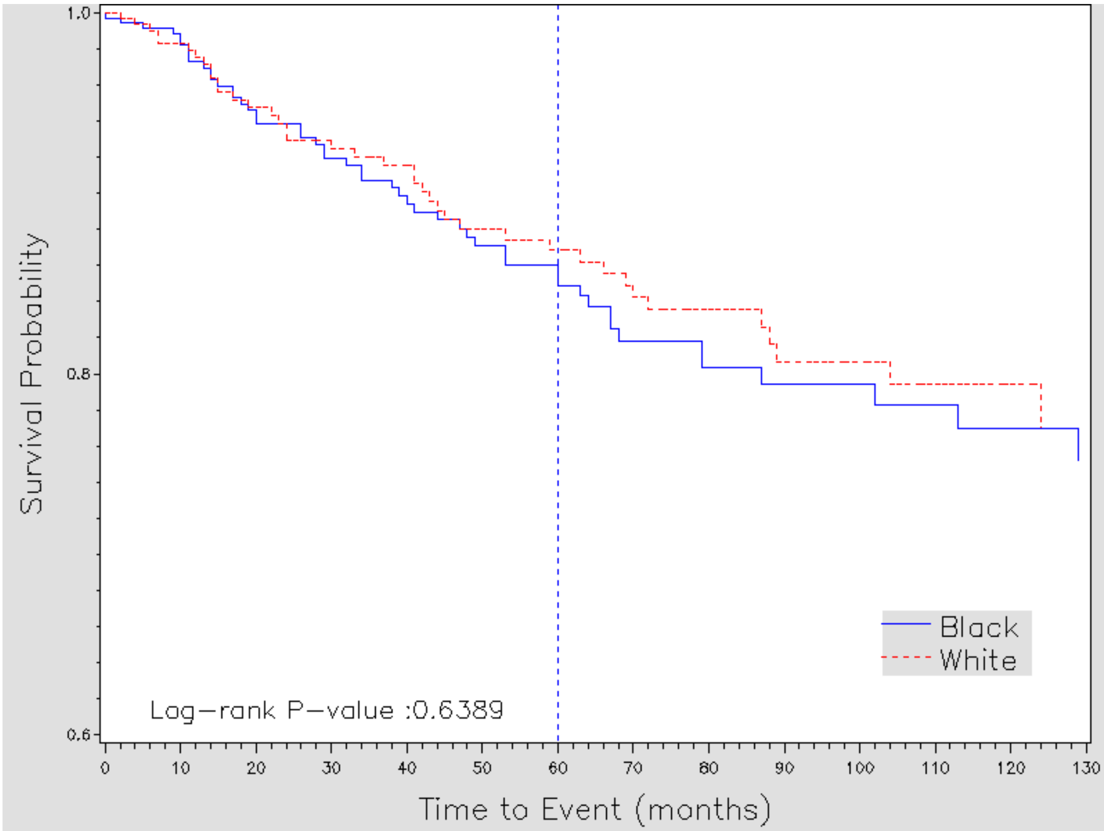

Figure 6.1: Breast Cancer Survival among Women in BCN, by Race

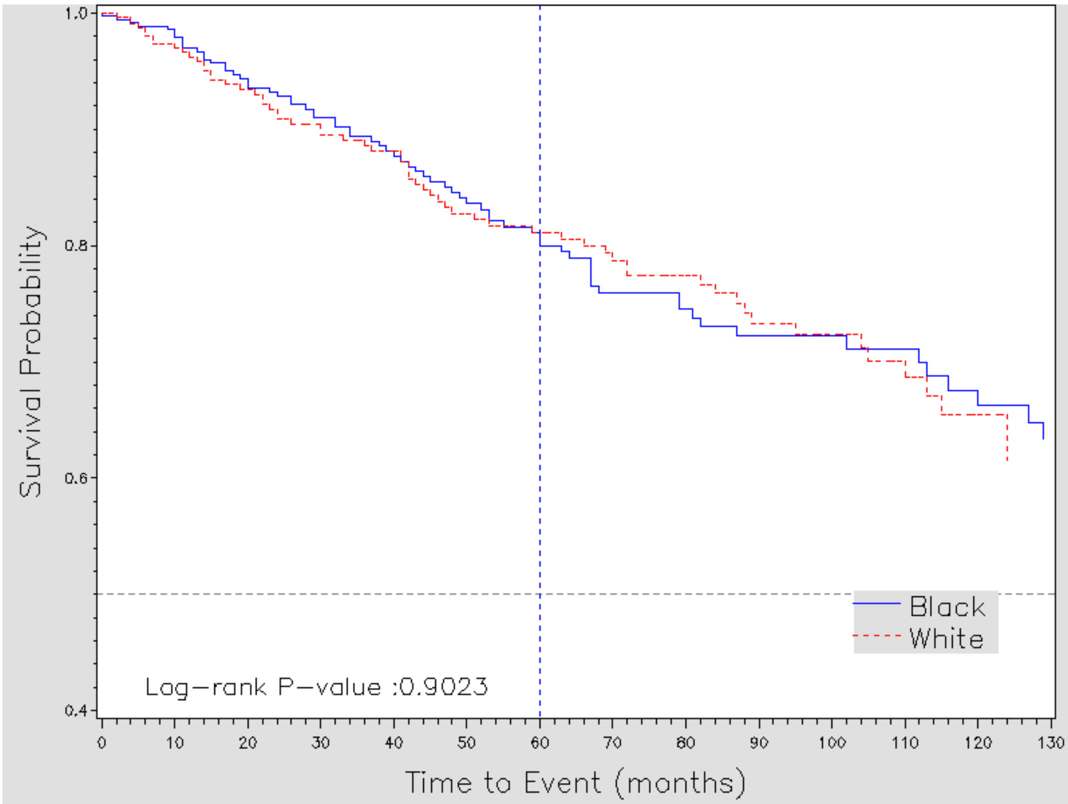

Figure 6.2: All-Cause Mortality Survival among Women in BCN, by Race

Table 6.2. Crude and Adjusted Hazard Ratios for Breast Cancer-Specific and All-Cause Mortality among Travel Distance 10+ miles Compared with < 10 Miles

	Breast Cancer Deaths				All Deaths			
Variables	**Deaths (n)**	**Person-Years**	**Crude HR (95% CI)**	**Adjusted HR (95% CI)***	**Deaths (n)**	**Person-Years**	**Crude HR (95% CI)**	**Adjusted HR (95% CI)***
Distance to Provider								
< 10 miles	36	1116	Referent	Referent	53	1158	Referent	Referent
10 + miles	27	833	1.03 (0.63-1.70)	1.03 (0.33-3.16)	36	856	0.93 (0.61-1.42)	0.86 (0.32-2.30)
Distance to Diagnosing Mammography								
< 10 miles	10	647	Referent	Referent	19	677	Referent	Referent
10 + miles	26	759	**2.32 (1.12-4.80)**	2.21 (0.68-7.21)	32	772	1.50 (0.85-2.65)	1.46 (0.58-3.65)
Distance to Closest Mammography								
< 10 miles	47	2129	Referent	Referent	79	2228	Referent	Referent
10 + miles	43	1045	**1.83 (1.21-2.77)**	2.14 (0.95-4.83)	54	1101	1.38 (0.98-1.96)	1.81 (0.89-3.69)

* Adjusted for race, age, estrogen receptor, marital status, income, insurance, treatment, and breast cancer stage at diagnosis
