DISPARITIES IN THE TREATMENT OF EARLY BREAST CANCER

by

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ABSTRACT OF THE DISSERTATION

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Context: Breast cancer is the most common cancer and the second leading cause of cancer death among US women. Compounding the impact of breast cancer are significant age and race differences that have been noted in the incidence and mortality of breast cancer. The elderly suffer disproportionately from the burden of breast cancer because they are a rapidly growing population in the US and they also have relatively higher mortality and morbidity from this disease. There is conclusive evidence of the efficacy of adjuvant systemic treatment in prolonging survival. However, very little is known about the frequency of use of this treatment in the elderly. On the other hand, racial differences in breast cancer reveal that although black women have lower incidence of breast cancer than whites, they sustain higher mortality rates. There is evidence that the reduced survival among blacks may be attributable more to differences in socioeconomic status and access to appropriate care, rather than to biological differences between the races. Therefore, it is apparent that the elderly and ethnic minority groups, especially black women, experience poorer outcomes from their breast cancers than their counterparts. Age and race disparities in treatment of early breast cancer may be one

mechanism by which these women suffer poorer outcomes. Therefore, the overall goal of this dissertation was to examine age and race disparities in the treatment of early breast cancer as articulated in the three specific aims described below.

Specific Aims: The aims of this dissertation were to: (1) determine the frequency of use of adjuvant systemic treatment for early breast cancer among women 65 years of age and older, (2) examine whether differences exist in receipt of standard treatment for early breast cancer between black and white women, and (3) examine whether differences exist in delays in initiation of treatment for early breast cancer between black and white women.

Design, Setting, and Patients: Aim 1 utilized data from the population-based New Jersey Cancer Registry (NJSCR) to ascertain the frequency of use of adjuvant systemic treatment among 200 women (100 fatal cases and 100 non-fatal cases) who were ≥ 65 years of age and diagnosed with early stage breast cancer during 1987-1998. Study subjects were stratified based on their estrogen receptor (ER) status into ER positive and ER negative cases. NJSCR data provided information on patient and tumor characteristics as well as information on treatment received and their providers. Cancer registry data are usually obtained from hospital tumor registrars, while adjuvant systemic treatment is frequently administered on an outpatient basis. Therefore, cancer registry data was supplemented with data obtained from patients' primary care physicians and oncologists.

For Aims 2 and 3 of this dissertation, a retrospective cohort study was designed using a linked NJSCR and New Jersey Medicaid dataset for the years 1997 through 2001. Participants in these studies were women 20-64 years of age who were diagnosed with early-stage breast cancer (SEER Summary Stage 'localized' and 'regional spread to lymph nodes') between January 1997 and December 2001. Women who were neither white nor black, who were diagnosed with other cancers, and whose breast cancer was not the primary cancer were excluded. The linked database was used to obtain diagnostic, prognostic, and treatment information on 237 black and 485 white women.

Descriptive analyses were done to characterize the study populations for all three aims. For Aim 1, the frequency of use of surgical therapy, hormonal therapy alone, chemotherapy alone, and hormonal therapy in combination with chemotherapy was calculated separately for subjects with ER positive and ER negative tumors. Multivariate logistic regression models were constructed to examine the predictors of adjuvant hormonal and chemotherapy use. For Aim 2, logistic regression models were constructed to compare receipt of standard treatment between blacks and whites. Racial differences in breast cancer specific and overall survival were evaluated using Cox proportional hazard models. For Aim 3, we compared blacks and whites with respect to delays in initiation of surgical treatment after confirmed diagnosis, of adjuvant radiation therapy after breast conserving surgery, and of adjuvant hormonal and chemotherapy after definitive surgery. Logistic regression models were constructed to examine the association between delays in initiation of surgical treatment ($\geq$1 month vs. <1 month), radiation treatment after breast conserving surgery ($\geq$2 months vs. < 2months), adjuvant

hormonal therapy and chemotherapy (≥1 month vs. <1 month, ≥2 months vs. <2 months, and ≥3 months vs. <3 months) and race.

Results: Aim 1 of this dissertation showed that 28% of elderly New Jersey women with early breast cancer received chemotherapy alone or in combination with hormonal therapy whereas 42% received hormonal therapy alone. Only 40% of the women with ER negative tumors received chemotherapy alone or in combination with hormonal treatment and 30% of patients did not receive any adjuvant therapy. Examination of racial differences in receipt of standard treatment (Aim 2) revealed no differences in receipt of surgical, radiation, or adjuvant systemic treatment. Breast cancer specific mortality (Hazard ratio=1.37; 95% confidence interval = 0.94 – 1.98) and all-cause mortality (Hazard Ratio=1.43; 95% confidence interval=1.08-1.89) were higher among blacks than whites. Although no racial differences were noted in receipt of standard treatment, Aim 3 showed that blacks as compared to whites more often experienced delays of 2 or more months and 3 or more months in initiation of adjuvant chemotherapy after definitive surgery. Also, delays of 2 or more months in adjuvant radiation therapy after breast conserving surgery were observed more frequently among blacks (76.7%) as compared to whites (63.0%). After controlling for other predictors, compared with white women, black women had 1.49-fold odds (95% confidence interval, 0.89, 2.50) of delay of 2 or more months and 1.90-fold odds (95% confidence interval, 0.92, 3.93) of delay of 3 or more months in adjuvant chemotherapy. Delays in adjuvant radiation and chemotherapy were also associated with poorer survival as compared to those who did not experience

such delays. No racial differences were observed in delays in initiation of surgical treatment and adjuvant hormonal therapy.

Conclusion: The research in this dissertation confirmed that significant age and race disparities exist in the treatment of early breast cancer and factors underlying these disparities need to be studied further. Among elderly New Jersey women, almost 40% of women with ER positive tumors did not receive adjuvant hormonal therapy, while 60% of women with ER negative tumors did not receive adjuvant chemotherapy. The frequency of use of adjuvant systemic therapy in the elderly New Jersey population is significantly lower than that reported among middle aged women from other reports. Efforts in increasing the use of hormonal and adjuvant chemotherapy may help to reduce the excess mortality burden among elderly women with early breast cancer. The results from Aims 2 and 3 show that although receipt of standard treatment for early breast cancer was similar between black and white New Jersey Medicaid beneficiaries with early breast cancer, blacks experienced delays in initiation of adjuvant radiation and chemotherapy more often than their white counterparts. This implies that when socioeconomic status and access to care are similar between blacks and whites, receipt of standard treatment is also similar. In spite of this, blacks experience longer delays in treatment initiation suggesting that other factors may also play a role. Identifying the reasons for this difference requires a more in-depth look at the role of several patient, physician, and care-process level factors involved in the complex management of patients with breast cancer.

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INTRODUCTION

Burden of disease

Breast cancer is the most common cancer and the second leading cause of cancer death among US women.[1] The American Cancer Society estimates that in 2007, 178,480 women will be diagnosed with breast cancer and over 40,000 will succumb to the disease.[1] There is a 12.7% chance that a woman will develop breast cancer sometime during her lifetime based on data from 2001-2003.[1] This equates to 1 in 8 women. Since the 1990s, remarkable reductions in breast cancer mortality have been observed.[1] This decline has been attributed to both improvements in early detection (through screening mammography) and breast cancer treatment (adjuvant systemic treatment).[2, 3] However, these trends mask important age and race differences.

Older women are diagnosed more often with breast cancer and sustain higher mortality from it than their younger counterparts.[4-8] In the US, 43% of all invasive breast cancer occurs in women 65 years of age and older, although only 14% of women are in this age group.[4, 7, 9] In contrast to recent progress in reducing mortality from breast cancer for women under age 65 (3.7% decline in the period 1975 to 2004), the breast cancer mortality rate for women 65 years or older decreased only by 1.4% during the same period.[10, 11] Because of the rapid growth of the elderly population in the US as well as the relatively higher mortality and morbidity due to breast cancer in this age group, breast cancer mortality in the elderly is an important public health problem.

