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CONSIDER US: ANALYSIS OF NATIONAL MAMMOGRAPHY SCREENING RECOMMENDATIONS ON AFRICAN AMERICAN WOMEN

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CONSIDER US: ANALYSIS OF NATIONAL MAMMOGRAPHY SCREENING RECOMMENDATIONS ON AFRICAN AMERICAN WOMEN

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Breast cancer is the second most common cause of cancer related death in women in the United States with one in eight women expected to develop the disease in their lifetime. Unfortunately, breast cancer is the leading cause of cancer related death among African American women. African American women are four times more likely to die from breast cancer that Caucasian women. Mammography screenings are the most effective method of reducing breast cancer mortality in African American women. This study aimed to determine if the changes made to the mammography screening recommendations put forth by the U.S. Preventive Services Task Force in November 2009 and later re-enforced in January 2016 create an increased burden of breast cancer diagnoses among African American women. The study does so by addressing whether changing the time interval between mammography screenings affects the likelihood of African American women being diagnosed with breast cancer and if African American women typically present with knowledge of their family history of breast cancer. The U.S. Preventive Services Task Force used the fact that the majority of women develop breast cancer in their 60s and the burden caused by false

positives to support their decision to change the screening recommendations, however, literature describes a higher incidence of aggressive breast cancers and earlier onset of disease in African American women. Data from the Breast Cancer Surveillance Consortium was used to run multivariate regression analyses of breast cancer diagnosis within a year of the previous mammography screening and the presence of knowledge of family history at the time of mammography screening. A significant association was not found between race and the likelihood of being diagnosed with either invasive or non-invasive breast cancer. However, African American women had a higher proportion of women without knowledge of their family history of breast cancer. This research fills an important gap in understanding how the recommendation changes can influence the mortality and morbidity of African American women that develop breast cancer. Its implications include potential policy changes on the mammography screening recommendations given specifically for African American women.

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INTRODUCTION

This dissertation seeks to determine if the changes made to the mammography screening recommendations in November 2009 and later re-enforced in January 2016 create an increased burden of breast cancer diagnoses among African American women.[1] While the argument has been made for the change in screening recommendations due to the majority of women developing breast cancer in their 60s and the burden caused by false positives, recent literature describes a higher incidence of aggressive breast cancers and earlier onset of disease in African American women.[2]

Much of the literature surrounding African American women and breast cancer has focused on the causes of increased mortality and morbidity of breast cancer among African American women compared to their Caucasian counterparts. Historically, researchers focused on these areas because African American women had higher rates of mortality and morbidity though Caucasian women were more likely to be diagnosed with breast cancer.[2-7] The literature has documented that African American women are more likely to be diagnosed with a late-stage breast cancer due to a myriad of reasons [2,8-27], but the impact of increasing the time interval between mammography screenings from one year to two years has not been reported. Therefore, this study will determine if the changes to the mammography screening recommendations has the potential to cause more African American women to be diagnosed with a breast cancer.

The study used mammography screening history and date of diagnosis as determinants of the threat of greater incidence. This research fills an important gap in understanding how the recommendation changes can influence the mortality and morbidity of African American women that develop breast cancer. Its implications include potential policy changes on the mammography screening recommendations given specifically for African American women.

BACKGROUND

Literature Review

Breast cancer is the second most common cause of cancer related death in women in the United States with one in eight women expected to develop the disease in their lifetime.[5] Breast cancer can be detected through physical examination of the breast[28] but is most commonly detected through mammography screenings. Other screening methodologies exist, such as ultrasound, digital breast tomosynthesis, and magnetic resonance imaging; however, mammography screenings are directly linked to reducing breast cancer mortality by discovering the cancer before signs and symptoms present and are the most effective method of reducing late-stage diagnoses in African American women.[10,29,30] For women aged 40-60 years, mammography screenings have been shown to reduce mortality from breast cancer by 15-32%.[9,31,32] Mammography screenings have also been found to be the most cost effective method of diagnosing breast cancer.[33] Staging is a method of categorizing the progression of the disease by describing the size, location, and spread of the breast cancer. There are five stages of breast cancer, zero through four. Stage zero is noninvasive ductal carcinoma in situ (DCIS). Stages one through four are invasive breast cancers and they are categorized by early/localized, locally advanced, and metastatic states.[28]

- Early or Localized: Stage I, Stage II, and Stage IIIA
- Locally Advanced: Stage IIIB and Stage IIIC
- Metastatic Breast Cancer: Stage IV

Stage is determined by the size of the tumor and whether or not the cancer has spread to neighboring tissues, lymph nodes, and distal parts of the body. Discovering the presence of the disease while it is categorized as Stage I or II yields a 100% and 93% 5-year survival rate,

respectively. Stage III has a 72% 5-year survival rate and Stage IV has only a 22% 5-year survival rate.[34] The drastic decline in survival likelihood has caused stage III and IV breast cancers to be termed late-stage breast cancers. The earlier a breast cancer is detected, the more likely a woman is to survive.

Incidence

In the United States, 12.8% of women can expect to develop breast cancer at some point in their lives.[4] There will be an estimated 268,600 new cases of breast cancer and 41,760 deaths in 2019.[35] Among African American women, there is an expected 33,840 cases and 6,540 deaths in 2019.[5] This study focuses on the difference between African American and Caucasian women because non-Hispanic black and non-Hispanic white women both have higher incidence and death rates for breast cancer than other races/ethnicities.[4] The incidence of breast cancer is increasing for both non-Hispanic whites and non-Hispanic blacks.[5] Speaking to the significance of late-stage diagnoses, Healthy People 2020 has separate goals for reducing breast cancer mortality and reducing the rate of late-stage cancer diagnoses.[14] African American women experience elevated death rates and poorer survival rates for breast cancer nationally.[4,5]

Treatments and Quality of Life

There are six types of standard treatments for breast cancer: surgery, radiation therapy, chemotherapy, hormone therapy, target therapy, and immunotherapy.[28] Breast-conserving surgery removes the cancerous tumor and some of the tissue surrounding the tumor but leaves the breast. These procedures can be referred to as a lumpectomy, partial mastectomy, segmental mastectomy, or quadrantectomy. The surgical removal of the entire breast is a simple or total mastectomy. When conducting a mastectomy, neighboring lymph nodes may also be removed. A modified radical mastectomy removes the entire breast as well as the lymph nodes under the arm,

the lining over the chest muscles, and a portion of the chest wall muscles. Radiation therapy uses high energy x-rays to kill the cancerous cells or prevent further growth of the tumor. Chemotherapy uses oral or intravenous drugs to kill the cancerous cells or prevent further growth of the tumor. Hormone therapy removes the hormones that aid in the tumor's growth through drugs, surgery, or radiation. Targeted therapy uses drugs, antibodies, and other substances to kill specific cancerous cells while not harming normal tissue. Lastly, immunotherapy uses the body's immune system to kill the cancer by using substances to boost or restore the body's defenses. For the purposes of this study, targeted therapies and chemotherapy will be reported together.[36]

Breast cancer treatments are tailored to the stage and type. An early or localized breast cancer is treated with surgery. The surgical treatment can range from either breast conserving to modified radical mastectomy. Postoperative radiation can also be given to ensure the cancer does not return. In the case of a locally advanced breast cancer, the prescribed treatment is usually surgery, chemotherapy before and/or after surgery, radiation therapy, and hormone therapy. Treatment of metastatic breast cancer includes all six treatment options with the surgical treatment being a total mastectomy and surgical removal of the cancerous tumors for other areas of the body. The complexity of treatment increases considerably for late-stage breast cancers.

There are also types of breast cancers that are defined by the biomarkers present on the cancerous cells. Biomarker testing identifies the presence of estrogen receptors, progesterone receptors, and human epidermal growth factor type 2 receptor (HER2). If the breast cancer cells have larger than normal amounts of HER2 receptors on their surface, the cancer cells are called HER2 positive (HER2+). If the breast cancer cells have a normal amount of HER2 on their surface, the cancer cells are called HER2 negative (HER2-). If the breast cancer cells do not have estrogen receptors, progesterone receptors, or an abnormally large amount of HER2 receptors,

the cancer cells are called triple negative. If the breast cancer cells do have estrogen receptors, progesterone receptors, and an abnormally large amount of HER2 receptors, the cancer cells are called triple positive. Triple negative breast cancer is treated with conventional chemotherapy, but adjuvant chemotherapy is recommended for tumors ≥6 mm and radiation therapy for tumors >5 cm.[37] Knowing the type of breast cancer helps inform how best to treat the cancer. HER2+ breast cancer is more likely to grow and divide faster than HER2- breast cancer.

Cancer treatments are designed to destroy cancerous cells and cannot always discriminate good cells from unwanted cells. The more advanced the cancer, the more invasive the treatment. The increase in each of these treatments causes more lasting damage to the body. Some of the side effects to cancer treatment are pain, nausea, vomiting, anemia, fatigue, physical limitations, infection, lymphedema, and depression.[38] Of these side effects breast cancer survivors report a diminished quality of life from lymphedema, sexual problems, restricted physical abilities, and depression.[39,40] These quality of life issues can remain long after the actual cancer treatments have been completed. Therefore, the costs of a late-stage cancer diagnosis extends beyond the physical treatment of the cancer.

