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Master of Public Health
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Study Design Project
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Impact of Financial Strength and Distance to Treatment on Initial Diagnostic Staging of Breast Cancer in African American Women Residing in Arkansas and Surrounding Areas

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Abstract

Breast cancer mortality in Arkansas is disproportionately increased for African American women compared to Caucasian women. This study aims to establish an association between distance to treatment and financial strength in the clinical staging of carcinoma at first diagnosis in African American women in Arkansas. Following a cross-sectional study design, researchers will survey African American women diagnosed with breast cancer in the last ten years. Participants will be prompted with questions about financial strength and distance to medical facilities. Furthermore, participants will be queried on the stage and type of breast cancer based on the original diagnosis. Data collected from surveys will be stratified to determine the strength of the association of distance, financial strength, and severity of breast cancer stage. It is expected that distance will have a proportional correlation to the tumor stage, while financial strength will be inversely proportional. The association of financial strength is favored to have a stronger association than distance on the initial tumor stage at initial diagnosis.

Background

Breast cancer is a serious disease costing an average of 16.2 years of life lost (YLLs) in the United States in 2019 (National Cancer Insititute, 2022). African American women suffer disproportionately higher mortality rates due to breast cancer, specifically, 40% higher nationally and 42% higher in Arkansas(Jatoi et al., 2022, Young et al.,2020, Foy et al.,2018). Between 2014-2018, 27.7 deaths per 100,000 were attributed to African American women. Caucasian women suffer 20.0 deaths per 100,000 (Jatoi et al., 2022). Adjusting for age, the breast cancer-specific mortality rate between 2015 and 2019 is 19.5 per 100,000 (95% CI (18.6,20.4)) (United States Department of Health and Human Services). For African American women, the disease-specific mortality rate for the same period is 28.1 per 100,000 (95% CI (25.2,31.3)) (United States Department of Health and Human Services). Caucasian women suffer a much lower rate at 18.6 per 100,000 (95% CI (17.7,19.6)) (United States Department of Health and Human Services). The age-adjusted incidence of breast cancer in Arkansas for all races is 119.5 per 100,000, while African American women carry 121.0 per 100,000 (95% CI (114.8,127.5) (American Cancer Society). Comparatively, the age-adjusted incidence rate for Caucasian women is 118.1 per 100,000 (95% CI (115.6,120.7) (American Cancer Society). The national incidence rate for African Americans of 125.8 per 100,000 is lower than that of Caucasian women at 139.2 cases per 100,000 women between 2014 and 2018. Therefore, there is a disparity in the burden of disease for breast cancer in Arkansas compared to the national metrics. It is estimated that in 2022, 2440 women will be diagnosed with breast cancer (American Cancer Society: Cancer Facts & Statistics, Holt & Fisher et al., 2020, U.S. Census Bureau).

In a study by Qinjin & Xiaobai et al., low survival rates from breast cancer among African American women are influenced by socioeconomic factors (Fan et al., 2021). Distances to cancer screenings and treatment locations are prohibitive for the substantially rural state (Young et al., 2020). Only 65% of women aged 45 years and older keep up with routine breast cancer screenings compared to the national average of 68% (American Cancer Society: Cancer Facts & Statistics). The national breast cancer mortality rate has decreased nationally due to preventative screenings and novel cancer treatments (Bevers et al., 2018). However, higher-grade tumors are often found in African American women (Monzavi-Karbassi et al., 2016).

Reducing the time to treatment initiation (TTI) is significant in cancer survival, and obstacles impeding accelerated diagnosis and treatment are critical to extended survival (Cone et al., 2020). Approximately 41% of Arkansas' population resides in rural areas, which increases the TTI for breast cancer care (Rural Development in Arkansas). An increased TTI metric positively correlates with a worse prognosis (Cone et al., 2020). Cone et al. estimated mortality increases from 9.7% to 11.0% for a TTI of 8-60 days and 61-120 days, respectively.

Socioeconomic factors impacting favorable prognoses for African American Women are varied. Some factors include a lack of clinical trial enrollment, hospital resources, clinical communication, and biased medical practices (Siddharth & Sharma, 2018). Other factors that affect breast cancer survival include medical comorbidities such as hypertension, diabetes, and heart disease (Siddharth & Sharma, 2018). Compared to Caucasian Americans, the African American population of Arkansas has a 14.1% higher proportion of hypertension (*PRC research: UAMS Fay W. Boozman college of public health*). Diabetes in African American women is 2.14 times more likely to be diagnosed than in Caucasian women (Carnethon et al., 2017). As previously mentioned, distance to health care facilities providing preventative medicine and cancer care increases TTI and, ultimately, the prognosis. African American women are disproportionately impacted by breast cancer compared to their Caucasian counterparts. Due to socioeconomic position, distance to treatment, reduced treatment options, and various comorbidities, the prognosis is poorer for this segment of the Arkansas population.