In addition to differences by age, there are remarkable racial differences in incidence and mortality of breast cancer. In the US from 1975-2004, the age-adjusted breast cancer incidence rates were higher among whites than blacks.[10] However, black

women under 40 years have a higher incidence than whites. Past age 40 years, whites have higher incidences than blacks.[10] In contrast, mortality from breast cancer is higher for blacks than whites at every age.[10]

Since the early 1990s, significant reductions in breast cancer specific mortality have been observed among both whites and blacks. Death rates from breast cancer were comparable in both races in the 1970s. However a widening disparity between the races has been noted since the early 1980s. During the period 1975-1990, white women had a 0.3% increase in mortality as compared to a 1.5% increase among blacks.[10] Even during the 1990s when mortality decreased for both races, the annual decrease in mortality among blacks (1.3%) was lower than among whites (2.2%).[10] Disparities in morality rates between the races have increased over the past decade.[12]

Treatment of early stage breast cancer

Treatment of early stage breast cancer [American Joint Commission on Cancer (AJCC) stages I, IIA, IIB, or IIIA] typically includes a combination of surgical options with adjuvant radiation therapy and/or adjuvant systemic treatment (hormonal and/or chemotherapy). The most commonly employed treatment options are described below.

<u>Mastectomy versus Breast Conserving Surgery (BCS) followed by Radiation therapy</u>

Several randomized clinical trials with extensive follow-up periods that have compared BCS (wide excision of the tumor with preservation of the breast) with total mastectomy have conclusively established no difference in survival between the less extensive BCS followed by radiation therapy and total mastectomy.[13-17] Radiation therapy is an integral part of BCS and has been recommended by the National Institutes

of Health (NIH) consensus panel.[18] Omission of radiation therapy after BCS is associated with increased risk of recurrence and mortality.[14]

Adjuvant Hormonal Therapy

The benefit of adjuvant systemic treatment in prolonging disease-free and overall survival has been demonstrated by several randomized trials in pre- as well as postmenopausal women irrespective of nodal status.[19-23] The 3rd Early Breast Cancer Trialists' Collaborative Group Overview which included more than 37,000 women with operable breast cancer in 55 randomized trials of adjuvant therapy with tamoxifen showed a 26% reduction in the annual recurrence rate and a 14% reduction in the annual death rate among women on tamoxifen.[19] These benefits were much greater in women with tumors expressing estrogen receptors.[19, 21]

Adjuvant Chemotherapy

Several randomized trials have shown a significant reduction in the odds of annual recurrence and death from breast cancer among women who received adjuvant chemotherapy compared with those who did not.[20, 23-29] These clinical trials also showed that the benefit of adjuvant chemotherapy was equally shared among node-positive and node-negative patients.[20, 26] In addition, the relative risk reductions for recurrence and for mortality were higher for women < 50 years compared to those older than 50 years.[20] Adjuvant chemotherapy also added to the effect of tamoxifen in postmenopausal women.[20, 22]

Based on the above findings, the NIH expert consensus panel developed evidence-based guidelines for early-stage breast cancer treatment in 1990, with a separate

publication specifically on adjuvant therapy in 2000.[30] Under that guideline, physicians are recommended to offer:

1. Surgical treatment either with BCS followed by radiation therapy or by total mastectomy.
2. Adjuvant hormonal treatment for estrogen receptor (ER) and/or progesterone receptor (PR) positive tumors, regardless of age, menopausal status, involvement of axillary lymph nodes, or tumor size
3. Adjuvant cytotoxic polychemotherapy to most women with ER and PR negative tumors, with lymph node metastases or with primary breast tumors larger than 1cm (both node-negative and node-positive) and negative for ER and PR.

There is evidence that non-adherence to consensus standard treatment is associated with higher recurrence and mortality from breast cancer.[31, 32]

Age disparities in treatment for early breast cancer

Breast cancer is becoming increasingly common in older age groups. However, less aggressive treatments may be recommended to older women because of concerns regarding tolerability of adverse effects especially among women with several concomitant diseases. Substantial variations in breast cancer treatment have been noted between younger and older women and these differences are more evident with increasing age of the patient.[33-36] Older women are less likely to receive postoperative radiation or adjuvant systemic therapy compared with younger women.[37] Under utilization of effective treatments may contribute to poorer outcomes among women in this age group.

Although age disparities in surgical and radiation use have been investigated previously[34-36] the actual use of adjuvant systemic treatment in older patients with early breast cancer is not studied as well. A recent study that used the New Mexico Tumor Registry data reported that the use of chemotherapy decreased substantially with increasing age across all tumor stages.[38] Overall, 66% of women younger than 45 years of age received chemotherapy compared with 44% of women between 50 and 54 years of age, 31% of women between 55 and 59 years of age, and 18% of women between 60 and 64 years of age.[38] In that study, the decreasing pattern of chemotherapy use with age continued even after adjustment was made for prognostic factors. Although there is some evidence that side effects of chemotherapy can be more troublesome in older than in younger women, most older women can tolerate hormonal or chemotherapy reasonably well.[21, 39, 40] Studies have shown that co-morbidity can only explain a small part of the variation observed in the treatment intensity of older women with breast cancer.[41, 42] There is also evidence that the effect of care that does not adhere to consensus standard is associated with higher mortality rate in older women as in younger women.[31, 32]

Thus, the objective of the first study of this dissertation was to report the frequency of use of adjuvant systemic therapy for early breast cancer among women 65 years of age or older in New Jersey. We conducted this study by collecting adjuvant systemic treatment information from patients' primary care physicians and oncologists. Cancer registry data are often used for surgical and radiation treatment information. The frequency of use of adjuvant systemic treatment, however, may be underreported by cancer registries. This is because cancer registry data are frequently obtained from

hospital discharge abstracts and are less likely to capture adjuvant systemic treatment which is often administered in an outpatient setting.

We believe that obtaining accurate data on the actual age-specific use of adjuvant hormonal and/or chemotherapy will add to the scant literature on the frequency of use of this efficacious treatment option for early stage breast cancer.

Racial/ethnic disparities in treatment for early breast cancer.

Black breast cancer patients have a shorter survival than their white counterparts. The poorer survival rate from breast cancer among black women could result from late stage at diagnosis,[43] lack of access to treatment, inadequate treatment,[44-46] or to greater likelihood of being diagnosed with more aggressive tumors.[47-50] The excess death rate among blacks appears to result from differences in access and quality of breast cancer treatment rather than biological differences between the races.[51-54] Treatment outcomes studies in settings where patients share equal access to treatment support that similar treatments among the races result in similar outcomes.[54-56]

Several studies have reported racial differences in the receipt of BCS.[15, 37, 57-64] Analysis of Medicare claims data for 1986,[62] 1990,[58] and 1994[60] and Surveillance, Epidemiology and End Results (SEER) data[63] revealed that elderly blacks were less likely than whites to receive BCS. Higher rates of BCS among black women as compared to whites have also been reported from the California Cancer Registry during 1988 through 1995[15] and from the SEER-Medicare linked data during 1988 through 1993.[64] However, several studies have also failed to show an association between race and receipt of BCS.[37, 57, 59, 65, 66] For instance, the National Cancer Institute Black/White

Cancer Survival Study for 1985 and 1986 demonstrated that after adjusting for tumor size and concomitant disease, significantly greater proportion of blacks underwent mastectomy compared with whites.[67]

Studies of racial disparity in breast cancer treatment are more consistent for receipt of adjuvant radiation therapy after BCS.[45] Blacks were less likely than whites to receive radiation therapy after BCS in studies that used the SEER data from 1983 through 1986,[57] from 1985 through 1989[37] and from 1988 through 1993.[64] Recent analyses of SEER data[68, 69] showed that black women who received BCS were less likely to receive follow-up radiation therapy in every 10-year age group with the exception of women who were older than 85 years.