Late effects appear months to years after breast cancer treatment. Recipients of radiation can experience lung inflammation, especially if chemotherapy was given at the same time as the radiation, arm lymphedema, and the development of breast cancer in the remaining breast for women under the age of 45. Chemotherapy can cause blood clots, premature menopause, heart failure, or the development of another cancer. Targeted therapy can also lead to heart failure.[28]

Incidence and Mortality in African American Women

Breast cancer is the most commonly diagnosed cancer in African American women and accounts for a third of all the cancer diagnoses.[5] Historically, non-Hispanic white women have

had a higher incidence of breast cancer than non-Hispanic black women. In recent years, the incidence rates of non-Hispanic white women and non-Hispanic black women have converged.[5] From 2005-2014 breast cancer incidence rates increased among non-Hispanic black women but remained stable for non-Hispanic white women.[4] Compared to non-Hispanic white women, non-Hispanic black women have a higher incidence of breast cancer before age 40 but lower incidence rates for the 65-84 age range.[4] Non-Hispanic black women have a higher incidence of breast cancer in their 40s than non-Hispanic white women. They also have a higher proportion of estrogen receptor negative breast cancer especially under the age of 50.[6] Previous studies found that the incidence rate of metastatic breast cancer among young non-Hispanic white and non-Hispanic black women, or early onset de novo metastatic breast cancer, were increasing.[41,42] However, DeSantis et al., found that when accounting for the sharp decrease in unstaged breast cancers the incidence rate among non-Hispanic white women levels off but continues to increase and remain statistically significant for non-Hispanic black women.[5]

Non-Hispanic black women are more likely to die from breast cancer at every age. The five-year breast cancer survival rate is lowest for non-Hispanic black women.[4] The highest mortality rates are seen among the age group with the smallest mortality disparity between non-Hispanic white women and non-Hispanic black women, age 65 and over.[6] Although the mortality rates are lower among women under 40 and women 40-49, the highest mortality disparity between non-Hispanic white and non-Hispanic black women was found in these two age groups.[6] Overall, 81% of breast cancers were diagnosed in women age 50 years or older with 89% of the deaths occurring in this age group. The median age of breast cancer diagnosis (White: 63 years, Black: 59 years) and death (White: 70 years, Black: 62 years) is lower in African American women.[4,5] Breast cancer survival rates for non-Hispanic black women are

81% for regional cancers and 26% for distant cancers compared to 89% and 37% for non-Hispanic white women.[4]

Disparity Causes

Personal Factors

Non-Hispanic black/African American women consistently have the highest prevalence of late-stage breast cancer diagnoses.[8,13,43] Mobley et al. named being categorized as Non-Hispanic black or African American as the number one predictor for being diagnosed with late-stage breast cancer.[16] The high mortality rate is due, in some part, to the point in disease progression at which African American women are diagnosed with breast cancer. African American women are more likely than Caucasian women to be diagnosed with a late-stage breast cancer, thereby decreasing their likelihood of survival.[16]

Behaviors causally linked to a late-stage cancer diagnosis are the same behaviors linked to developing breast cancer in general. These are smoking, alcohol consumption, a lack of breastfeeding, use of hormone therapy, having a body mass index over 25, and a lack of physical activity,[9] all of which are prevalent in the African American community.[5]

An additional risk factor for being diagnosed with late-stage breast cancer is having a low socioeconomic status. With the presence of health insurance being a major contributing factor to the utilization of preventive health services among African American women, the lack of health insurance becomes a barrier for the women of this population.[18] The perceived prohibitive costs prevents some employers from providing health insurance to all of their employees.[44] The presence of employer-sponsored health insurance, specifically, directly affects the use of health care services even in people with known high susceptibility to developing cancer.[45]

Under insured or uninsured women under the age of 65 are most at risk for being diagnosed with late-stage breast cancer.[16] Some women with low socioeconomic statuses have to choose between going to a doctor's appointment or receiving a full day's pay.[10] Women living near and below the poverty line are more likely to be diagnosed with later-stage breast cancer and African American women are twice as likely to live below the federal poverty limit as white women.[5]

Mammography screenings are directly linked to reducing breast cancer mortality by discovering the cancer before signs and symptoms present.[29] For women aged 40 – 60 years, mammography screenings have consistently shown to reduce mortality from breast cancer by 15-32%.[9] The research has found a plethora of reasons low-income minority women fail to receive mammography screenings in a timely enough fashion to prevent late-stage breast cancer diagnosis.[10] Reasons can effectively be grouped by construct to get a sense of thematic patterns driving behavior. Behavior capability is an issue with a majority of women reporting that merely knowing where to go to receive a mammography screening, scheduling screenings, and not having adequate information regarding the screening were issues preventing them from completing mammography screenings.[46] Likewise, self-efficacy is an obstacle. Women reported the struggle of taking time off from work, finding adequate transportation, and needing to care for children and/or elders. For women with knowledge of the mammography screening process, there were preventive outcome expectations such as women who expressed fear of having the screening result be a positive diagnosis for breast cancer.[46] Women diagnosed with breast cancer at any stage report a fear of dying.[47] A late-stage breast cancer diagnosis would only exacerbate this fear as a late-stage diagnosis decreases a woman's chance of survival compared to an early stage cancer. Even still, women reported perceived barriers such as the cost of screening and the

possible pain and discomfort experienced during mammography. Social norms generated in a segregated community were also found to be a hindrance to receiving a mammography screening particularly when that norm is to not conduct health promoting behaviors.[13,48] All of these factors are compounded by the ongoing feelings of distrust in health care providers in the African American community as a whole.[49-51] The woman's utilization of health care resources also depends on the social norms to which the woman subscribes.[13,48]

Research has found that spatial access to primary health care facilities was more impactful on late-stage breast cancer diagnoses than was access to mammography screenings in minority and low-economic status areas.[18,52] Access to preventive health services within the community becomes particularly salient when you consider the additional barrier of access to transportation. Low socioeconomic African American women are less likely to have personal vehicles.[17] With primary care physicians (PCP) being the first line of defense for preventive services, it stands to reason that they would also be a key player in reducing the likelihood of receiving a late-stage breast cancer diagnosis.[19] Societal attitudes that led to a decline in the number of PCPs and a decline in mammography screening rates coupled with the increased demand in the use of primary care preventive procedures and services create a unique circumstance where more vulnerable populations could be left without access to mammography screenings.[53,54]

Environmental Factors

Interpersonal environmental factors impacting African American women's likelihood of receiving a mammography screening include fear of losing a partner, lack of support from family and friends, and access to transportation.[10,55] The presence of positive social support from intimate partners, family, and friends contributes to the improvement of the quality of life. In

lower socioeconomic communities, reduced personal vehicle ownership potentially makes travel dependent on social relationship.[17]

Access to care is the most debilitating environmental factor with regards to women receiving mammography screenings.[10,13,16] The lack of spatially accessible primary care clinicians is directly related to late-stage cancer diagnosis. African American women with a lower socioeconomic status without geographical access to preventive services are at an increased risk of being diagnosed with late-stage breast cancer. [18] Breast cancer diagnoses and outcomes are improved by utilization of physicians that were not primary care providers as well suggesting a health promoting benefit from having access to see any desired physician.[19]

Being under or uninsured greatly influences the likelihood of a woman pursuing preventive and diagnostic services.[16,19] Many women do not have the option to get a mammogram without having at least being seen by a PCP.[16] The use of mammography exclusively because of affordability compared to other tests leaves women who require more sensitive testing measures susceptible to a late-stage diagnosis.[16] Regular utilization of preventive health care services, such as going to see a PCP, has been found to reduce the chance of late-stage breast cancer.[10,29] Research has shown that women with at least 10 visits to a PCP enjoyed a 50% decreased likelihood of being diagnosed with a late-stage breast cancer, thus reducing their risk of breast cancer mortality by 41%.[19] Without these visits, patients are unable to be alerted to the signs and symptoms of breast cancer, how to recognize them, and recommendations for formal screenings. Failure to make the recommended annual preventive care visits can result in not only the PCP not catching developing symptoms, but the patient missing patient education delivered during these visits. Women with increased primary care visits also have a 27% decreased overall mortality rate.[19]

Biological Factors

The type of breast cancer with which a woman is diagnosed can impact her likelihood of being diagnosed with a late-stage breast cancer and her chance of survival. African American women have a higher incidence of triple negative breast cancer. Triple negative breast cancer is an aggressive breast cancer and is associated with a worse prognosis.[56-59]

African American women have been found not to have knowledge of familial cancer history.[24] First- and second-degree relatives with breast cancer spell increased risk of developing breast cancer; however, African American women with an elevated risk are unable to alert health care providers of their need for early screenings. The lack of knowledge of family medical history among African American women is of particular concern for screening recommendations that delay the start of initial screenings for average risk women.

Current Recommendations

The U.S. Preventive Services Task Force (USPSTF) published their recommendations and were met with much debate.[60] The USPSTF provided an update to their mammography screening recommendations for average risk women in November 2009. In January 2016, the USPSTF provided further justification of their recommendations citing that women 60-69 are the age group of women most likely to avoid breast cancer mortality through mammography screening and mammography screening at ages 40-49 only avoids a small number of deaths due to breast cancer, but poses a greater number of harms. They define average risk as a woman lacking a personal history of breast cancer, a genetic mutation known to increase breast cancer risk, and/or a history of exposure to chest radiation in childhood. When these conditions are met, the USPSTF recommends receiving a mammography screening biennially for women 50-74 years. Regardless of the thorough explanation the USPSTF gave for their stance, the published

recommendations from prominent professional bodies are still quite mixed. Organizations have sided with U.S. Preventive Services Task Force, others have chosen to continue to recommend women begin screening at 40, and one organization has developed a completely different recommendation.