HR=Hazard ratios; CI=Confident Intervals

Table 6.3. Crude and Adjusted Hazard Ratios for Breast Cancer-Specific Mortality among Travel Distance 10+ miles Compared with < 10 Miles, by Race

	African American				European American			
Variables	**Deaths (n)**	**Person -Years**	**Crude HR (95% CI)**	**Adjusted HR (95% CI)***	**Deaths (n)**	**Person -Years**	**Crude HR (95% CI)**	**Adjusted HR (95% CI)***
Distance to Provider								
< 10 miles	25	596	Referent	Referent	11	520	Referent	Referent
10 + miles	9	394	0.59 (0.27-1.26)	3.32 (0.42-26.04)	18	439	1.92 (0.91-4.08)	3.64 (0.52-25.68)
Distance to Diagnosing Mammography								
< 10 miles	6	365	Referent	Referent	4	281	Referent	Referent
10 + miles	14	355	2.61 (1.00-6.79)	2.71 (0.59-12.47)	12	404	2.17 (0.70-6.75)	2.18 (0.07-68.69)
Distance to Closest Mammography								
< 10 miles	26	1109	Referent	Referent	21	1020	Referent	Referent
10 + miles	24	573	**1.75 (1.00-3.05)**	1.53 (0.51-4.59)	19	472	**1.93 (1.04-3.60)**	3.44 (0.91-12.93)

* Adjusted for age, ER, marital status, income, insurance, treatment, and breast cancer stage at diagnosis

Interaction: Distance to provider*race=0.69; Interaction: Distance to diagnosing mammography facility= 0.96;Interaction: Distance to closest mammography facility= 0.49