Although extensive research has been done in the area of racial/ethnic differences in surgical and radiation therapy for breast cancer, fewer studies have been conducted so far to investigate racial disparities in the use of adjuvant hormonal and chemotherapeutic regimes. SEER-Medicare linked data for women ≥65 years of age diagnosed with breast cancer in 1991 and 1992 showed no association between race and receipt of chemotherapy.[70] However, the completeness of Medicare data on adjuvant systemic therapies remains unclear as these treatments are mostly provided in an outpatient setting, and Medicare did not cover outpatient drugs in the study years. A more recent study by Bickell et al reported statistically significant differences in under use of appropriate adjuvant therapy between black (34%) and white women (16%) with early stage breast cancer after adjustment for demographic (age), clinical (stage, comorbidity), and access (lack of insurance, referral to oncologist) factors.[71] This study was conducted in a

handful of hospitals located in a single geographic area (New York city), thus representing a distinct population and limiting its generalizability.

In addition to under utilization of efficacious treatments, longer delays in initiating appropriate treatment after diagnosis among blacks may also contribute to their poorer prognosis from breast cancer. Few studies have examined racial differences in treatment delays.[72-75] A metropolitan Atlanta study showed a 2.3 fold increase in treatment delay (≥ 1 month vs. < 1 month) for blacks compared to whites after accounting for poverty index, insurance status, and marital status. The treatments considered in the calculation of treatment delay in that study only included surgical treatment and adjuvant chemotherapy. Adjuvant hormonal therapy as well as adjuvant radiation after BCS were not evaluated in that study. In addition, it was not clear why the authors did not adjust for education level and number of comorbid disease even though these were shown to be associated with treatment delay in their univariate analyses.[75] Another study conducted at Yale-New Haven Medical Center found that 33% of black women had not started treatment within 30 days of the diagnosis compared with 21% of white women ($p=0.056$). This comparison only achieved borderline statistical significance and also did not adjust for important confounding factors.[73] A more recent study conducted in an insured population, i.e. Medicare beneficiaries, using the linked SEER-Medicare claims database showed that compared with white women, black women had a 1.64-fold increased odds (95% confidence interval, 1.40-1.91) of treatment delay beyond 1 month.[74] That study also did not include adjuvant hormonal therapy in their definition of treatment delay.

The literature reviewed here points to significant variations in the treatment of breast cancer by race which includes several studies reporting that treatment differs between black and white women. However, there is evidence to suggest that differences in treatment and survival may be more attributable to socioeconomic differences or differences in access to care rather than to race.[61, 76, 77] Some studies have shown that the overall effect of race on survival is greatly reduced or absent when factors such as socioeconomic status, access to care, and health insurance are included as adjusting variables.[58, 78] The data used for most studies demonstrating racial differences came from either a specific geographic location or managed care plan or they stem from the population-based SEER registry linked with Medicare claims files. These data are good sources for patient characteristics (e.g., age, race, and cancer-related variables), but do not provide good measures of socioeconomic status (e.g., income) or access to care (e.g., insurance status). This may contribute to the large variation in results of studies examining racial disparities in breast cancer treatment and survival.

For Aims 2 and 3 of this dissertation, we linked the New Jersey Cancer Registry data with Medicaid claims data. By studying Medicaid beneficiaries we examined a relatively homogeneous group of women with respect to socioeconomic status, thus limiting the effect of SES on receipt of standard treatment and survival. Also, both studies were conducted in a population insured through Medicaid, thus accounting for the effect of access to care and insurance status. In addition, the Medicaid data allowed us to identify claims for adjuvant hormonal and chemotherapy treatments that are often not captured in cancer registries, while the NJSCR data provided information on diagnostic

and prognostic cancer-related variables as well as supplemented our information on surgical, adjuvant radiation, and adjuvant systemic treatment.

The overall goal of this dissertation was to examine age and race disparities in the treatment of early breast cancer. Our specific aims were to examine:

1. The frequency of use of adjuvant systemic treatment for early breast cancer among women 65 years of age or older.
2. If there were differences in treatment of early breast cancer and survival between black and white women.
3. If there were differences in delays in treatment of early breast cancer between black and white women.

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USE OF ADJUVANT SYSTEMIC THERAPY FOR EARLY BREAST CANCER AMONG WOMEN 65 YEARS AND OLDER

by

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USE OF ADJUVANT SYSTEMIC THERAPY FOR EARLY BREAST CANCER AMONG WOMEN 65 YEARS AND OLDER

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ABSTRACT

The National Institutes of Health (NIH) consensus statement recommends adjuvant therapy for early breast cancer irrespective of age. However, the actual use of such therapy is not well documented among women over 65 years. This study reports the frequency of use of adjuvant therapy in this age group. Receipt of adjuvant therapy was ascertained for 200 women aged ≥65 years diagnosed with early breast cancer who were identified from the New Jersey State Cancer Registry. In this population, 28% of patients received chemotherapy alone or in combination with hormonal therapy whereas 42% received hormonal therapy alone. Less than half of the women with ER negative tumors received chemotherapy alone or in combination with hormonal treatment. Adjuvant therapy was not prescribed to 30% of patients. Despite NIH recommendations, the frequency of use of adjuvant therapy in New Jersey is low among women over 65 years regardless of their receptor status.

ABBREVIATIONS USED

NIH – National Institutes of Health

ER – Estrogen receptor

NJSCR – New Jersey State Cancer Registry

AJCC – American Joint Commission on Cancer

SEER – Surveillance, Epidemiology, and End Results

PR – Progesterone receptor

USE OF ADJUVANT SYSTEMIC THERAPY FOR EARLY BREAST CANCER AMONG WOMEN 65 YEARS AND OLDER

Introduction

Because of the rapid growth of the elderly population and the higher mortality due to breast cancer in this age group, breast cancer in the elderly is a major public health problem. Initial adjuvant systemic therapy for breast cancer has been extensively evaluated in clinical trials and its efficacy in prolonging survival has been established.[1] Based on these findings, the National Institute of Health (NIH) expert-consensus panel developed evidence-based guidelines for early-stage breast cancer treatment.[2] The consensus recommended that adjuvant systemic treatment for stage I or stage II breast cancer include: (a) hormonal treatment for receptor positive tumors of less than or equal to 1 cm regardless of involvement of axillary lymph nodes; (b) polychemotherapy (≥ 2 agents) for receptor negative tumors larger than 1 cm (both node-negative and node-positive); (c) hormonal treatment plus polychemotherapy (≥ 2 agents) for receptor positive tumors larger than 1 cm (both node-negative and node-positive).[2]

Although side effects of chemotherapy can be more troublesome in older than in younger women, the majority of older women can tolerate hormonal or chemotherapy reasonably well.[3] There is also evidence that medical care that does not adhere to consensus standard treatment is associated with a higher mortality rate both in older and younger women,[4] Although the frequency of use of adjuvant systemic treatment in patients with early breast cancer is largely unknown, a recent study that used the New Mexico Tumor Registry data reported that only 11 percent of women with stage I, 47

percent with stage II, and 68 percent with stage IIIA received chemotherapy.[5] Furthermore, across all tumor stages, the use of chemotherapy decreased substantially with increasing age. Overall, 66 percent of women younger than 45 years of age received chemotherapy compared with 44 percent of women between 50 and 54 years of age, 31 percent of women between 55 and 59 years of age, and 18 percent of women between 60 and 64 years of age.[5] In that study, the decreasing pattern of chemotherapy use with age continued even after adjustment was made for prognostic factors.[5]

Cancer registry data are frequently obtained from hospital discharge abstracts. Since adjuvant systemic treatment is often administered in an outpatient setting, it is likely that such treatment may be underreported by cancer registries. The objective of this study was to report the frequency of use of adjuvant systemic therapy for early breast cancer among women 65 years of age or older in New Jersey.

Materials and Methods

Breast cancer cases used for this study were originally selected from the New Jersey State Cancer Registry (NJSCR) for a pilot study designed to assess whether adjuvant chemotherapy is effective in reducing mortality among older patients.