The USPSTF notes that the initiation of regular, biennial mammography screenings before the age of 50 is an individual decision that should bring into account the benefits and harms of mammography screenings. The task force conceded the inability to assess the benefits and harms of mammography screenings in women 75 years of age and older.[1] The American Academy of Family Physicians state that their recommendations mirror those of the U.S. Preventive Services Task Force.[61] Likewise, the American College of Physicians (ACP) suggests clinicians discuss the potential benefits and harms and a woman's preferences for mammography screening in average-risk women age 40 to 49. They also make special note that the potential harms outweigh the benefits in most women age 40 to 49. They recommend biennial mammography screenings for women age 50 to 74 and the discontinuation of screening in women age 75 or older and women with a life expectancy of 10 years or less.[62]

The American Medical Association (AMA), National Comprehensive Cancer Network (NCCN), and American College of Obstetrics and Gynecology (ACOG) all recommend women begin screening at age 40. It is also important to note the language the organizations use when presenting their recommendations because the language shows the value placed on other organizations recommendations. Some organizations, such as the American Cancer Society (ACS) and the ACP, state that they use other organization's recommendations in their evaluations for their own mammography screening guidelines.[62,63] Other organizations state that their recommendations mirror that of other professional organizations. The AMA state that their

policy agrees with the guidelines of the following organizations: ACOG; the American College of Radiology; ACS; the National Cancer Institute; and the NCCN. Their published guidelines are to initiate annual mammography screenings starting at age 40 for average risk women.[64] The NCCN recommends women aged 40 and older receive mammography screenings but concedes that the screening interval for women age 40 to 49 is still controversial. In light of that declaration, they state that the NCCN's panel has elected to follow the American Cancer Society's guidelines of annual mammography screenings.[65] The ACOG recommends average risk women be offered mammography screenings starting at age 40. In the event screening has not been initiated in their 40s, women should begin mammography screenings by age 50. Average risk women should have mammography screenings every one or two years based on an informed, shared decision-making process that includes a discussion of the benefits and harms of annual or biennial screening and incorporates patient values and preferences. Screening beyond age 75 should be based on a shared decision-making process between patient and provider informed by the woman's health status and longevity.[66]

Lastly, there is the hybrid recommendation of the ACS. With average risk being defined similarly to that of the USPSTF, the ACS recommends average risk women undergo annual mammography screenings beginning at the age of 45 and continuing until age 54. Women age 55 and older should begin screening biennially or have the opportunity to continue screening annually. Women age 40 through 44 should have the opportunity to begin annual screening. Women should continue mammography screenings as long as they are in good health and they have a life expectancy of at least 10 years.[67,68]

Cause of Recommendation Change

The USPSTF assessed the benefits and harms of mammography screenings. They found the sensitivity of mammography screening is 77-95% and the specificity is 94-97%.[1] False positives are common and lead to the need for additional imaging tests and invasive procedures like biopsies. False positives are more common for women age 40-49.[1] Aside from false positives there is overdiagnosis. Overdiagnosis occurs when an early stage invasive breast cancer is found in a woman that will likely die from another cause before succumbing to the breast cancer, most commonly seen in older women. In younger women it is when the detected DCIS breast cancer will never progress to an invasive cancer.[1] Ultimately, the number of women that would need to be screened to prevent one death from breast cancer is 1904 among women age 39-49. The number of women that would need to be screened to prevent one death from breast cancer is 1339 among women age 50-59. The number of women that would need to be screened to prevent one death from breast cancer is 377 among women age 60-69.[1]

Screening Controversy

Of all the behaviors impacting the development of late-stage breast cancer diagnosis, the most influential behavioral factor on late-stage diagnoses is mammography screening.[10,29] In order to prevent the disease's progression to the third or fourth stage, the disease would have to be found and treated earlier. To accomplish this, breast cancer needs to be detected before it can be felt by the woman or clinicians.[9] Not only is mammography screening the most effective measure to prevent late-stage diagnosis among all women, it is the measure most effective among African American women.[30] The recommendations for breast cancer screenings generated by organizations like the USPSTF, World Health Organization, ACOG, and ACS directly impact the likelihood and frequency of a woman in this population getting

mammography screenings. Unfortunately, leading professional organizations do not all agree on the best mammography screening guidelines.

Studies of the USPSTF's 2009 recommendations for mammography screening for the general population with normal risk of developing breast cancer has been varied but show little association mortality reduction though it has been studied through various data sources.[32] Amy Wang et al. conducted a retrospective, interrupted time-series analysis using insurance claims to determine the impact of the 2009 recommendation change from annual to biennial screenings on insured women's mammography screening practices. They found that there was a small drop in the 40-49 age group but no impact on the 50-64 age group.[69] Qin et al. also looked at medical insurance claims and found mammography screening rates among US women age 40-49 decreased following the 2009 recommendation change from USPSTF.[70] A decrease was also found in mammography screening rates among Medicare Part B patients following the screening recommendations.[71]

Looking at patient records for a large non-profit Oregon Health system, Nelson et al. found that mammography screening among women aged 50-74 increased, while decreasing for patients under the age of 50 and over the age of 74 in accordance with the new screening recommendations. The population in this study was mostly insured with only 3.2% without commercial or public insurance and only 2.3% covered by Medicaid.[72] Sprague et al. studied the impact of the USPSTF recommendations on mammography screening among Vermont women using a statewide registry. They noted a decrease in mammography screening after the 2009 recommendations were released.[73] Chang et al. found little change in mammography use in surveyed Medicare recipients before and after the recommendation change except for African American women in which they found no change at all.[74] Lee et al. studied mammography use

among African American and white community members in Arkansas. They found that there was a decline in mammography use for white women but no significant change in mammography use among African American women except for older women with no post-secondary education.[75]

Looking at data from the Breast Cancer Surveillance Consortium, Wernli et al. found that the screening interval between mammography screenings did not increase following the USPSTF guideline changes. It is important to note that their study population in the post period was more likely to have a college education, be in the highest quartile income level and live in an urban environment.[76] Using National Health Interviews Surveys, Fedewa et al. found that mammography screenings only decreased for higher socioeconomic younger women.[77] Block et al. looked at the mammography use specifically among women age 40-49 in the year following the recommendation changes and found no change using BRFSS data.[78] Gray and Picone also found that USPSTF recommendations lead to a reductions in mammography screening rates across all age groups using the BRFSS.[79] However, Dehkordy et al. found a decrease in mammography screening rates among all age groups with similar trends among insured women using data from the BRFSS.[80]

The impact of the change of the recommendations on actual mammography screening practices has been examined multiple times, but the actual impact of the change on breast cancer stage at diagnosis has been examined at an Atlanta hospital and through national registries. Simulating cancer stage distributions from patient records for the tumor registry of a large safety net hospital in Atlanta, GA, Habtes et al. found that the USPSTF recommendations lead to later breast cancer stages than the ACS.[81] They broaden the reach of the study and still found the ACS guidelines produce a higher proportion of stage I breast cancers and decreased the proportion of

stage II and III breast cancers compared to USPSTF guidelines. The ACS guidelines also offered higher 5-year survival estimates than the USPSTF guidelines. They also found that the ACS guidelines would produce a greater savings ($5,528) than the USPSTF guidelines. They felt their findings supported the use of ACS guidelines among low-income African American women treated in public urban hospitals.[82] In contrast to the study completed by Farley et al., O'Donoghue et al. found that the USPSTF guidelines resulted in substantial savings over current practices and annual screenings for 85% of the population. Specifically, a savings of $5.4 billion and $7.7 billion annually could be seen compared to current mammography screening practices and annual mammography screenings, respectively.[83] Instead of looking at a single hospital, Guo et al. looked at national cancer registries and found that the change in mammography screening guidelines from USPSTF slightly increased in situ, localized, and distant breast cancers, but decreased the incidence of regional cancer.[84] The literature has covered insured women at length, but analysis of the effect of the recommendation change on the uninsured is lacking. The question then becomes what impact does the change in recommendations have on African American women that are already more likely to have a late-stage diagnosis?

Family History

All of the mammography screening recommendations are contingent on a woman having average risk of developing breast cancer. An integral component of determining that risk is family history of breast cancer. Family history is associated with an increased risk of more than 60% for developing breast cancer and the percentage of people with a first-degree family member with a history of breast cancer has increased from 11% to 16% since the 1980s.[85]

Audrain-McGovern et al. found that as much as a third of women were not aware of the added risk a family history of breast cancer poses and women with family history of breast

cancer overestimate their risk.[86] Knowing the importance of familial health history is only useful if it is acted upon and 96% of people studied believed that knowledge of their family history was important to their health but only 40% were actively collecting the information.[87,88]

Though having awareness of their family health history my increase risk reducing behaviors in African Americans the majority of African American families have been found to not discuss health conditions.[89] Family members did not feel obliged to offer health information and wanted to have control over which family members received the information. In other instances, the lack of traditional familial relationships prevent family members from know the health history of even first-degree relatives.[90]

Public Health Significance

Guide Leadership Decision Making

The decision makers for non-profits, insurance companies and funding agencies base their activities on the recommendations of trusted health organizations. They put their faith in the health organizations to provide the best recommendations based on the most accurate information available. These non-profits and funding agencies are the ones directly impacting whether some women get screened or not. For example, a funding agency that is following the USPSTF recommendations will set the requirement that organizations using their funds can only provide screenings to women that have not had a mammogram in the past 24 months. Initially, it will appear as though they are able to assist twice as many women by screening biennially. However, if a subset of their population suffers because the recommendations have not taken into consideration their unique circumstances, they may be causing unknown harm.