HR=Hazard ratios; CI=Confident Intervals

Table 6.4. Crude and Adjusted Hazard Ratios for All-Cause Mortality among Travel Distance 10 + Miles Compared with < 10 Miles, by Race

Variables	African American				European American			
	Deaths (n)	Person -Years	Crude HR (95% CI)	Adjusted HR (95% CI)*	Deaths (n)	Person -Years	Crude HR (95% CI)	Adjusted HR (95% CI)*
Distance to Provider								
< 10 miles	34	616	Referent	Referent	19	542	Referent	Referent
10 + miles	10	399	**0.49 (0.24-0.98)**	1.34 (0.23-7.97)	26	456	1.65 (0.91-2.98)	2.83 (0.60-13.27)
Distance to Diagnosing Mammography								
< 10 miles	12	391	Referent	Referent	7	286	Referent	Referent
10 + miles	16	364	1.49 (0.70-3.14)	1.69 (0.51-5.63)	16	408	1.64 (0.67-3.99)	1.98 (0.47-8.31)
Distance to Closest Mammography								
< 10 miles	39	1160	Referent	Referent	40	1067	Referent	Referent
10 + miles	31	611	1.51 (0.94-2.42)	1.33 (0.50-3.56)	23	490	1.25 (0.75-2.09)	2.59 (0.86-7.86)

* Adjusted for age, ER, marital status, income, insurance, treatment, and breast cancer stage at diagnosis

Interaction: Distance to provider*race=0.92; Interaction: Distance to diagnosing mammography facility=0.21 ;Interaction: Distance to closest mammography facility= 0.65

HR=Hazard ratios; CI=Confident Intervals

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CHAPTER 7

SUMMARY

Breast cancer is the most commonly diagnosed cancer and is the second cause of cancer-related mortality among women in the United States (1). In South Carolina, breast cancer is the most common cancer diagnosed and is the second largest cause of cancer deaths among women in the state (2). Statewide, the age-adjusted incidence of breast cancer from 2002-2006 have remained stable at around 119 per 100,000 women (2), with a higher age-adjusted incidence among European American women compared to African American women (127.6 and 111.3 per 100,000 women, respectively) (2, 3). However, African American women had a 39% higher mortality rate compared to European American women (4). This disparity may be due to breast cancer tumor characteristics (5, 6) and difference in access/utilization of early detection and treatments among African American women (7, 8).

Early screening is the single most effective method in reducing mortality from the disease (1). Annual mammography with adequate follow-up is estimated to result in reductions in mortality ranging from 25% to 44% (9-15). Despite the benefit of mammography, many women do not maintain annual adherence to screening mammograms (16) and complete follow-up after having an abnormal mammogram screening (17, 18).

Minority, uninsured, and lower socioeconomic status women often do not have access to early detection (19). These women are less likely to utilize mammography screening (19-21), less likely to have timely and complete follow-up after an abnormal mammography screening (22), more likely to be diagnosed with advanced-stage breast cancer (23), and have poorer survival (24). To reduce the disproportionate burden of breast cancer among women in South Carolina, the Best Chance Network (BCN) was established to offer screening and follow-up services to disadvantaged women in the state.

This dissertation was designed to assess travel distance to the health facilities (screening referral provider, diagnosing mammography facility, closest mammography facility) and its relationship with completion of abnormal mammography follow-up, breast cancer stage at diagnosis, and mortality among women in the BCN program. A retrospective cohort study that covers a period of 14 years between 1996 and 2009 was used to investigate travel distances (to the screening referral provider, diagnosing mammography facility, and closest mammography facility) and completion of abnormal mammography follow-up, breast cancer stage at diagnosis, and mortality among women in the BCN program.

In the following pages, the results from each aim are summarized and discussed.

Aim 1(Chapter 4): Travel distance to screening facilities and completion of abnormal mammography follow-up among disadvantaged women

In aim 1, we examined the relationship between travel distance to the screening referral provider, diagnosing mammography facility, closest mammography facility, and

completion of abnormal mammogram follow-up among women in the BCN program. Inadequate screening or incompletion of abnormal mammogram follow-up after an abnormal mammogram screening can contribute to poor cancer survival. Factors associated with mammography and inadequate screening have been scrutinized in numerous studies, which includes patients characteristics, socioeconomic status, insurance status, having a primary health care provider, recommendations for screening from primary health care providers, lack of transportation, language barriers, concern about the effects of radiation, and fear of cancer (25-30). From a recent review of the literature, there has been no study examining distance to the screening referral provider, mammography facilities, and its effect on completion of abnormal follow-up. The finding from this aim contributes to some of the known factors relating to inadequate breast cancer screening.