Selection of Fatal Cases

Fatal cases were women who died of breast cancer at 65-85 years of age in New Jersey during the period 1987-1998 and were initially diagnosed with breast cancer that was either localized or with regional spread to lymph nodes as defined by the Surveillance Epidemiology and End Results (SEER) Summary Staging System. This corresponds to the American Joint Commission on Cancer (AJCC) stages I (T1N0M0), IIA (T1N1M0, T2N0M0), IIB (T2N1M0, T3N0M0) or IIIA (T1N2M0, T2N2M0, T3N1M0, T3N2M0).[6] The Tumor (T), Node (N), and Metastasis (M) in the above staging system are defined as follows: T1 = tumor ≤2.0 cm in greatest dimension, T2 = tumor >2.0 cm but ≤5.0 cm in greatest dimension, T3 = tumor >5.0 cm in greatest dimension, N0 = no regional lymph node metastasis, N1= metastasis to movable ipsilateral axillary lymph node(s), N2 =metastasis to ipsilateral axillary lymph node(s) fixed or matted, or in clinically apparent ipsilateral internal mammary nodes in the *absence* of clinically evident lymph node metastasis, M0 = no distant metastasis, and M1= distant metastasis.[6]

Cases were then stratified based on their receptor status into ER positive and ER negative cases. Of all women meeting these criteria, we randomly selected 50 ER positive and 50 ER negative breast cancer cases. Women whose ER status was not recorded in the registry were excluded.

Selection of Non-Fatal Cases

Non-fatal cases were selected from breast cancer survivors who were alive at least until the date of death of the fatal case. One non-fatal case with no known recurrence of breast cancer was matched to each fatal case. These were randomly chosen from all women who matched the fatal cases on date of diagnosis (± 1 year), age at diagnosis (five-year age groups), SEER Summary Stage of breast cancer (localized or regional spread to lymph nodes), and ER status (positive or negative). Fatal and non-fatal cases who were not New Jersey residents and non-fatal cases who, upon receipt of medical information from providers, were found to have probable evidence of recurrence in their breast cancer were excluded. In those cases, non-fatal cases were selected to match to fatal cases from a back-up pool of non-fatal cases.

Construction of a Representative Sample of Elderly NJ Women with Breast Cancer

The case-control sampling method heavily represents cases (50% of our sample were cases). Thus, combining the non-fatal and fatal cases to determine the frequency of use of adjuvant systemic therapy is inappropriate. To reconstruct a sample that was representative of the elderly NJ women with early breast cancer, we obtained the distribution of fatal and non-fatal cases of early breast cancer among women 65 to 84 years of age at diagnosis from the population-based NJSCR. In order to estimate the frequency of use of adjuvant systemic therapy in New Jersey, we calculated a weighted average using the proportion of fatal and non-fatal ER positive (6.6 and 93.4%) and ER negative (13.3 and 86.7%) early breast cancer cases diagnosed during the years 1987 through 1998 from all records available in the NJSCR among women 65 years of age and older. On the basis of this information, we gave less weight to the fatal cases and more

weight to the non-fatal cases in our sample. This enabled us to reconstruct a representative sample of elderly NJ breast cancer patients in the community.

Ascertainment of Adjuvant Systemic Treatment and Confounding Variables

The NJSCR computerized files provided information on demographic characteristics (age, race, ethnicity, and marital status), tumor characteristics (date of diagnosis, stage, receptor status, grade, and histological type), as well as treatment received (surgery, radiation therapy, chemotherapy, and hormonal therapy with tamoxifen) by the study subjects. Additional information was sought from patients' treating physicians on adjuvant systemic treatment. Physicians of patients included in the study were mailed a questionnaire requesting them to verify existing information obtained from the NJSCR and to provide information that was missing on the NJSCR file. In instances when information obtained from the NJSCR differed from that provided by the treating physicians, we considered the physician's information to be more accurate. Using this method, we were able to obtain information on use of adjuvant systemic therapy for 80% of the study population. Physicians were also requested to provide information on the presence of comorbid diseases for their patients. We used this information to calculate the Charlson's comorbidity index for each patient.[7] This study was approved by the Institutional Review Boards of the University of Medicine and Dentistry of New Jersey and the New Jersey Department of Health and Senior Services.

Statistical Analysis

We examined the distribution of demographic and patient factors (age at diagnosis, race/ethnicity, marital status and Charlson's comorbidity index) as well as tumor characteristics (ER receptor status and progesterone receptor (PR) status, tumor grade, histological type, and SEER summary stage of the tumor) in the study population. We, then, determined the frequency of use of surgical therapy, hormonal therapy alone, chemotherapy alone, and hormonal therapy in combination with chemotherapy separately for subjects with ER positive and ER negative tumors. Subjects with missing treatment information were not included in the calculation of this frequency. Multivariate logistic regression models were constructed with use of adjuvant hormonal and chemotherapy as dependent variables and ER status, PR status, stage, comorbidity index, patients' age, and race as independent variables. All analyses were done using the SAS statistical software, version 9.1.[8]

Results

Patient Characteristics

The demographic characteristics of the study subjects are shown in Table 1. The study population comprised mostly of women aged 70-79 years, who were predominantly non-Hispanic whites, and were either married or widowed. 75 percent of the women in the study had a Charlson's comorbidity score of zero. We also calculated the frequency of occurrence of specific co-morbidity. Among subjects who were reported as having at least one comorbid condition, 62.4 percent suffered from various cardiovascular conditions including coronary artery disease, hypertension, congestive heart failure, myocardial infarction and cerebrovascular accidents. Another 21.2 percent had a history of cancers other than their breast cancer. A further 12.9 percent of the study subjects suffered from respiratory conditions like asthma, chronic emphysema and bronchitis while 10.6 percent had a history of diabetes mellitus. There were no substantial differences in demographic characteristics between fatal and non-fatal cases.

Tumor Characteristics

The distribution of tumor characteristics in the study population is displayed in Table 1. As a result of the stratification by ER status in the study design, the proportion of breast cancer patients with receptor positive and receptor negative tumors was equal. The distribution of subjects with PR positive and negative tumors was similar. Most women whose tumors expressed estrogen receptors were also PR positive (63 percent). Similarly, 73 percent of women with ER negative tumors were also negative for progesterone receptors. Breast cancer patients were diagnosed with poorly differentiated or anaplastic tumors more often than with well or moderately differentiated tumors. When stratified by ER status, a higher percentage of women with well/moderately

differentiated tumors expressed estrogen receptors (44 percent) versus 20 percent that were negative for estrogen receptors. Among those with poorly differentiated or anaplastic tumors, 54 percent were ER negative while only 20 percent were receptor positive. Infiltrating duct carcinoma was the most common histological type observed among the study subjects. Other histological types included lobular carcinoma, adenocarcinoma, and mucinous adenocarcinoma. More than half of the subjects had localized disease with about 40 percent having regional spread to lymph nodes.

Receipt of Surgical and Radiation Therapy

Approximately 90 percent of the women in our study population underwent either a lumpectomy or a mastectomy for their breast cancers. Table 2 describes the use of surgical treatment for breast cancer by ER status. Among women with ER positive or negative tumors, the receipt of mastectomy was higher among non-fatal cases whereas lumpectomy was performed more often among fatal cases. Radiation therapy was administered to 35 percent of the women in the study.

Receipt of Adjuvant Systemic Therapy

Overall, 42 and 14 percent of the study subjects received hormonal therapy alone and chemotherapy alone respectively. Chemotherapy in combination with hormonal therapy was reported for another 14 percent of the subjects and approximately 30 percent received no adjuvant systemic treatment. Table 2 shows the frequency of use of adjuvant systemic therapy separately for ER positive and ER negative subjects. About 49 percent of the subjects whose tumors were ER positive received hormonal therapy alone while 11 percent received hormonal therapy in combination with chemotherapy. On the other hand, 35 percent of women with ER positive tumors were not prescribed any adjuvant

therapy. Among women whose tumors did not express estrogen receptors, the prevalence of use of chemotherapy alone or in combination with hormonal therapy was 23 and 17 percent respectively. When the use of adjuvant therapy was stratified by stage of breast cancer at diagnosis, we observed that hormonal therapy alone was prescribed more often for localized breast cancer (67.2% vs. 37.5%). On the other hand, a significantly higher percentage of subjects whose tumors had spread to regional lymph nodes as compared to those that were localized (62.5% vs. 32.8% respectively, p=0.0015) received chemotherapy alone or in combination with hormonal therapy. Thus, our results indicated a higher use of chemotherapy or combination therapy among those who had node positive breast cancer.