Objectives:

This study aims to measure the association between the initial clinical breast cancer stage to two exposures: distance to treatment and financial strength. Furthermore, a determination will be sought whether financial strength or distance to treatment have a stronger association with the initial breast cancer stage at initial diagnosis.

Materials and Methods

Study design:

A cross-sectional study design was chosen for this research as it will compare two exposures: distance to treatment and the financial strength of the patient. The study will look at the exposures and outcomes simultaneously at one point. This study will look at the exposure variables' prevalence and impact on the outcomes. A case-control study is ideal for rare diseases, and data can be easily pulled from patient records; however, temporality does not need to be established. Since no medical intervention will be performed, a randomized control study is excluded. A cohort study is excluded as a potential design due to the high resource demand. However, a cohort study could be used to analyze exposures from known breast cancer outcomes.

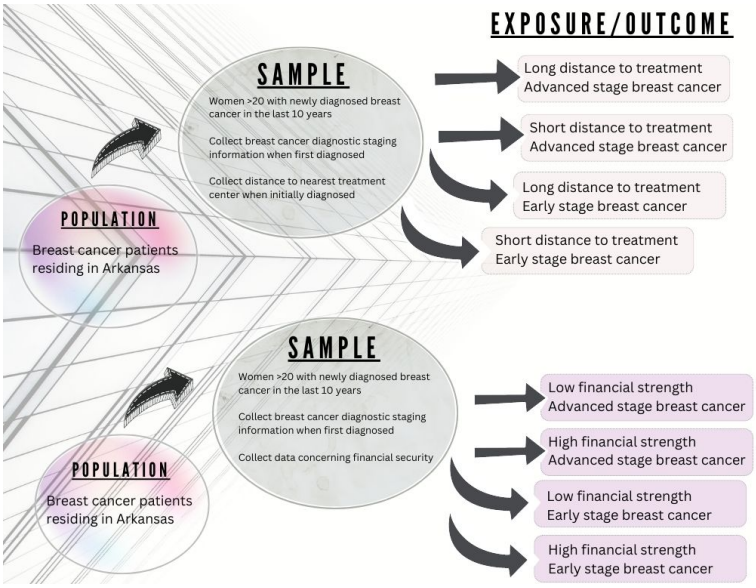

Figure 1. Diagram illustrating cross-sectional experimental design.

Study participants:

Researchers will Utilize living patient records from Baptist Health Breast Center and the University of Arkansas Women's Breast Center. A sample of African American patients newly diagnosed with breast cancer in the last ten years over the age of 20 will be selected.

Data collection

An electronic questionnaire will be disseminated via emails on record. If an email cannot be located, the questionnaire will be mailed to the physical mailing address with links to the

electronic questionnaire or provide the option for the patient to complete the questionnaire and mail it back with paid postage. Two separate exposures will be analyzed in this study. The first exposure will be the distance to medical treatment, which will be assessed by geographical software that will measure the distance from the patient's address of record to the nearest clinical setting appropriate for initial testing. The address of the record will be compared to the survey response to ensure accuracy. Distances less than 10 miles will be considered a short distance to treatment, while >10 miles to treatment will be extended. The second exposure addresses financial strength, which will be assessed utilizing a measure adopted by the Center for Financial Services Innovation and applied as a measure by Weida et al. (Weida et al. 2020). Indicators that will be implemented in this questionnaire will center around spending habits, level of liquid capital, investments, debt, income, and emergency money. For the analytical purposes of this study, participants will be categorized as having weak and strong financial strength using the measure mentioned above.

Two outcomes are considered for this study, early stage and advanced stage. These outcomes were derived from the four clinical stages of cancer: stage 0: non-invasive; stage 1: limited invasion into surrounding breast tissue, possible lymph node involvement; stage 2: Invasion into a larger area of the breast, possible lymph node involvement; Stage 3: Extensive invasion into the breast, lymph node involvement and possible skin and chest wall involvement, stage 4: lymph node involvement, distant metastatic disease (Memorial Sloan Kettering Cancer Center). Stages 0-2 will be considered the early stage, while stages 3-4 will be considered the late stage. Patients will be directed to indicate the disease stage rendered by their respective medical institutions.