We found that women who lived further from their diagnosing mammography facility had longer day to resolution (completion of abnormal mammographic finding) compared to those who lived the closest (p=0.05). AA women had significantly longer day to resolution compared to EA women; the largest difference in median day to resolution was in travel distance to the diagnosing mammography facility (28 days for AA women vs. 22 days for EA women). We also found that women who lived closest to the diagnosing mammography facility were more likely to have an abnormal mammographic follow-up completion compared to those who lived the farthest. When stratified by race, we still see the association among AA and EA women for the adjusted model.

One important aspect of this aim was our sensitivity analysis using travel distance to the diagnosing mammography facility compared with travel distance to the closest mammography facility. We observed no association between completion of abnormal mammogram follow-up and travel distance to the closest mammography facility, but we found an association with travel distance to the diagnosing mammography facility. Women were more likely to have their abnormal mammogram follow-up completed if they were living closest to their diagnosing mammography facility. Choosing a facility for screening may not always be the closest to home due to various factors, such as personal preference, neighborhood characteristics, and hours of operation. Relying on the closest mammography facility to calculate the travel distance may not portrait an accurate distance.

Aim 2(Chapter 5): Travel distance to screening facilities and breast cancer stage at diagnosis among disadvantaged women

The purpose of this aim was 1) to investigate whether travel distance to the screening provider and mammography facility was associated with stage of breast cancer at diagnosis, 2) are there racial disparities in breast cancer stage at diagnosis among women in BCN, and 3) are there a difference in the distribution of breast cancer stage at diagnosis among BCN participants and non-BCN participants? Breast cancer stage at diagnosis is an important factor in survival and mortality (1). Women with breast cancer diagnosed at advanced stage have limited treatment options and poorer survival compared to women with early stage breast cancer. The 5-year relative survival rate among women whose breast cancer is diagnosed while in the regional stage are nearly

four times greater than those of women whose cancer has spread to distant (distant stage) lymph nodes or organs at the time of diagnosis (84% vs. 23%) (1). Many studies have examined travel time/distance to health care or mammography facility and breast cancer stage at diagnosis (31-39); however, findings have been inconsistent between the studies. The inconsistent results may be due to geographical locations and density of population or mammography facilities in the area. Nevertheless, almost all of these studies used the closest mammography facility to calculate the travel distance/time. In our study, we were able to use all three health facilities (screening referral provider, diagnosis mammography facility, and closest mammography facility).

In the crude models, we found no significant relationship between travel distance and breast cancer stage at diagnosis. However, when we adjusted for age, race, income, insurance status, and marital status, we found that women living 10-15 miles from their diagnosing mammography facility were 2.25 times (95% CI=1.04-4.83) more likely to be diagnosed with late stage breast cancer compared to those living less than 5 miles from their diagnosing mammography facility. We found no association (both in the crude and adjusted model) among EA and AA women in the BCN.

Among women in the BCN, there was no difference in the distribution of cancer stages and race (p-value=0.45). However, there was statistically significant difference between breast cancer stage at diagnosis and race among non-BCN women (p-value<0.01), with AA women had higher percentage of regional and distant breast cancer at diagnosis compared to EA women.

Our null findings, though not what we expected, is similar to six studies that found no association between travel distance to the mammography facility and breast cancer stage at diagnosis (31-36). From a literature search, there were three studies that found an association (37-39). However, all of them used the closest mammography facility as the facility of utilization and they used zip code centroids to compute the travel distance.

All of these studies that examined this relationship had no information on patients' mammography utilization. By using the nearest mammography facility, a patient may not utilize this facility due to various reasons. Relying on the closest mammography facility may underestimate the true travel distance between patients' residence and actual mammography usage if the closest facility is not the one being utilized.

Aim 3(Chapter 6): Travel distance to screening referral provider, mammography facility, and breast cancer mortality among women in a state breast cancer screening program

In aim 3, we investigated the association between travel distance to the screening referral provider, mammography facility, and cancer-specific and all-cause mortality among women in BCN. We also contrasted and compared breast cancer-specific and all-cause survival between European-American and African-American women in BCN. Stage at diagnosis, age, race, socioeconomic status, lifestyle, and tumor characteristics are all associated with breast cancer mortality and survival (37-45). The association between geographic proximity to the screening referral provider, mammography facility, and breast cancer mortality has not been elucidated.