Table 3 presents the results from multivariate logistic regression models with adjuvant hormonal and chemotherapy as dependent variables. Patients with cancers that had spread to regional lymph nodes were significantly more likely to receive adjuvant chemotherapy as compared to those with localized tumors [Odds ratio (OR) 4.75, 95% confidence interval (CI) 2.10 - 10.78] as were patients with progesterone receptor negative tumors [OR= 3.27, 95% CI: 1.08, 9.94]. These estimates were adjusted for ER status, Charlson's comorbidity index, and patients' age and race/ethnicity.

Contrary to the recommendations in the NIH consensus statement[2], a significant proportion of women with ER negative tumors (34 percent, n=22) were prescribed hormonal therapy alone. A closer look at the data revealed that eight women who were classified as ER negative in the NJSCR files were subsequently reported to be ER positive by their physicians and/or hospitals. However, these cases were analyzed as per their original assignment at the design stage and weights were calculated accordingly. In

addition, three women were positive for progesterone receptors. Data on use of adjuvant systemic treatment was not available for 20 ER positive and 20 ER negative subjects. This was predominantly due to two reasons. First, for some patients, the NJSCR could not identify the treating physicians. Therefore, no additional information could be obtained. Second, the treating physicians could not locate the medical records of some of the patients. This was either because the medical records were destroyed or because the office staff could not find the necessary information.

Discussion

Our study documents the pattern of use of adjuvant systemic therapy among women 65 years and older with early breast cancer**.** Overall, 42 and 14 percent of the study subjects received hormonal therapy alone and chemotherapy alone respectively. Chemotherapy in combination with hormonal therapy was reported for 14 percent of the subjects and approximately 30 percent received no adjuvant systemic treatment. Hormonal therapy was the most frequently used treatment modality irrespective of hormonal receptor status. Chemotherapy alone or in combination with hormonal therapy was prescribed to less than half the women with ER negative tumors.

In this study, we found that approximately 42 percent of New Jersey women 65 years of age and older with early breast cancer received hormonal therapy alone. This is in line with the results obtained from other studies in which the use of this treatment ranged between 17 and 81 percent among this age group.[5, 9-13] Previous research has also demonstrated that the frequency of use of chemotherapy alone or in combination with hormonal therapy among elderly women with early breast cancer varies from as low as 2 percent to as high as 33 percent.[5, 9-13] In our study, about 28 percent of the subjects received adjuvant chemotherapy alone or in combination with hormonal therapy, which is consistent with previous research.

An interesting finding of this study was that, contrary to NIH guidelines[2], a high proportion of ER negative women received hormonal therapy alone (34 percent) or in combination with chemotherapy (17 percent). Several clinical trials that published their data in the 1980s demonstrated an overall benefit of tamoxifen in reducing breast cancer mortality for both ER positive and negative tumors.[14-18] The increased use of adjuvant

hormonal therapy for receptor negative tumors in our population of women diagnosed during 1988-1998 may reflect the evidence available to physicians at that time. However, with better assays available for ER and PR tests, recent research has shown no benefit of tamoxifen use among women with receptor negative tumors.[19] Also, it has been suggested that ER negative women with a positive PR assay might benefit from tamoxifen.[2, 20] In our study, we found that 7 out of the 22 women with ER negative tumors who received hormonal therapy alone were PR positive. In such cases, the decision to prescribe hormonal treatment may have been driven by patients' positive PR status.

In the present study, we found that eight women who were classified as ER negative based on the NJSCR data were reported to be ER positive by their treating physicians and hospitals. Studies have reported considerable variability in techniques of measurement of ER status between laboratories[21, 22] as well as in the definitions for ER positivity.[23] It has also been postulated that tamoxifen may have mechanisms of action other than its role of binding to ER protein. It has been suggested that tamoxifen may have an effect on insulin-like growth factor I levels, thus extending it's therapeutic benefit to postmenopausal ER negative women.[24] There is some evidence that women whose tumors express low, but still detectable amounts of ER protein may show a favorable response to tamoxifen in spite of being reported as ER negative.[2, 22]

Our study has its limitations; one of which is the lack of information on tumor characteristics and treatment for some patients. This was primarily due to three reasons. First, information on women diagnosed with breast cancer more than 7 years after diagnosis was not available from the physicians, either because their records were

archived at an off-site location or were destroyed. Second, names and contact information of attending physicians and/or oncologists for some study subjects were not available from the registry data, thus making it impossible to obtain additional treatment information; and lastly, for some patients, the physicians identified from the registry had not contributed to the patients' breast cancer care and did not have any information on other physicians who may have evaluated the patient for their cancer treatment. In spite of these limitations, the adjuvant treatment information obtained from the physicians was superior to that available in the registry data, thus providing a better estimate of the frequency of use of adjuvant systemic treatment for early breast cancer among women 65 years and older residing in New Jersey.

In conclusion, only about a quarter of women 65 years of age and older in New Jersey received adjuvant chemotherapy. More significantly, less than half of the women with ER negative tumors were reported to have received adjuvant chemotherapy. Efforts in increasing the use of hormonal and adjuvant chemotherapy may help to reduce the excess mortality burden among elderly women with early breast cancer.

Table 1: Patient and Tumor Characteristics of the study subjects

	Fatal cases (n=100)	Non-fatal cases (n=100)	Weighted average*
Patient Characteristics			
Age at diagnosis in years, (%)			
65-69	23.0	21.0	21.2
70-74	28.0	31.0	30.7
75-79	33.0	32.0	32.1
80-85	16.0	16.0	16.0
Race/Ethnicity, (%)			
White Non-Hispanic	89.0	91.0	90.8
Black Non-Hispanic	8.0	4.0	4.5
Hispanic	2.0	2.0	2.0
Unknown	1.0	3.0	2.8
Marital Status, (%)			
Single	8.0	10.0	9.8
Married	39.0	38.0	38.1
Widowed	49.0	39.0	40.2
Separated / divorced	2.0	9.0	8.2
Unknown	2.0	4.0	3.8
Charlson's co-morbidity index, (%)			
0	75.0	75.0	75.0
1	10.0	8.0	8.2
2	12.0	13.0	12.9
≥ 3	3.0	4.0	3.9
Tumor Characteristics			
Estrogen receptor status, (%)			
Positive	50.0	50.0	50.0
Negative	50.0	50.0	50.0
Progesterone receptor status, (%)			
Positive	39.0	42.0	41.7
Negative	43.0	39.0	39.5
Unknown	18.0	19.0	18.9
Tumor grade, (%)			
Well / Moderately differentiated	18.6	32.0	30.4
Poorly differentiated / Anaplastic	43.3	37.0	37.7
Unknown	38.1	31.0	31.8
Tumor histology, (%)			
Infiltrating duct carcinoma	78.0	70.0	70.9
Lobular carcinoma	7.0	10.0	9.7
Adenocarcinoma	2.0	6.0	5.5
Mucinous adenocarcinoma	4.0	1.0	1.3
Other	9.0	13.0	12.5
SEER summary stage, (%)			
Localized	60.0	60.0	60.0
Regional spread to lymph nodes	40.0	40.0	40.0

*Percentages reported are calculated as a weighted average of the proportion of fatal (0.116) and non-fatal cases (0.884) having the specific characteristic

Table 2: Receipt of Surgical and Adjuvant Systemic Therapy among study subjects

	Frequency and Percentage of women receiving adjuvant systemic therapy†		Weighted Average‡
	Fatal Cases (n=100)	Non-fatal Cases (n=100)	
ER* positive subjects			
Surgical Therapy			
Mastectomy	9 (21.4)	14 (29.2)	28.7
Lumpectomy	31 (73.8)	27 (56.3)	57.5
No surgery	2 (4.8)	7 (14.6)	14.0
Unknown§	8	2	
Adjuvant therapy			
Hormonal therapy only	15 (45.5)	23 (48.9)	48.7
Chemotherapy only	5 (15.2)	2 (4.3)	5.0
Hormonal plus chemotherapy	8 (24.2)	5 (10.6)	11.5
No adjuvant therapy	5 (15.2)	17 (36.2)	34.8
Unknown§	17	3	
ER* negative subjects			
Surgical Therapy			
Mastectomy	11 (22.0)	20 (40.0)	37.6
Lumpectomy	32 (64.0)	27 (54.0)	55.3
No surgery	7 (14.0)	3 (6.0)	7.1
Unknown§	0	0	
Adjuvant therapy			
Hormonal therapy only	8 (19.1)	14 (36.8)	34.4
Chemotherapy only	9 (21.4)	9 (23.7)	23.4
Hormonal plus chemotherapy	10 (23.8)	6 (15.8)	16.9
No adjuvant therapy	15 (35.7)	9 (23.7)	25.3
Unknown§	8	12	

*ER=Estrogen Receptor

†Numbers reported are N (%)

§In the calculation of percentages, subjects with unknown surgical, hormonal and chemotherapy information are excluded.