Preventing Health Disparities

The disparity in rates of late-stage breast cancer between African American and Caucasian women has been well documented.[2,20-22,26,59] We know African American women have a lower lifetime incidence rate but have a higher mortality rate. We also know the gap between the incidence rate is closing so as the incidence rate for Caucasian women plateaus the rate for African American women is increasing.[2] This could be due to the increased efforts to get more African American women to complete regular mammography screenings. Regardless, holding off mammography screenings for two years could potentially cause a widening of the disparity because of the type of breast cancers with which African American women often present. African American women present with breast cancers that are fast growing and resistant to treatment. That coupled with the fact that African American women have a higher incidence of breast cancer for ages 44 and younger could mean women likely to have an aggressive, difficult to treat cancer would have to wait longer to be screened.[11] The possibility of catching their breast cancer in an early stage is drastically reduced if not eliminated entirely. The reduction in opportunities for early cancer detection causes the number of late-stage cancer diagnoses and/or the mortality rate to increase.

Specific Aims and Research Questions

Aims

Aim 1: Determine the impact of mammography screening frequency on breast cancer diagnosis in African American women age 35 and older.

Aim 2: Determine if African American women age 35 and older typically have knowledge of their family history of breast cancer.

Research Questions

1. Does changing the time interval between mammography screenings affect the likelihood of African American women being diagnosed with breast cancer?
2. Do African American women typically present with knowledge of their family history of breast cancer?

METHODS

Data Source(s)

A publicly available data set of patient level data was retrieved from the Beast Cancer Surveillance Consortium (BCSC) - https://www.bcsc-research.org/. The BCSC is a network of eight breast imaging registries comprised of racially/ethnically and geographically diverse populations. Registries included are The Kaiser Permanente WA Registry, Colorado Mammography Advocacy Project, Metro Chicago Breast Cancer Registry, Vermont Breast Cancer Surveillance System, New Hampshire Mammography Network, Carolina Mammography Registry, New Mexico Mammography Project, and San Francisco Mammography Registry. The data set includes the data from 2,392,998 screening mammograms. The women included in the data set did not have a history of breast cancer and had received previous mammography screenings in the five years prior to the index mammography screening, but not nine months before the screening. Breast cancer diagnoses and pathology data were linked to the registry data within a year of the mammography screening using SEER programs and tumor registries. Risk factors (age, family history, race/ethnicity, height, weight, and health history) were self-reported at the time of the indexed mammography screening.

Study Variables

This study focused on the development of breast cancer during the time interval between screenings. The time interval between screenings was defined as the time from the date of diagnosis to the most recent prior mammography screening. Age at diagnosis is reported in five year increments for ages 35-84. The breast cancer diagnosis variable is a dichotomous variable: invasive or in situ breast cancer and no invasive or in situ breast cancer. Family history is recorded as a categorical variable for zero, one, and two or more for the number of first-degree relatives with a history of breast cancer. For the purposes of this study, the variable was converted into a dichotomous variable for the presence or absence of knowledge of family history.

Study Subjects

Inclusion criteria was being a non-Hispanic white or black woman age 35 years or older at the time of breast cancer diagnosis from one of the mammography service providers participating in the study. Exclusion criteria was being under the age of 35, missing diagnosis information such as the date and stage of diagnosis, missing previous mammography history (except for women 40 years old and younger), and identifying as any race/ethnicity other than African American/black/non-Hispanic black or non-Hispanic white. The aim was to have a sample size of 1025 African American/black/non-Hispanic black women and non-Hispanic white women for a total of 2050 women.

Sample Size Calculation

$$\frac{z^2 pq}{d^2} = n$$

$$\frac{1.96^2 \cdot 0.1214 \cdot 0.8786}{0.02^2} = 1024.38 = n$$

Data Collection

The de-identified data was collected via electronic download. No personal health information was retrieved. Data was stored on a firewall-protected server within the UTHealth School of Public Health. At no time was the data be downloaded to portable devices such as a USB drive. Data was de-identified before given to the researcher.

Data Analysis

STATA was used to run descriptive statistics and regression analyses. Summary statistics and plots was used to study the data and any trends or outliers that may exist. For Aim 1, a multivariate analysis of age, family history, previous mammogram result, breast density, and hormone therapy use was conducted using Chi-square and z-tests for proportions to assess the significance of any differences in the proportion of women diagnosed with breast cancer will be conducted. For Aim 2, a multivariate analysis of age, previous mammogram result, breast density, and breast cancer diagnosis will be conducted using Chi-square and z-tests for proportions to assess the significance of any differences in the proportion of women diagnosed with breast cancer was conducted.

Human Subjects Considerations

The study utilized retrospective patient level data. The protocol was submitted to IRB for approval and received exempt status (HSC-SPH-19-1023).

Results Dissemination

Results will be presented to participating organizations to inform their clinical practices. Results will also be written up for publication. The completed manuscript could be submitted to one of the following peer reviewed journals American Journal of Preventive Medicine, Annals of

Internal Medicine, American Journal of Public Health, Cancer, Journal of General Internal Medicine, Women's Health Issues, or The Breast Journal.

JOURNAL ARTICLE 1

The Impact of Mammography Screening Frequency on Breast Cancer Diagnosis in African American Women

American Journal of Preventive Medicine

Introduction

Breast cancer is the second most common cause of cancer-related death in women in the United States, with one in eight women expected to develop the disease in their lifetime.[1] There will be an estimated 268,600 new cases of breast cancer and 41,760 deaths in 2019.2 Among African American women, there are an expected 33,840 new cases diagnosed and 6,540 deaths will have occurred in 2019.[1] The incidence of breast cancer is increasing for both non-Hispanic whites and non-Hispanic blacks, while mortality rates have remained stable for non-Hispanic white women.[1] Further, black and white women both have higher incidence and death rates for breast cancer than other races/ethnicities.[3] African American women are more likely to be diagnosed with a late-stage breast cancer due to a myriad of reasons, such as lack of preventive care, higher prevalence of aggressive cancers, and access to care.[4-24] Breast cancer can be detected through physical examination of the breast[25] but is most commonly detected through mammography screenings. Other screening methodologies exist, such as ultrasound, digital breast tomosynthesis, and magnetic resonance imaging; however, mammography screenings are directly linked to reducing breast cancer mortality. Mammography discovers the cancer before signs and symptoms present and thus, remains the most effective method of reducing late-stage diagnoses in African American women.[7,26,27]

Discovering the presence of the disease while it is categorized as Stage I or II yields a 99% and 93% 5-year survival rate, respectively. Stage III has a 72% 5-year survival rate and Stage IV has only a 22% 5-year survival rate.[28] For women aged 40-60 years, mammography screenings have been shown to reduce mortality from breast cancer by 15-32%.[6,29,30] At every stage of diagnosis, African American women have a lower 5-year survival rate than white women. White women have a 98% and 97% 5-year survival rate for stages I and II. They have 76% 5-year survival rate for stage III and 27% for stage IV. African American women have 97%, 88%, 64%, and 19% 5-year survival rates for stages I-IV, respectively. African American women specifically have a 40% increased risk of dying from breast cancer than their Caucasian counterparts, though they now have similar incidence rates.[1] Though numerous factors play into their mortality disparity such as personal behavioral risk factors, socioeconomic status, and access to care, African American women also present with more aggressive breast cancers that are more difficult to treat and grow more rapidly.[31-35]

Mammography screenings have been found to be the most cost effective method of diagnosing breast cancer.[36] Organizations such as the U.S. Preventive Services Task Force (USPSTF) have made recommendations that women of a certain age get mammography screenings in an effort to reduce, if not prevent, breast cancer mortality. The recommendations for breast cancer screenings generated by organizations such as USPSTF, World Health Organization, American Congress of Obstetricians and Gynecologists, and American Cancer Society directly impact the likelihood that and frequency with which a woman gets mammography screenings. Prior to November 2009 the USPSTF recommendation was that women complete annual mammography screenings starting at age 40.[37,38] In November 2009, and later reinforced in January 2016, USPSTF changed the recommendation to biennial

mammography screenings for women aged 50-74. The USPSTF was unable to conduct individual analyses of the impact of the screening interval on different racial and ethnic groups. In fact, the USPSTF stated that there was not enough evidence to fully support the biennial screening recommendation.[39] Several studies have looked at the change in general screening practices post recommendation change, but the results have been mixed. A few studies have noted that they saw no change in the African American population but that could be due to the same issues and barriers that prevent these women from adhering to mammography screenings in the first place.[40,41] Lee et al, compared the mammography usage of African American and white women in Arkansas before (2007–2010) and after (2011–2013) the mammography recommendation change. They found no change in mammography screening practices for African American women aged 40-74. Chang et al studied the change in mammography screening practices in the 3-year period before and after the mammography screening guideline recommendation change in women with Medicare and found that the African American women were the only group not to decrease their mammography usage. In modeling the outcomes of African American women adhering to the USPSTF's recommendations, Habtes et al. found that the recommendations lead to an increase in late stage diagnoses as opposed to the American Cancer Society's recommendations.[42] Therefore, this study will evaluate the proportion of African American women that were diagnosed with breast cancer within one year of a previous mammography screening prior to the implementation of the mammography screening guideline changes from USPSTF to explore the potential for the guideline change to have impacted this specific high-risk population.