We found no significant difference in the survival proportions for breast cancer-specific and all-cause among AA and EA women. In the crude model, we found that women living 10+ miles from the diagnosing mammography and closest mammography facility had ~2-fold increase risk of death from breast cancer compared to those living <10 miles. However, we found no association when adjusted for race, age, estrogen receptor, marital status, income, insurance, treatment, and breast cancer stage at diagnosis. We also found no association between travel distance to the screening referral provider, diagnosing mammography facility, closest mammography facility and all-cause mortality between EA and AA women. Though we did not find any study that investigated travel distance to healthcare facility and breast cancer survival in the United States, a study in Northern England had similar finding (46); they found no association between travel time to the general practitioners and breast cancer survival. Our finding shows that travel distance to the screening referral provider and mammography facility may not be a risk factor for breast cancer mortality and survival among women in BCN. Since our finding from aim 2 did not find any convincing evidence that travel distance to the screening referral provider and mammography facility was associated with breast cancer stage of diagnosis, we were not surprised with these null findings.

Implications

This dissertation provides significant contributions to the better understanding of geographical level barriers to abnormal mammographic follow-up and breast cancer morbidity and mortality, especially in South Carolina. Mammography screening rates have improved among women; however, barriers affecting timely follow-up from an

abnormal mammogram and breast cancer morbidity and mortality are still serious public health concerns. The study showed that travel distance from patient residence to the diagnosing mammography facility affects completion of abnormal mammographic finding; women living farther from the facility had longer days to resolution (completion of abnormal mammographic finding) compared to those who living the closest. This study provides a geographical dimension that needs to be considered when developing effective intervention to make sure women are having timely abnormal mammographic finding. Due to the low-income population of the BCN program, some women may not have reliable transportation. Hence, providing transportation, such as a shuttle, for patients to and from the facility may be an effective intervention.

The establishment of BCN was to provide service delivery and ensures timely and complete diagnostic follow-up and treatment initiation for underserved women screened through the program. Since we found evidence of racial disparity in the time to completion of abnormal mammogram work-up (AA women had longer days to completion compared with EA women), additional support to the BCN program to expand services should be promoted to reduce the disparity in days to completion of abnormal mammographic finding among EA and AA women.

Living farther from the screening referral provider and mammography facility did not increase the chance of late-stage breast cancer at diagnosis and mortality among women in BCN. There were also no racial disparities in the breast cancer stage at diagnosis and mortality among the women. These findings reveal that the program is meeting established program standards of reducing health disparities among racial/ethnic

groups. However, the findings in this study may be unique, because our population was from a program that was established to provide adequate screening and follow-up among women who enter the program; therefore, it may not be generalized to the general population.

Another explanation for these null findings could be related to the geography of South Carolina. The state is relatively a rural state and women may seek health services no matter the distance. Due to the extensive BCN network providing service throughout the state, travel distance may not be an issue for these women; the mean travel distance to the screening provider is 10.9 miles (SD=10.5), diagnosing mammography facility is 14.6 miles (SD=15.8), and closest mammography facility is 8.1 miles (SD=6.5). Overall, this study has shed some light on geographical proximity to some of the health facilities and completion of abnormal mammographic finding and breast cancer morbidity and mortality among women with homogenous socioeconomic status. This study adds to some of the breast cancer disparities research in South Carolina.

Recommendations for Future Research

This research is the first study to use geospatial method to examined travel distance to the screening provider, mammography facility, and completion of abnormal mammography follow-up among a low-income population who have access to screening at no cost. It is also one of the few research studies to examined travel distance to the screening provider, mammography facility, and breast cancer morbidity and mortality. This research measured the distance to mammography facilities using road network. However, the variation of the route, speed limits or other barriers to travel was not

considered. Future research that examines the relationship between travel distance to mammography facility or health facilities should consider these barriers, because it affects travel distance. Capturing an accurate measurement of travel distance/time will help better understand whether location of the health facilities affect health outcome. Other important factors to consider are the mode of transportation utilized by patients, availability and frequency of transport services, quality of service provided in the mammography facilities, and the nature of social constraints related to mammography utilization.

This study was conducted on a population that came from a relatively rural area. The attitude regarding health care services may be different from people living in more urban areas. Further study on similar program like the BCN in other geographical location and larger study from the general population should be investigated to confirm the findings.

Though this research focused on the geographic aspect (travel distance) from the patient's residence to the health facilities, future research should also seek qualitative aspects focusing on the provider-patient communications to follow-up. The patient, provider, and system can all contribute to inadequate follow-up and morbidity and mortality. A multi-discipline will not deepen our knowledge about barriers affecting completion of abnormal mammographic finding and breast cancer morbidity and mortality, but it may also suggest avenues of intervention to decrease the health disparities related to breast cancer.

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