‡Weighted average for ER positive subjects = (0.066 x proportion of fatal cases receiving specific adjuvant therapy) + (0.934 x proportion of non-fatal cases receiving specific adjuvant therapy)
Weighted average for ER negative subjects = (0.133 x proportion of fatal cases receiving specific adjuvant therapy) + (0.867 x proportion of non-fatal cases receiving specific adjuvant therapy)

Table 3: Factors related to use of adjuvant systemic therapy

	Odds Ratio (95% CI)
Adjuvant hormonal therapy	
Estrogen receptor status	
Positive	1.00
Negative	0.63 (0.25, 1.54)
Progesterone receptor status	
Positive	1.00
Negative	0.54 (0.21, 1.42)
Unknown	0.57 (0.20, 1.61)
Stage	
Localized	1.00
Regional spread to lymph nodes	1.33 (0.62, 2.83)
Charlson's comorbidity index	1.45 (0.98, 2.14)
Patients' age	1.03 (0.97, 1.11)
Race/Ethnicity	
Non-hispanic white	1.00
Non-hispanic black	0.98 (0.24, 3.97)
Hispanic	0.64 (0.08, 5.35)
Unknown	0.73 (0.09, 5.73)
Adjuvant chemotherapy	
Estrogen receptor status	
Positive	1.00
Negative	0.73 (0.25, 2.11)
Progesterone receptor status	
Positive	1.00
Negative	3.27 (1.08, 9.94)
Unknown	0.64 (0.17, 2.46)
Stage	
Localized	1.00
Regional spread to lymph nodes	4.75 (2.10, 10.78)
Charlson's comorbidity index	0.98 (0.71, 1.37)
Patients' age	0.88 (0.82, 0.96)
Race/Ethnicity	
Non-hispanic white	1.00
Non-hispanic black	1.03 (0.22, 4.80)
Hispanic	0.81 (0.10, 6.68)
Unknown	0.77 (0.06, 9.33)

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RACIAL DIFFERENCES IN TREATMENT OF EARLY BREAST CANCER AMONG MEDICAID BENEFICIARIES

by

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ABSTRACT OF MANUSCRIPT 2 OF 3

RACIAL DIFFERENCES IN TREATMENT OF EARLY BREAST CANCER AMONG MEDICAID BENEFICIARIES

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ABSTRACT

Background: Black breast cancer patients have a shorter survival compared to their white counterparts. The shorter survival among blacks could be due to their advanced stage at presentation or lack of optimal treatment. Medicaid enrolled patients provide an opportunity to examine racial disparity in the treatment of breast cancer minimizing the roles of access to health care and socioeconomic status. This study compared breast cancer treatment and survival in black and white women enrolled in Medicaid.

Methods: We linked the New Jersey Cancer Registry and the Medicaid Research files to obtain diagnostic, prognostic, and treatment information on 237 black and 485 white women 20-64 years of age diagnosed with early stage breast cancer between January 1997 and December 2001. Logistic regression models were constructed to compare treatment utilization between blacks and whites. Racial differences in breast cancer specific and overall survival were evaluated using Cox proportional hazard models.

Results: There were no differences in receipt of surgical, radiation, or adjuvant systemic treatment between blacks and whites. Breast cancer specific mortality (Hazard

ratio=1.37; 95% confidence interval = 0.94 – 1.98) and all-cause mortality (Hazard Ratio=1.43; 95% confidence interval=1.08-1.89) were higher among blacks than whites. Conclusion: In this study of Medicaid enrolled women with similar socioeconomic status and health care access, blacks and whites received similar breast cancer treatment. In spite of similar treatment, blacks have higher breast cancer and all-cause mortality than whites. Our findings suggest that factors other than treatment differences contribute to the racial disparity in mortality.

RACIAL DIFFERENCES IN TREATMENT OF EARLY BREAST CANCER AMONG MEDICAID BENEFICIARIES

Background

The American Cancer Society estimates that in 2007 alone, 178,480 women in the United States (US) will be diagnosed with breast cancer and over 40,000 will succumb to the disease.[1] Breast cancer mortality rates have shown a steady decline during the 1990s. However, this trend masks important racial differences. While the age-adjusted incidence of breast cancer during 2000-2004 was lower among blacks (118.3 per 100,000) compared to whites (132.5 per 100,000), the age-adjusted mortality rates were higher among blacks (33.9 per 100,000) compared to whites (25.0 per 100,000).[2] Although there has been a steady decline in mortality rates from 1995-2004 for both blacks and whites, racial disparities in these rates have increased over the past decade.[2] For instance, between 1992 and 2000, breast cancer mortality declined by 2.6% per year among Whites, but the yearly decrease was only by 1.1% among African Americans.[2]

Several studies examining the efficacy and/or effectiveness of initial breast cancer treatment such as breast-conserving therapy (BCS), radiation following surgery, adjuvant tamoxifen, and chemotherapy have demonstrated equal benefits from these therapies among both white and black women.[3-5] In view of this, one possible explanation for existing racial disparity in mortality is the lack of receipt of optimal treatment among blacks. Extensive research has been done in the area of racial/ethnic differences in surgical as well as radiation therapy following BCS for early breast cancer.[6-18] Racial disparities in the receipt of adjuvant systemic therapy have been studied less.[19, 20]

Although biologic differences in tumor aggressiveness can not be discounted, socioeconomic status and access to care may play an important role in treatment differences between the races. Cancer registry data linked with Medicaid provides a unique opportunity to study racial disparities in standard treatment of early breast cancer by minimizing the role of socioeconomic status and access to care. While the cancer registry provides access to accurate data on diagnostic and prognostic variables as well as surgical and radiation therapy, the Medicaid file captures adjuvant systemic treatment claims. Previous studies have been unable to capture this information as adjuvant systemic therapy is often provided in outpatient settings and requires resources intensive medical record reviews from outpatient visits. Therefore, the objective of this study was to examine racial differences in treatment for early breast cancer and survival among Medicaid beneficiaries.

Methods

Data Sources

A retrospective cohort study was conducted using data from the New Jersey Cancer Registry (NJSCR) linked with the New Jersey Medicaid Research file. The NJSCR database provided information on socio-demographic variables (age, race, marital status), on tumor characteristics (histologic type, grade or differentiation, and cancer stage), on cancer treatment (mastectomy or BCS, radiation therapy, adjuvant hormonal therapy, and adjuvant chemotherapy), and on patients' vital status (alive or dead). If the patient had died, the date of death and the cause of death were also available. The accuracy of tumor registry data has been examined by comparing it with data collected from patients' treating physicians and hospitals for a breast cancer quality improvement project.[21] While the tumor registries and the quality improvement project had similar information on tumor stage and surgery type, receipt of radiation and adjuvant systemic treatment were less accurate from tumor registries.[21]

Encounter data from the New Jersey Medicaid research file was used to supplement information on adjuvant systemic treatment obtained from the cancer registry data. New Jersey Medicaid is a health care program for the poor and is financed with state and federal dollars. The State of New Jersey Medicaid Management Information System (NJMMIS) is a comprehensive database that encompasses all medical encounter claims submitted by providers for the care of Medicaid enrollees.[22, 23] Under a cooperative agreement between the federal government and states, the NJMMIS and 38 other states submit Medicaid data to the Centers for Medicare and Medicaid Services (CMS). CMS checks the quality and completeness of data received from each state and

converts the State Medicaid data to State Medicaid Research Files (SMRF) for the years prior to 1999 or the Medicaid Analytic Extract (MAX) files for the years 1999 and later.