Methods

Data Source

Data came from a de-identified, patient-level public dataset from the Breast Cancer Surveillance Consortium (BCSC) - https://www.bcsc-research.org/.[43-47] The BCSC is a network of eight breast imaging registries comprising racially/ethnically and geographically diverse populations. Seven mammography registries, Carolina Mammography Registry, Colorado Mammography Project, Group Health Cooperative's Breast Cancer Surveillance Project, New Hampshire Mammography Network, New Mexico Mammography Project, San Francisco Mammography Registry, and the Vermont Breast Cancer Surveillance System, contributed data that has been used in over 700 studies.[43] The data set includes the data from 2,392,998 screening mammograms collected between January 1, 1996-December 31, 2002. The women included in the dataset did not have a history of breast cancer and had received previous mammography screenings in the five years prior to, but not in the nine months before, the index mammography screening. Breast cancer diagnoses and pathology data were linked to the registry data within a year of the mammography screening using SEER programs and tumor registries. Risk factors (age, family history, race/ethnicity, height, weight, and health history) were self-reported via questionnaire at the time of the indexed mammography screening. Lastly, breast density was determined by a radiologist based on the mammography films included in the registry.

Study Participants

The study sample was limited to women identified as white or African American aged 35 years or older at the time of breast cancer diagnosis from one of the mammography service providers participating in the study. African American women have been found to present with early onset breast cancers more frequently than other racial groups.[31-35] For this reason, women

aged 35-39 have been included in this study even though most mammography screening guidelines do not recommend women begin screening until age 40. The initial sample consisted of a total of 766,119 women. The University of Texas Health Science Center's Committee for the Protection of Human Subjects reviewed the protocol for this study and deemed the study exempt.

Variables

The independent variable of this study was the race of the women undergoing screening and include white and black women. The dataset also includes a variable for ethnicity to denote whether a woman identified as Hispanic white or Hispanic black, but since an equal percentage of participates had an unknown ethnicity (7.22%) as identified as Hispanic (7.44%) the author deemed this variable unreliable. To address the issue of the accuracy and consistency of ethnicity reporting, all participants that identified as Hispanic were dropped from the data set (n= 55,304). This decision was made based on the assumption that individuals were more likely to answer yes when they are sure of their Hispanic heritage and unknown and/or no when there were no Hispanic ties.

The dependent variable of this study was the diagnosis of breast cancer after receiving a mammography screening within a year of their previous mammography screening. Breast cancer diagnosis data was collected as a dichotomous variable (Diagnosis/No diagnosis).

Covariates in this study were age, breast density, number of first degree relatives diagnosed with breast cancer, previous mammogram result, and use of hormone therapy.[47-52] Age was collected as an ordinal variable with 10 five-year age categories ranging from 35-84. The breast density variable was an ordinal variable based on the Breast Imaging Reporting and Data System (BI-RADS) coding system's four breast density codes (Almost entirely fat, scattered fibroglandar

densities, heterogeneously dense, and extremely dense). BI-RADS classifications describe the degree of attenuation of mammography screenings due to the composition of breast tissue. As breast tissue density increases, the sensitivity of mammography screenings decreases. The sensitivity is highest for breasts that are categorized as almost entirely fat and lowest for breasts that are categorized as extremely dense.[53] The variable denoting the number of first-degree relatives diagnosed with breast cancer is an ordinal variable ranging from zero to two or more. The result of the participant's previous mammogram was collected as a dichotomous variable to denote whether or not the participant received a false positive from her previous mammography screening. The use of hormone therapy was collected as a categorical variable based on the woman's use of hormone therapy (Yes, No, and Unknown).

Statistical Analysis

Descriptive statistics were run to get unadjusted proportions (%) on dependent and independent variables as well as the covariates in the model. Chi-square tests were run to evaluate the differences between breast cancer diagnosis for all variables and between races. Z-tests for proportions was used to assess the significance of any differences in the proportion of women diagnosed with breast cancer. To examine the association between breast cancer diagnosis and race, logistic regression analyses were conducted. The multivariate analysis controlled for age, breast density, the number of first degree relatives that have been diagnosed with breast cancer, the result of the participant's previous mammogram, and the use of hormone therapy.

Sensitivity Analysis: For the sensitivity analysis, the regression analysis was conducted looking at any possible associations among women below the age of 50. The sample was limited to women that were aged 35-49 at the time of their mammography screening. The results of the

crude and adjusted odds ratios were then compared to the initial results of the multivariate analysis.

STATA, Version 16 was used to conduct the analyses.

Results

We found that the data set, as expected, had considerably more participants that identified as white than as African American. The majority of the sample fell between the ages of 40-59 (62.6%), had scattered fibroglanduar densities (33.38 %) or heterogeneously dense breast (29.90%), if known, had no first degree relatives with a previous breast cancer diagnosis (72.38%) and had unknown hormone therapy usage (43.65%). Table 2.1 shows the breakdown of study variables stratified by race.

The proportions of women in each age group were significantly different for white and African American women both overall and at every age group. Although the majority of the study population fell between the ages of 40 and 59, 62.5% of white and 65.1% of African American women fell in these age groups. There was a significantly higher proportion of African American women in the 35-39 (p=0.0000), 40-44 (p=0.0000), and 45-49 (p=0.0000) age groups when compared to the proportion of white women in the same age groups.

For African American women specifically, the 35-39 (p=0.002), 40-44 (p=0.006), 45-49 (p=0.005), 75-79 (p=0.029), and 80-84 (p=0.037) age groups were statistically different from the African American study population. The 40-44 and 45-49 age groups had a significantly higher proportion of women in them when compared to the overall group. The 35-39, 75-79, and 80-84 had a significantly lower proportion of women in them when compared to the overall group. The 35-39, 40-44, 45-49, 50-54 age groups had a lower proportion of women diagnosed with breast cancer. Whereas the 55-59, 60-64, 65-69, 70-74, 75-79, and 80-84 age groups all

experienced an elevated proportion of women diagnosed with breast cancer. Women under the age of 50 were also significantly less likely to have developed breast cancer within a year of their previous mammography screening.

The sample saw an elevated odds ratio for women with breasts composed almost entirely of fat (1.20, CI 1.16-1.24) more so than for women with scattered fibroglandular densities and heterogeneously dense breasts (1.16, CI 1.14-1.18). The African American women in the study had a lower odds ratio for having extremely dense breasts (0.81, CI 0.78-0.84).

The probability of receiving a cancer diagnosis within a year of having received a mammography screening for each race was analyzed via logistic regression. Table 2.2 shows the crude and adjusted odds ratios from the logistic regression analyses. A significant association was not found between race and the likelihood of being diagnosed with either invasive or non-invasive breast cancer. The covariates, however, were all significant apart from the number of first-degree relatives diagnosed with breast cancer.

Discussion

Our findings show that African American women are not at an increased risk of developing breast cancer within the year between mammography screenings compared to their Caucasian counterparts. Interestingly, we showed a reduced risk of developing breast cancer within a year in women with dense breast tissue. This result is contradictory to the existing literature that has found women with higher density breast more likely to develop breast cancer.[54,55]

This study differs from others studying this topic in that we included women aged 35-39 in our analysis.[40,41,56-58] Although none of the previous or current recommendations include women in the 35-39 age group, the more aggressive breast cancers African American women

tend to present start developing at a younger age.[31-35,59-63] To analyze the potential threat of being diagnosed with a breast cancer within a year, this younger age group needed to be included as well.

Habtes et al. found that the USPSTF's recommendations lead to an increased number of late stage breast cancer diagnoses among African American women compared to having women follow the American Cancer Society's mammography screening recommendations.[42] The difference in our findings could be that Habtes et al. compared the change in the number of diagnoses within a single population whereas we are comparing the difference in diagnoses between two populations.

We did see a greater proportion of African American women under the age of 50 being diagnosed with breast cancer. Attention must be paid to this group of women. Additional research is needed to see when breast cancer is developing to determine if following the USPSTF's guidelines would have a potential negative impact on this group of women and if so, what can be done to challenge this problem. Additional research should look for commonalities among this population to identify the potential for interventions, such as genetic testing, a more detailed risk assessment, or a different time interval for screening.

Our unique contribution to the research is exploration of the impact of screening time on a racial subgroup of women. The USPSTF stated they were not able to identify the recommendation needs of each racial group individually. Since the African American population already has an increased risk of breast cancer mortality, it is important to explore all opportunities to exacerbate this risk.

From our research it appears healthcare leadership and funding agencies can continue to follow the USPSTF's recommendations. However, these findings do not guarantee an absence in

increase in later stage breast cancer diagnoses. In the small percentage of women in our study population that did develop breast cancer within a year, there is still the potential for the breast cancer to progress should mammography screening be delayed for another year.

Strengths and Limitations

A strength of our study is that we used BCSC data. The USPSTF also utilized data from the BCSC to conduct their analysis before changing the mammography screening recommendations making our populations comparable. A limitation of this dataset is that it lacked staging information and exact mammography screening dates to tell if there was a common screening interval within which women were presenting with breast cancer or the stage at which most women at a particular screening interval were diagnosed. It also lacks a good representation of registries in the portion of the country with higher densities of African American residents. Thus the dataset lacks a representative sample of African American women overall. White women made up ~60% of the sample, which is close to the national percentage of white women, but African American women only made up ~5%, which is substantially below the 13% national percentage of African American women.