Confounding variables may include carcinogenic agents, which may induce aggressive tumors that grow slowly. The Triple-Negative breast cancer (TNBC) subtype accounts for 15% of breast cancers and is known to be the most aggressive and could be potentially found at higher stages compared to those with ER, PR, and HER2 markers (Ensenyat-Mendez et al., 2021, American Cancer Society). Inflammatory breast cancer is another aggressive subtype that may lead to more advanced stages upon new diagnosis (American Cancer Society). Aggressive breast cancers can be accounted for and excluded from the analysis. Further confounders could include mental health complications preventing a patient from seeking care promptly and other unexpected delays. Clinical performance and medical errors may also lead to delays in diagnosis and treatment. Unforeseeable delays may confound all exposures leading to more advanced breast cancer staging. Finally, a confounder that will need to be addressed is age.

Older women, such as those living in assisted living environments, may not be able to obtain clinical treatment promptly (Rosen & Sten et al., 2018). This confounder can be addressed by age-adjusting the data.

Possible sources of errors

Selection bias may be a potential issue if wealthier patients leave Arkansas to seek treatment. The same bias could impact those participants who live at a greater distance from medical care and opt to go out of state for care. Potential errors may arise in the participant responses regarding initial breast cancer diagnosis, including stage and when they were diagnosed. Measurement bias may be an error of concern if patients do not appropriately recall financial information or provide erroneous distance to treatment. Such bias would disproportionately impact representation based on wealth, distance, or both. Recall bias may be mitigated by utilizing medical records to supplement participant responses. Errors grounded in observer bias will not be anticipated as the survey will be electronic and not rely on in-person response recording. Follow-up bias will not impact the research as no follow-up will be required. Non-differential misclassification bias cannot be excluded due to the potential of staging errors due to pathological diagnostic errors. Early-stage breast cancer could mistakenly be classified as advanced or vice versa (Wu et al., 2021).

Time frame

Due to the nature of the study and the reliance upon electronic response forms, the study should not require substantial completion time. However, participants must be given adequate time to respond, approximately six months. Gaining permission to review patient records is expected to take up to 6-8 months. Analyzing records would take only 2-3 weeks with adequate staffing. Therefore, the study is anticipated to take approximately 1-2 years to gather data and produce a final written paper sufficiently.

Ethical consideration

Patient confidentiality will be preserved under the Health Insurance Portability and Accountability Act of 1996 (HIPPA) guidance. Therefore, written consent must be gathered from patients mediated through the covered entities (U.S. Department of Health & Human Services, 2022). Identifiable patient information will be kept confidential, with all relevant information redacted from the study. FDA regulations regarding biomedical research will be strictly adhered to, including obtaining approval from the Institutional Review Board (IRB) before initiating research (Center for Drug Evaluation and Research, 2019). All relevant regarding the experimental design will be submitted for ethical approval by the IRB.

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Proposed Main Findings and Possible Impact of the Study

Measurement of disease burden will include the stage-specific prevalence of early-stage (0,1,2) and advanced-stage (3,4) breast cancer in the study population at initial diagnosis. In addition, age-specific Prevalence of early-stage (0,1,2) and late-stage (3,4) breast cancer in the study population at initial diagnosis will be utilized.

The odds ratio will be the measure of association for this study. The odds ratio for distance to treatment: odds of long distance to treatment with advanced-stage breast cancer to the odds of long distances with early-stage breast cancer (Table 1). The odds ratio for financial strength: odds of weak financial strength to advanced-stage breast cancer to the odds of weak financial strength to early-stage breast cancer (Table 2). Finally, the two odds ratios will be compared to find whether distance to treatment or financial strength has a more significant impact on the severity of the disease at initial diagnosis.

Distance to Treatment	Cases of Advanced Stage Breast Cancer	Cases of Early Stage Breast Cancer
Long	A	B
Short	C	D
	A+C	B+D
Odds Ratio	(A/C)/(B/D)	

Financial Strength	Cases of Advanced Stage Breast Cancer	Cases of Early Stage Breast Cancer
Weak	A	B
Strong	C	D
	A+C	B+D
Odds Ratio	(A/C)/(B/D)	

Table 1. Odds ratio calculation for distance and initial breast cancer staging. Table 2. Odds ratio calculation for financial strength and initial breast cancer staging.