The SMRF/MAX has four separate files: (1) the personal summary file, (2) the inpatient file, (3) the other therapy file, and (4) the drug file. Table 1 provides information available in each of these files. Each file contains a unique identifier for each Medicaid eligible enrollee. This unique patient identifier was used to merge these four data files.

The Medicaid drug file has been validated against primary source data (e.g. medical and pharmacy records) and the agreement was found to be high.[24-26] Furthermore, the use of Medicaid data to identify drug utilization is believed to be more comprehensive than either patient recall or physician's prescribing records. The likelihood of having gaps in breast cancer treatment claims due to changes in eligibility is low as a result of the "Breast and Cervical Cancer Prevention and Treatment Act of 2000" enacted by New Jersey under which medical assistance is provided through Medicaid for women diagnosed with breast cancer in the national screening program for low-income women.[27]

Study Participants

Participants in this study were women 20-64 years of age who were diagnosed with early-stage breast cancer (SEER Summary Stage 'localized' and 'regional spread to lymph nodes') between January 1997 and December 2001. This corresponds to the American Joint Commission on Cancer (AJCC) stages I, IIA, IIB or IIIA.[28] We excluded women who were neither white nor black, who were diagnosed with other cancers, and whose breast cancer was not the primary cancer.

Linkage of NJSCR and Medicaid files

Women who met the above criteria were identified from the New Jersey Cancer Registry and linked with the New Jersey Medicaid File for the same years using probabilistic record linkage methodology. This method does not require linkage variables (social security number, date, month, and year of birth, gender, race, zip code of residence) from the two files to match exactly. In order to determine a matched or unmatched pair, each variable contributes some information, i.e., weight. Weights take into account the reliability of the linkage variable and the probability of random agreement of the variable in the two files. The total weight for each linked record was used to classify records as matched, not matched, or uncertainly matched (clerical pairs) based on whether the statistical probability of a match exceeded a certain threshold.

To accomplish the record linkage duplicate records were first deleted. Linked records that had a higher weight associated with them were accepted as 'matched'. Records that were uncertainly matched were examined manually and evaluated using a set of rules developed by the research team. Records that met these rules were selected as 'matches'. The final linked database included 722 women with early stage breast cancer (485 white and 237 black).

Definition of standard treatment

Receipt of standard treatment for early breast cancer was defined on the basis of the National Institutes of Health consensus report.[29] A woman diagnosed with early stage breast cancer was considered as having received standard treatment if she (i) was treated surgically either with breast conserving surgery (BCS) followed by radiation therapy or by total mastectomy. BCS was defined as excision of primary tumor and adjacent breast

tissue. The procedure is also referred to as lumpectomy, segmental mastectomy, or partial mastectomy; (ii) received hormonal treatment regardless of involvement of axillary lymph nodes for estrogen receptor (ER) and/or progesterone receptor (PR) positive tumors; (iii) received polychemotherapy for ER and PR negative tumors (both node-negative and node-positive); (iv) received hormonal treatment plus polychemotherapy for ER and/or PR positive tumors (both node-negative and node-positive). For instance, a woman who was diagnosed with a receptor positive tumor was considered to have received standard treatment if she underwent either mastectomy or BCS followed by radiation therapy and also received adjuvant hormonal therapy alone or in combination with chemotherapy. On the other hand, a woman who was diagnosed with a receptor negative tumor was considered to have received standard treatment if she underwent either mastectomy or BCS followed by radiation therapy and also received adjuvant chemotherapy.

Standard polychemotherapy regimens include a combination of doxorubicin, cyclophosphamide and 5-fluorouracil or epirubicin, cyclphosphamide, and 5-fluorouracil. Hormonal therapy includes any of the following most commonly prescribed drugs; tamoxifen or raloxifene, anastrozole or letrozole, and goserelin or leuprolide. These drugs are listed in the Medicaid data either as National Drug Codes (NDC) or as Healthcare Common Procedure Coding Systems (HCPCS) J-codes. The Food and Drug Administration requires that drug manufacturers identify and report all drug products using a unique, three-segment number, called the National Drug Code (NDC), which is a universal product identifier for human drugs.[30] The HCPCS is a standardized coding system developed by the Centers for Medicare and Medicaid Services to identify medical

services and procedures furnished by physicians and other health care professionals.[31] We used the Lexicon database[32] to identify all possible NDC and HCPCS J-codes for adjuvant hormonal therapy and adjuvant chemotherapy. This database includes several relational databases of drug names, drug product information, disease names and coding systems (NDC, HCPCS, and others).[32] Drugs can be identified from this database using the drug name, brand description, or active ingredients. Each drug name is associated with a unique drug identifier, which was used to identify the relevant codes. We then, linked the codes identified from Lexicon to NDC and J-codes available in claims records of the Medicaid files. This enabled us to identify all claims for adjuvant hormonal and chemotherapy treatments from the Medicaid claims files.

Confounding variables

The decision to prescribe adjuvant systemic therapy depends on several prognostic variables. In addition to stage of cancer at diagnosis, these include tumor histology, grade (well differentiated, moderately differentiated, poorly differentiated, or anaplastic), and receptor status (positive or negative). The above clinical information was obtained from the cancer registry files and was used to adjust for the effect of these prognostic indicators on the receipt of standard treatment. The presence of comorbid conditions may also influence a physician's decision in prescribing adjuvant systemic therapy for breast cancer. Comorbid conditions were identified from the Medicaid inpatient and other therapy files using ICD-9 codes. Comorbidity was classified by computing the Charlson's comorbidity index;[33] which is a weighted measure of number and severity of comorbid conditions. This index was originally developed in a cohort of

breast cancer patients to assess the effect of comorbidity on breast cancer mortality. Since then, it has been applied widely to several clinical scenarios in medical research.

This study was approved by the Institutional Review Boards of the University of Medicine and Dentistry of New Jersey and the New Jersey Department of Health and Senior Services.

Statistical Analysis

We first compared the distribution of demographic variables (age at diagnosis, marital status) and tumor characteristics (histology, grade, ER and PR status) between whites and blacks. Receipt of standard breast cancer treatment was the dependent variable and race (black vs. white) was the main independent variable. The receipt of standard breast cancer treatment was compared between black and white women using logistic regression models after adjusting for the confounding effects of age, marital status, presence of comorbid conditions, tumor stage, histology, and grade.

We also compared differences between blacks and whites in surgery (BCS or mastectomy versus no surgery) and the type of surgery performed (BCS versus mastectomy). For those with BCS, we examined whether RT was delivered or not. Similarly, for ER and/or PR positive patients, we compared the receipt of hormonal therapy versus no therapy. In this group, we also compared the receipt of hormonal therapy alone versus hormonal therapy plus chemotherapy. For ER and PR negative patients, we compared the receipt of chemotherapy versus no treatment. Multivariate logistic regression models accounting for demographic and clinical confounding variables were constructed for all the above comparisons.

We also performed survival analysis using the Kaplan-Meier method to evaluate if racial/ethnic differences existed in the rates of breast cancer specific and overall survival. Survival time was computed as the difference between date of diagnosis and date of death for decedents or the date of last follow-up for survivors. We constructed Cox proportional hazards models to compare breast cancer specific and overall survival between blacks and whites. Hazard ratios and their 95% confidence intervals were

estimated using these models. Analyses were performed with the use of SAS software, version 9.1.