The study used the development of breast cancer within a year of a previous mammography screening and before the age of 50 as a proxy for determining if African American women would be at risk for developing a more advanced breast cancer if following the USPSTF's recommendations. Our study was only able to look at the development of breast cancer within a year of a previous mammography screening. As a result, we suggest more research be done looking at the number of African American women diagnosed with breast cancer within two years of their previous mammography screening to determine the effects of delaying mammography screenings for two years.

Conclusion

These findings suggest that though they are more likely to be diagnosed at a younger age, African American women are not more likely to be diagnosed with breast cancer within a year of a previous mammography screening. Thus, the recommendation that women receive mammography screenings every two years appears to be appropriate for the majority of women.

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Table 1.1: Study Demographics

	White		Black		
	N	percentage	N	percentage	p-value
	656,489	92.4%	54,326	7.6%	
Age					<0.0001
35-39	17,870	2.7%	1,914	3.5%	
40-44	100,561	15.3%	9,315	17.1%	
45-49	112,448	17.1%	10,442	19.2%	
50-54	113,495	17.3%	9,199	16.9%	
55-59	83,093	12.7%	6,406	11.8%	
60-64	63,369	9.7%	5,033	9.3%	
65-69	55,879	8.5%	4,454	8.2%	
70-74	49,843	7.6%	3,642	6.7%	
75-79	37,890	5.8%	2,542	4.7%	
80-84	22,041	3.4%	1,379	2.5%	
Young					<0.0001
No	425,610	64.8%	32,655	60.1%	
Yes	230,879	35.2%	21,671	39.9%	
Density					<0.0001
Almost entirely fat	38,653	5.9%	3,801	7.0%	
Scattered fibroglandular densities	217,437	33.1%	19,837	36.5%	
Heterogeneously dense	194,673	29.7%	17,862	32.9%	
Extremely dense	40,800	6.2%	2,773	5.1%	
Unknown	164,926	25.1%	10,053	18.5%	
Number of Relatives					<0.0001
Zero	476,857	72.6%	37,661	69.3%	
One	81,448	12.4%	5,019	9.2%	
Two or more	3,999	0.6%	154	0.3%	
Unknown	94,185	14.3%	11,492	21.2%	
Family History					<0.0001
Known	562,304	85.7%	42,834	78.8%	
Unknown	94,185	14.3%	11,492	21.2%	
Previous Mammogram					<0.0001
Negative	438,547	66.8%	34,509	63.5%	
False Positive	9,207	1.4%	840	1.5%	
Unknown	208,735	31.8%	18,977	34.9%	
Hormone Use					<0.0001
No	189,699	28.9%	21,748	40.0%	
Yes	180,356	27.5%	8,749	16.1%	
Unknown	286,434	43.6%	23,829	43.9%	
Invasive Breast Cancer					0.097
No	652,360	99.4%	54,016	99.4%	
Yes	4,129	0.6%	310	0.6%	
Breast Cancer					0.161
No	651,430	99.2%	53,937	99.3%	
Yes	5,059	0.8%	389	0.7%	

Table 1.2: Crude Regression Models for Demographics

	OR	CI 95%	p-value
Age			
35-39	1.30	1.24-1.37	<0.0001
40-44	1.14	1.12-1.17	<0.0001
45-49	1.15	1.13-1.18	<0.0001
50-54	0.98	0.95-1.00	0.035
55-59	0.92	0.90-0.95	<0.0001
60-64	0.96	0.93-0.99	0.003
65-69	0.96	0.93-0.99	0.012
70-74	0.87	0.84-0.91	<0.0001
75-79	0.8	0.77-0.84	<0.0001
80-84	0.75	0.71-0.79	<0.0001
Young	1.22	1.20-1.25	<0.0001
Density			
Almost entirely fat	1.20	1.16-1.24	<0.0001
Scattered fibroglandular densities	1.16	1.14-1.18	<0.0001
Heterogeneously dense	1.16	1.14-1.18	<0.0001
Extremely dense	0.81	0.78-0.84	<0.0001
Unknown	0.68	0.66-0.69	<0.0001
Family History	0.62	0.61-0.64	<0.0001
Previous Mammogram	1.16	1.13-1.18	<0.0001
Hormone Use	0.61	0.60-0.62	<0.0001

Table 2.1: Crude and Adjust Logistic Regression Models for Cancer

	Crude			Adjusted		
	OR	CI 95%	p-value	OR	CI 95%	p-value
Age				1.16	1.15-1.18	<0.0001
35-39	0.36	0.27-0.47	<0.0001			
40-44	0.40	0.36-0.44	<0.0001			
45-49	0.62	0.57-0.67	<0.0001			
50-54	0.84	0.78-0.91	<0.0001			
55-59	1.21	1.12-1.31	<0.0001			
60-64	1.37	1.26-1.48	<0.0001			
65-69	1.56	1.44-1.69	<0.0001			
70-74	1.59	1.46-1.73	<0.0001			
75-79	1.68	1.53-1.85	<0.0001			
80-84	1.57	1.38-1.77	<0.0001			
Young	0.43	0.40-0.46	<0.0001	0.46	0.42-0.50	<0.0001
Density				1.06	1.05-1.07	<0.0001
Almost entirely fat	0.41	0.34-0.48	<0.0001			
Scattered fibroglandular densities	0.82	0.77-0.87	<0.0001			
Heterogeneously dense	1.13	1.07-1.20	<0.0001			
Extremely dense	1.10	0.98-1.22	0.0886			
Unknown	1.25	1.18-1.33	<0.0001			
Family History	0.96	0.89-1.03	0.2837			
Previous Mammogram	1.17	1.11-1.24	<0.0001	1.02	1.02-1.03	<0.0001
Hormone Use	0.79	0.74-0.83	<0.0001	0.99	0.98-0.99	<0.0001
Number of Relatives				1.00	0.99-1.01	0.662
Race	0.93	0.84-1.03	0.1611	0.98	0.88-1.09	0.728

Table 2.2: Crude and Adjust Logistic Regression Models for Invasive Cancer

	Crude			Adjusted		
	OR	CI 95%	p-value	OR	CI 95%	p-value
Age				1.17	1.16-1.19	<0.0001
35-39	0.34	0.25-0.46	<0.0001			
40-44	0.37	0.33-0.42	<0.0001			
45-49	0.59	0.53-0.65	<0.0001			
50-54	0.81	0.75-0.88	<0.0001			
55-59	1.24	1.14-1.35	<0.0001			
60-64	1.37	1.25-1.50	<0.0001			
65-69	1.55	1.42-1.70	<0.0001			
70-74	1.69	1.54-1.85	<0.0001			
75-79	1.75	1.58-1.94	<0.0001			
80-84	1.66	1.45-1.90	<0.0001			
Density				1.06	1.05-1.07	<0.0001
Almost entirely fat	0.43	0.36-0.52	<0.0001			
Scattered fibroglandular densities	0.84	0.79-0.90	<0.0001			
Heterogeneously dense	1.11	1.04-1.19	0.0009			
Extremely dense	1.04	0.92-1.17	0.5769			
Unknown	1.27	1.19-1.35	<0.0001			
Number of Relatives				1.00	1.00-1.01	0.331
Family History	0.94	0.87-1.02	0.1495			
Previous Mammogram	1.17	1.10-1.25	<0.0001	1.02	1.02-1.03	<0.0001
Hormone Use	0.77	0.72-0.82	<0.001	0.98	0.97-0.99	<0.0001
Young	0.4	0.37-0.44	<0.0001	0.44	0.40-0.48	<0.0001
Race	0.91	0.81-1.02	0.0972	0.96	0.85-1.08	0.476

JOURNAL ARTICLE 2

The Knowledge of Family History of Breast Cancer among African American Women

American Journal of Preventive Medicine

Introduction

Breast cancer is the second most common cause of cancer-related death in women in the United States with one in eight women expected to develop the disease in their lifetime.[1] As the most commonly diagnosed cancer in African American women, it accounts for a third of all cancer diagnoses. Black women have a 40% increased risk of dying from breast cancer than their White counterparts.[1] Several factors contribute to the mortality disparity that exists between Black and White women including, but not limited to, access to care.[2-6] Mammography screenings are known to reduce breast cancer mortality by 15-32% so receiving timely mammography screenings is critical for all women and especially African American women.[7-9] The appropriate time to engage in screening is an area of much debate. Several recommendations exist for when a woman should receive a mammogram. The American Cancer Society suggests that women of average risk undergo annual mammography screenings beginning at the age of 45 and continuing until age 54. Women age 55 and older should begin screening biennially or have the opportunity to continue screening annually. Women age 40 through 44 should have the opportunity to begin annual screening. Women should continue mammography screenings as long as they are in good health and they have a life expectancy of at least 10 years.[10,11] The American College of Obstetrics and Gynecology recommends women of average risk should begin mammography screenings at age 40.[12] The U.S. Preventive Services Task Force (USPSTF) recently affirmed their revision to mammography screening recommendations. Contrary to their previous recommendations that women aged 40 and older receive annual mammography

screenings, the USPSTF now recommends average risk women receive a mammography screening biennially from ages 50-74.[13]