Stage-specific prevalence (Table 1) will be calculated to elucidate the breast cancer stage distribution at initial diagnosis. Together with distance data, initial staging at first diagnosis will illuminate the prevalence of an advanced stage at initial diagnosis and the correlating distance to treatment. The proportion of advanced stage at initial diagnosis is expected to be low in the study population. Age-specific prevalence (table 2) will show the effects of age on initial staging at first diagnosis.

Stage-specific prevalence of early stage (0,1,2) and advanced stage (3,4) breast cancer in the study population at initial diagnosis		
Stage	Cases	Prevalence
0	X_0	$X_0/(X_0+X_1+X_2+X_3+X_4)$
1	X_1	$X_1/(X_0+X_1+X_2+X_3+X_4)$
2	X_2	$X_2/(X_0+X_1+X_2+X_3+X_4)$
3	X_3	$X_3/(X_0+X_1+X_2+X_3+X_4)$
4	X_4	$X_4/(X_0+X_1+X_2+X_3+X_4)$
Early Stage	$X_0+ X_1+X_2$	$(X_0+ X_1+X_2)/ (X_0+X_1+X_2+X_3+X_4)$
Late Stage	$X_3+ X_4$	$(X_3+ X_4)/ (X_0+X_1+X_2+X_3+X_4)$

Table 1. Prevalence calculations for the stage-specific prevalence of breast cancer in the study population.

Age-specific prevalence of early stage (0,1,2) and late-stage (3,4) breast cancer in the study population at initial diagnosis.

Age group	Total # Early Stage (E)	Total # Late Stage (L)	Total All Stages (E+L)
20-29	E_{20-29} /$(E+L)_{20-29}$	L_{20-29} /$(E+L)_{20-29}$	$(E+L)_{20-29}$
30-49	E_{30-49} /$(E+L)_{30-49}$	L_{30-49} /$(E+L)_{30-49}$	$(E+L)_{30-49}$
50-59	E_{50-59} /$(E+L)_{50-59}$	L_{50-59} /$(E+L)_{50-59}$	$(E+L)_{50-59}$
60-69	E_{60-69} /$(E+L)_{60-69}$	L_{60-69} /$(E+L)_{60-69}$	$(E+L)_{60-69}$
70-79	E_{70-79} /$(E+L)_{70-79}$	L_{70-79} /$(E+L)_{70-79}$	$(E+L)_{70-79}$
80-89	E_{80-89} /$(E+L)_{80-89}$	L_{80-89} /$(E+L)_{80-89}$	$(E+L)_{80-89}$
90+	E_{90+} /$(E+L)_{90+}$	L_{90+} /$(E+L)_{90+}$	$(E+L)_{90+}$
			Total # of Study Participants

Table 2. Age-specific prevalence of early-stage vs late stage in the study population.

Confounders involving tumor types known to be more aggressive will be excluded based on histopathological data obtained from final pathology reporting. Those tumors will include triple-negative, inflammatory breast cancers. Survey data will be crosschecked with patient records provided by the relevant health system. Confounders involving mental health complications will be eliminated by ensuring that patients with adverse mental health diagnoses before breast cancer diagnosis will be excluded from the data. Confounders involving medical errors or clinical performance will be addressed by ensuring that delay in initial diagnosis due to clinical errors is excluded from the study. Including this data would be harmful to the study because a delay in obtaining tissue will provide time for the tumor stage to be more advanced when initially diagnosed. The data will be utilized if the error is resolved and a correct diagnosis is rendered on the original histopathological specimen rather than through a repeat procedure. This research will use the amended diagnosis if corrected reports are issued. Adjusting the data for age will address some confounding impacts of age-related mental health deterioration. Eliminating carcinogenic exposures will not be possible, as recall bias would be too impactful.

If there is a correlation between increasing distance to clinical care and the initial stage of breast cancer at first diagnosis, this would be helpful to data for breast cancer prevention. Many Arkansas residents live in rural environments and are more likely than not at an increased risk for healthcare delay. Mobile healthcare units could help alleviate the travel burden on those living in rural destinations. Furthermore, guidance in providing free or low-cost transportation to rural residents could reduce the exposure to long distances to care. Assessing an association of financial strength and initial tumor stage is expected to correlate and help substantiate socioeconomic position's impact in healthcare. If shown to be accurate, financial assistance could alleviate the financial roadblocks to rural residents to assist with clinical work-up to give the best outcome for potential breast cancer cases.

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