The common thread among the recommendations is that they are intended only for women of average risk. Average risk is defined as a woman lacking a personal history of breast cancer, a genetic mutation known to increase breast cancer risk, and/or a history of exposure to chest radiation in childhood.[12] Based on this, a woman's knowledge of her family history of breast cancer is critical. Family history is associated with an increased risk of more than 60% for developing breast cancer.[14] Also, the proportion of women with a first-degree family member with a history of breast cancer has increased from 11% (1980s) to 16% (2010).[14] Lack of knowledge of family history and risk is a concern in women of screening age. Audrain-McGovern et al. found that as much as a third of women are unaware of the additional risk a family history of breast cancer poses to their health.[15] Studies found that although 96% of people studied believed that knowledge of their family history was important to their overall health, only 40% of people who believe it is important were actively collecting the information.[16,17]

Familial communication style also impacts knowledge of history and risk. Hovick et al. conducted focus groups and interviews with African Americans in Houston, Texas to assess family communication styles related to health issues. They found that few participants reported having good communication. The majority were found not to discuss health issues with their families for a variety of reasons. Individuals that did not want their information spread to unknown people felt it necessary to forgo sharing it at all. Participants expressed feelings of sole ownership of their health history and it was not anyone else's business. Others did not want to burden family members with their issues and thus kept the information regarding their health to themselves. Frequently, there was an absence of knowledge sharing because the family members

had no way of getting the information, either the family members with diseases did not go to the doctor and did not know the information or family members were not in contact with their relatives. The authors further stated that non-communication came up in every focus group and every interview.[18] Studies have found that African American women are less likely to discuss family health issues and/or have genetic testing as compared to other groups,[18,19] which leads to our research question. We know that women with a family history of breast cancer are more likely to get mammography screenings, but how many African American women attend their mammography screening appointment knowing their family history of breast cancer?

Methods

This study used data from the Breast Cancer Surveillance Consortium (BCSC) https://www.bcsc-research.org/,[14,20-23] a publicly available dataset of de-identified, patient-level data collected from the BCSC's seven breast imaging registries. Carolina Mammography Registry, Colorado Mammography Project, Group Health Cooperative's Breast Cancer Surveillance Project, New Hampshire Mammography Network, New Mexico Mammography Project, San Francisco Mammography Registry, and the Vermont Breast Cancer Surveillance System contributed data.[24] The dataset included data from 2,392,998 screening mammograms collected between January 1, 1996-December 31, 2002. The women included in the dataset did not have a history of breast cancer. Breast cancer diagnoses and pathology data were linked to the registry data within a year of the mammography screening using SEER programs and tumor registries. Risk factors (age, family history, race/ethnicity, height, weight, and health history) were self-reported via questionnaire at the time of the indexed mammography screening. Lastly, breast density was determined by a radiologist based on the mammography films included in the registry.

Study Participants

The study sample was limited to women identified as white or black aged 35 years or older at the time of breast cancer diagnosis from one of the mammography service providers participating in the study. We dropped participants that identified as Hispanic from this study. African American women have been found to present with early onset breast cancers more frequently than other racial groups.[25-29] For this reason, women aged 35-39 have been included in this study even though most mammography screening guidelines do not recommend women begin screening until age 40. The sample consisted of a total of 766,119 women. The University of Texas Health Science Center's Committee for the Protection of Human Subjects reviewed the protocol for this study and deemed the study exempt.

Variables

The independent variable of this study was the race of women receiving mammography screenings, categorized as white and black women. The data sources only categorized women as white and black, so the assumption was made that the black category includes women that identify as African American. The dataset also includes a variable for ethnicity to denote whether a woman identified as Hispanic white or Hispanic black, but since an equal percentage of participates had an unknown ethnicity (7.22%) as identified as Hispanic (7.44%) the author deemed this variable unreliable. To address the issue of the accuracy and consistency of ethnicity reporting, all participants that identified as Hispanic were dropped from the dataset (n= 55,304) leading to a sample size of (n=710,815) for this analysis. This decision was made based on the assumption that individuals were more likely to answer yes when they are sure of their Hispanic heritage and unknown and/or no when there were no Hispanic ties.

The dependent variable of this study was the knowledge of breast cancer diagnoses among first degree relatives. The number of first degree relatives that have been diagnosed with breast cancer data was collected as an ordinal variable with responses for 0 relatives, 1 relative, 2 or more relatives, and unknown. The variable was then converted into a dichotomous variable, knowledge of breast cancer diagnoses among relatives versus absence of knowledge of breast cancer diagnoses among relatives.

Covariates in this study were age, breast density, the number of first degree relatives that have been diagnosed with breast cancer, and the result of the participant's previous mammogram. Age was collected as an ordinal variable with 10 five-year age categories ranging from 35-84. The breast density variable was an ordinal variable based on the Breast Imaging Reporting and Data System (BI-RADS) coding system four breast density codes (Almost entirely fat, scattered fibroglandar densities, heterogeneously dense, and extremely dense). BI-RADS classifications describe the level of sensitivity of mammography screenings for each common type of breast tissue composition. The sensitivity of mammography screenings decreases as breast tissue density increases. The sensitivity is highest for breasts that are categorized as almost entirely fat and lowest for breasts that are categorized as extremely dense.[30] The result of the participant's previous mammogram was collected as a dichotomous variable to denote whether or not the participant received a false positive from her previous mammography screening.

Statistical Analysis

Descriptive statistics were run to get unadjusted proportions (%) on the dependent variable, the independent variable, and the covariates in the model. Chi-square tests were run to evaluate the differences between women with a knowledge of family breast cancer diagnoses for all variables and between races. Z-tests for proportions were used to assess the significance of

any differences in the proportion of women diagnosed with and without knowledge of family breast cancer diagnoses. To examine the association between knowledge of family breast cancer diagnoses and race, logistic regression analyses were conducted. The multivariate analysis controlled for age, breast density, and the result of the participant's previous mammogram.

Sensitivity Analysis: For the sensitivity analysis, the regression analysis was conducted looking at any possible associations among women with knowledge of family breast cancer diagnoses by the number of relatives with breast cancer diagnoses. The analysis utilized the data as collected, as an ordinal variable with responses for 0 relatives, 1 relative, 2 or more relatives, and unknown. The results of the crude and adjusted odds ratios were then compared to the initial results of the multivariate analysis.

STATA, Version 16 was used to conduct the analyses.

Results

The dataset had considerably more participants that identified as white (92.36%) than as black (7.64%). The majority of the sample also fell between the ages of 40-59 (62.6%), had scattered fibroglandular densities (33.38 %) or heterogeneously dense breast (29.90%), if known, had no first degree relatives with a previous breast cancer diagnosis (72.38%) and had unknown hormone therapy usage (43.65%). Table 3.1 shows the breakdown of study variables stratified by race.

The proportions of women in each age group were significantly different for white and black women both overall and at every age group. Although the majority of the study population fell between the ages of 40 and 59, 62.5% of white and 65.1% of black women fell in these age groups. There was a significantly higher proportion of African American women in the 35-39

(p=0.0000), 40-44 (p=0.0000), and 45-49 (p=0.0000) age groups when compared to the proportion of white women in the same age groups.

For African American women specifically, the 35-39 (p=0.002), 40-44 (p=0.006), 45-49 (p=0.005), 75-79 (p=0.029), and 80-84 (p=0.037) age groups were statistically different from the African American study population. The 40-44 and 45-49 age groups had a significantly higher proportion of women in them when compared to the overall group. The 35-39, 75-79, and 80-84 had a significantly lower proportion of women in them when compared to the overall group.

The 35-39 (p=0.0000), 40-44 (p=0.0000), 55-59 (p=0.0454), 60-64 (p=0.0000), 65-69 (p=0.0000), 70-74 (p=0.0000), and 80-84 (p=0.0048) age groups had a significantly higher proportion of women without knowledge for their family history of breast cancer. Although ages 45-49 (p=0.1271), 50-54 (p=0.6457), 75-79 (p=0.0753) did not have a significantly higher proportion of women without family history knowledge, women under the age of 50 as a whole did have a significantly higher proportion of women without that knowledge (p=0.0000).

In our sample, 85.13% of women had knowledge of their family history of breast cancer with 85.65% of the white women in the study having this knowledge compared to 78.85% of African American women. African American women had a higher proportion of women without knowledge for their family history of breast cancer. Looking specifically at the study participants with familial knowledge, the breakdown of the number of known first degree relatives with a breast cancer diagnosis was similar between white and African American women. We found that 72.64% of white women reported having no first degree relatives with a previous breast cancer diagnosis compared to 69.32% of African American women. Also, 12.41% of white participants and 9.24% of African American participants reported having one first degree relative with a previous breast cancer diagnosis. Very few women reported having two or more first

degree relatives with a previous breast cancer diagnosis with only 0.61% for white women and 0.28% for African American women.

Women who had received a false-positive from a previous mammography screening also were more likely to know their family history of breast cancer.

We used logistic regression to analyze the probability of a woman knowing her family history of breast cancer at the time of her mammography screening. Table 3.2 shows the crude and adjusted odds ratios from the logistic regression analyses. A significant association was found between race and the likelihood of a woman knowing her family history of breast cancer at the time of her mammography screening (p=0.0000). All of the covariates, with the exception of actual cancer diagnosis, were significant (p=0.0000). African American women are significantly less likely to know their family history of breast cancer. Women under the age of 50 were 10% more likely to know their family history of breast cancer.

Discussion

These findings show that African American women do not typically present to their mammography screening appointments with knowledge regarding family history of breast cancer diagnoses. There was no association between the women that presented with family history knowledge and those that developed breast cancer within a year of their previous mammography screening. In agreement with Shiyanbola et al., we found an association between having first degree relatives with a breast cancer diagnosis and the diagnosis of breast cancer among study participants. Our study population had a lower percentage of women with at least one first degree relative with a previous breast cancer diagnosis than the 16% Shiyanbola et al. reported at just 12.74%.[14]

The significantly lower proportion of African American women with a knowledge of relatives' previous breast cancer diagnoses speaks to Hovick et al.'s findings that African American families seldom discuss health histories. The literature offers conflicting views as to where the issue lies regarding the transferal of family health information. Hovick et al. suggested that older individuals choose not to share the information while Koehly et al. found older African Americans more likely to gather the information.[18,31] Hovick et al. and Forrest et al. also found that younger individuals elect not to hear the information.[18,32] Our results seem to be in line with their findings as our participants aged 45-54 were found to have knowledge of familial breast cancer diagnoses.

We did see a statistically significant higher proportion of women with knowledge of their family history that had previously received a false positive mammography screening. This may be due to women being more inclined to discuss their family history of breast cancer with their relatives when they receive a false positive mammography screening.

In establishing clinical procedures for healthcare providers, leadership should consider paying close attention to the manner in which health histories are gathered from their patients. Perhaps patients could be counseled on exploring both breast cancer and overall health histories with their families in prior to their mammography screening appointment by their primary care physician. This conversation could alert healthcare providers to the lack of knowledge of some of their patients and alter the manner in which they provide care.[14-18,33] The knowledge of familial histories would determine when clinicians would recommend women begin mammography screenings.

This study's strength is that we used BCSC data. The USPSTF utilized the BCSC's data to conduct their analysis before electing to change the recommendations for mammography

screening making our analyses comparable. However, as with any research study, there are limitations. The primary limitation in this study is the limited race/ethnic representation of registries in parts of the country with higher densities of African Americans. Thus the dataset lacks a representative sample of African American women. White women made up ~60% of the sample but black women only made up ~5%. 60% is close to the national percentage of white women, but 5% is nowhere near the 13% needed for black women.

Conclusion

The results from this study show that the previous breast cancer diagnoses of first degree family members is not something African American women have knowledge of when they come in for their mammography screening. However, though African American women do not typically present with knowledge of familial breast health, they are coming in for mammography screenings and the motivation for their action could be useful information in the fight to end the breast cancer mortality disparity.

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Table 3.1: Crude and Adjust Logistic Regression Models for Knowledge of Family History

	Crude			Adjusted by Breast Cancer			Adjusted by Invasive Cancer		
	OR	CI 95%	P value	OR	CI 95%	P value	OR	CI 95%	P value
Age				0.96	0.96-0.97	<0.0001	1.04	1.03-1.04	<0.0001
35-39	1.24	1.19-1.29	<0.0001						
40-44	1.11	1.09-1.13	<0.0001						
45-49	1.02	1.00-1.04	0.0229						
50-54	1.01	0.99-1.03	0.3191						
55-59	0.98	0.96-1.00	0.1011						
60-64	0.94	0.92-0.96	<0.0001						
65-69	0.90	0.88-0.92	<0.0001						
70-74	0.92	0.89-0.94	<0.0001						
75-79	0.97	0.94-0.99	0.0162						
80-84	1.03	0.99-1.07	0.1621						
Density				0.85	0.85-0.86	<0.0001	1.11	1.11-1.11	<0.0001
Almost entirely fat	1.46	1.42-1.51	<0.0001						
Scattered fibroglandular densities	1.52	1.50-1.55	<0.0001						
Heterogeneously dense	1.50	1.47-1.52	<0.0001						
Extremely dense	1.73	1.68-1.79	<0.0001						
Unknown	0.37	0.36-0.37	<0.0001						
Previous Mammogram	0.85	0.83-0.86	<0.0001	0.97	0.97-0.97	<0.0001	1.02	1.01-1.02	<0.0001
Young	1.10	1.09-1.12	<0.0001	1.18	1.17-1.20	<0.0001	1.18	1.17-1.20	<0.0001
Race	0.62	0.61-0.64	<0.0001	0.57	0.55-0.58	<0.0001	1.24	1.22-1.27	<0.0001
Breast Cancer	0.96	0.89-1.03	0.2837	1.06	0.99-1.15	0.105			
Invasive Cancer	0.94	0.87-1.02	0.1495				1.05	0.96-1.14	0.296

Table 3.2: Crude and Adjust Logistic Regression Models for Number of Relatives with Breast Cancer

	Crude			Adjusted by Breast Cancer			Adjusted by Invasive Cancer		
	OR	CI 95%	P value	OR	CI 95%	P value	OR	CI 95%	P value
Age				1.04	1.03-1.04	<0.0001	1.04	1.03-1.04	<0.0001
35-39	1.64	1.59-1.68	<0.0001						
40-44	0.85	0.84-0.86	<0.0001						
45-49	0.92	0.91-0.93	<0.0001						
50-54	0.92	0.91-0.93	<0.0001						
55-59	0.98	0.96-0.99	0.0038						
60-64	1.03	1.02-1.05	0.0002						
65-69	1.10	10.8-1.12	<0.0001						
70-74	1.14	1.12-1.16	<0.0001						
75-79	1.16	1.14-1.19	<0.0001						
80-84	1.14	1.11-1.18	<0.0001						
Density				1.11	1.11-1.11	<0.0001	1.11	1.11-1.11	<0.0001
Almost entirely fat	0.79	0.77-0.80	<0.0001						
Scattered fibroglandular densities	0.77	0.76-0.78	<0.0001						
Heterogeneously dense	0.80	0.79-0.81	<0.0001						
Extremely dense	0.78	0.77-0.80	<0.0001						
Unknown	1.93	1.91-1.96	<0.0001						
Previous Mammogram	1.07	1.06-1.09	<0.0001	1.02	1.01-1.02	<0.0001	1.02	1.01-1.02	<0.0001
Young	0.92	0.91-0.93	<0.0001	0.89	0.88-0.90	<0.0001	0.89	0.88-0.90	<0.0001
Race	1.17	1.15-1.20	<0.0001	1.24	1.22-1.27	<0.0001	1.24	1.22-1.27	<0.0001
Breast Cancer	1.3	1.22-1.37	<0.0001	1.21	1.14-1.28	<0.0001			
Invasive Cancer	1.3	1.22-1.39	<0.0001				1.21	1.14-1.28	<0.0001

CONCLUSION

This dissertation was initiated with the goal of determining whether or not the U.S. Preventive Services Task Force's (USPSTF) recommendation for women aged 50-74 to receive biennial mammography screening negatively impacts African American women, a group with existing mortality disparities. The study does so by examining whether changing the time interval between mammography screenings affects the likelihood of African American women being diagnosed with breast cancer and if African American women typically present with knowledge of their family history of breast cancer.

The analysis of breast cancer incidence showed that African American women are not at an increased risk of developing breast cancer within the year between mammography screenings when compared to their Caucasian counterparts. However, results showed a greater proportion of African American women under the age of 50 being diagnosed with breast cancer. This is concerning because this age group is completely omitted from mammography screening practices when adhering to the most recent recommendations. Findings also showed that African American women do not typically present to their mammography screening appointments with knowledge regarding the past breast cancer diagnoses of their first degree relatives. Additional research is needed to see when the breast cancer is developing to determine if following the USPSTF's guidelines would have the potential to negativity impact this group of women and what can be done to challenge this problem. Research would need to look for commonalities between impacted women to identify potential areas for interventions.

Given the current evidence, it appears healthcare leadership and funding agencies can continue to follow the USPSTF's recommendations with the caveat that the recommendations do

not guarantee prevention of later stage breast cancer diagnoses in the women that develop breast cancer between scheduled mammography screenings. In establishing clinical procedures for health care providers, leadership should pay close attention to the manner in which health histories are gathered from their patients. Clinicians should advise patients to discuss health histories with their families in both the area of breast cancer and overall health.

APPENDICES

Appendix A: Committee for Protection of Human Subjects Approval Letter

UTHealth
The University of Texas
Health Science Center at Houston

Committee for the Protection of Human Subjects
6410 Fannin Street, Suite 1100
Houston, Texas 77030

Gayla Ferguson
UT-H - SPH - Mgmt, Policy and Comm Health

December 04, 2019

HSC-SPH-19-1023 - *Consider Us: Analysis of National Mammography Screening Recommendations on African American Women*

The above named project is determined to qualify for exempt status according to 45 CFR 46.101(b)

CATEGORY #4 *: Research, involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified directly or through identifiers linked to the subjects.*

CHANGES: Should you choose to make any changes to the protocol that would involve the inclusion of human subjects or identified data from humans, please submit the change via iRIS to the Committee for the Protection of Human Subjects for review.

INFORMED CONSENT DETERMINATION:
Waiver of Consent Granted

HEALTH INSURANCE PORTABILITY and ACCOUNTABILITY ACT (HIPAA):
Exempt from HIPAA

STUDY CLOSURES: Upon completion of your project, submission of a study closure report is required. The study closure report should be submitted once all data has been collected and analyzed.

Should you have any questions, please contact the Office of Research Support Committees at 713-500-7943.

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