Results

Table 1 provides the distribution of patient and tumor characteristics between blacks and whites. Blacks were more likely than whites to have characteristics that indicated a poor prognosis. Blacks were younger, never married (single), and were diagnosed more frequently with tumors that had spread to lymph nodes, were receptor negative, and were poorly differentiated or anaplastic.

Overall, only about 60% of patients received the standard initial treatment for their cancers. The vast majority of patients (97%) underwent either BCS or mastectomy. However, only about half of those who underwent BCS received radiation therapy. 59% (n=193) of women with receptor positive tumors received adjuvant hormonal therapy whereas 70% (n=101) of women with receptor negative tumors received adjuvant chemotherapy.

The proportion of black and white patients who received standard initial treatment for early breast cancer is shown in Table 2. There were no differences in the proportion of black and white women receiving surgical treatment (BCS or mastectomy), radiation after BCS, or adjuvant therapy (hormonal and/or polychemotherapy). Results from logistic regression analyses showed no racial/ethnic differences in receipt of standard initial treatment after adjusting for age, marital status, comorbidity, tumor stage, grade, and histology (see Table 3).

A total of 226 deaths occurred in this study population. Of these, 138 women (61%) died as a result of their breast cancer. Cox proportional hazards models showed that breast cancer specific mortality [Hazard ratio (HR) = 1.37; 95% confidence interval (CI) 0.94 – 1.98)] as well as all-cause mortality (HR=1.43; 95% CI 1.08-1.89) were higher

among blacks than whites. Figures 1 and 2 show the adjusted survival curves for breast cancer specific and overall survival respectively.

Discussion

In this population of Medicaid-enrolled patients with breast cancer, we found that only 60% of the women received the standard initial treatment for their breast cancer. This reflects the socioeconomic marginalization of this population. In spite of the overall low rate of receipt of standard treatment, we did not find any differences in its use between blacks and whites. Several studies have shown disparities in breast cancer treatment between blacks and whites.[6-9, 12, 13, 15-18] However, there is also evidence that these disparities are significantly reduced or eliminated when factors such as socioeconomic status and health insurance are taken into account.[6, 11, 34, 35] We studied Medicaid beneficiaries who are relatively homogeneous with respect to socioeconomic status as most enrollees have income levels below the federal poverty line. In addition, Medicaid enrollees are also likely to have similar access to care as they can avail of inpatient and outpatient services through their enrolment in Medicaid. Therefore, by studying this population, we were able to minimize the effect of socioeconomic status and access to care on receipt of standard treatment and survival. Our results indicate that women who with similar medical insurance are likely to be treated equally for their breast cancer. However, this may not necessarily translate to survival benefits between the races.

In our study, blacks as compared to whites were 37% more likely to die of breast cancer and 43% more likely to die of all-causes. The hazard ratio associated with breast cancer specific mortality did not achieve statistical significance. However, examination of the different causes of death revealed that the underlying cause of death for almost 61% (138 of 226) of all deaths was breast cancer. Thus, breast cancer deaths contribute

significantly to the hazard ratio for all-cause mortality which was statistically significant. These findings suggest that the increased risk of death among blacks may be a result of being diagnosed with more aggressive tumors.

Receipt of initial standard treatment for early breast cancer (as defined earlier) includes a combination of surgical, radiation, adjuvant hormonal, and chemotherapy, as appropriate. Of these treatment modalities, extensive research has been done in the area of racial differences in surgical and radiation therapy for early breast cancer.[6, 11-13, 15, 16, 36] However, relatively little population-based information is available on racial differences in adjuvant hormonal and chemotherapy. This is primarily because adjuvant therapy is mostly given in outpatient settings and obtaining this information is difficult. By linking the NJSCR file with the Medicaid file, we were able to supplement the outpatient hormonal and chemotherapy utilization information in the NJSCR file, thus adding to the scant literature on racial differences in adjuvant therapy.

In conclusion, there were no differences in surgical, radiation, adjuvant hormonal, or chemotherapy utilization between black and white women with early breast cancer who were insured with Medicaid. However, in spite of similar treatment, blacks have higher breast cancer and all-cause mortality than whites. Our findings suggest that factors other than treatment differences contribute to the racial disparity in mortality.

Table 1: Description of data available from the New Jersey State Medicaid files

Filename (description)	Variables extracted
Personal summary file (patient-level)	Date of birth Date of death Gender Race/ethnicity County code Zip code Social security number
Inpatient file (claims-level)	Date of admission Primary and secondary diagnoses codes Procedure dates Procedure codes
Drug file (claims-level)	Type of drug Number of days supplied Date of prescription Date filled Quantity of drug National Drug Code (NDC) number
Other therapy file (claims-level) Outpatient and emergency services	Date of service Type of service Primary and secondary diagnoses codes Procedure code Drug codes for injections

Table 2: Descriptive Characteristics of the Study Population

Characteristics	white (n=485)	black (n=237)
Patient Characteristics		
Age in years, n (%)		
< 40	85 (17.5)	52 (21.9)
40-44	84 (17.3)	40 (16.9)
45-49	79 (16.3)	30 (12.7)
50-54	84 (17.3)	33 (13.9)
55-59	70 (14.4)	36 (15.2)
60-64	83 (17.1)	46 (19.4)
Marital status, n (%)		
Single	133 (27.4)	111 (46.8)
Married	173 (35.7)	39 (16.5)
Widowed/Separated/Divorced	158 (32.6)	73 (30.8)
Unknown	21 (4.3)	14 (5.9)
Charlson's Comorbidity Index, n (%)		
0	329 (67.8)	152 (64.1)
1-2	114 (23.5)	59 (24.9)
3 or greater	42 (8.7)	26 (11.0)
Tumor Characteristics		
SEER summary stage, n (%)		
Localized	275 (56.7)	126 (53.2)
Regional spread to lymph nodes alone	210 (43.3)	111 (46.8)
Receptor status, n (%)		
ER* or PR** positive	247 (51.6)	98 (42.2)
ER and PR negative	81 (16.9)	63 (27.2)
ER and PR not done	32 (6.7)	14 (6.0)
ER and PR unknown	119 (24.8)	57 (24.6)
Tumor grade, n (%)		
Well differentiated	45 (9.3)	16 (6.8)
Moderately differentiated	146 (30.1)	61 (25.7)
Poorly differentiated	205 (42.3)	126 (53.2)
Anaplastic	6 (1.2)	6 (2.5)
Unknown/unstaged	83 (17.1)	28 (11.8)
Tumor histology, n (%)		
Infiltrating ductal	391 (80.6)	196 (82.7)
Lobular	34 (7.0)	6 (2.5)
Adenocarcinoma	11 (2.3)	1 (0.4)
Mucinous adenocarcinoma	7 (1.4)	4 (1.7)
Other	42 (8.7)	30 (12.7)

*ER – estrogen receptor, PR – progresterone receptor

Table 3: Standard initial treatment for early breast cancer by race/ethnicity, 1997-2001

Treatment Received, n (%)	**Whites**	**Blacks**
	n=328	n=161
Standard breast cancer treatment*	195 (59.4)	98 (60.9)
Surgery	n=485	n=237
Breast conserving surgery (BCS) or mastectomy	470 (96.9)	229 (96.6)
No surgery	12 (2.5)	7 (3.0)
Other surgery	3 (0.6)	1 (0.4)
Of those with surgery:	n=470	n=229
BCS	230 (48.9)	119 (52.0)
Mastectomy	240 (51.1)	110 (48.0)
Of those with BCS:	n=230	n=119
Radiation	121 (52.6)	61 (51.3)
No radiation	109 (47.4)	57 (47.9)
Adjuvant Therapy		
ER positive or PR positive	n=247	n=98
Hormonal therapy alone	110 (44.5)	47 (48.0)
Hormonal therapy plus chemotherapy	34 (13.8)	12 (12.2)
Chemotherapy alone	53 (21.5)	23 (23.5)
No therapy	50 (20.2)	16 (16.3)
ER negative and PR negative	n=81	n=63
Chemotherapy alone	55 (67.9)	41 (65.1)
Hormonal therapy plus chemotherapy	3 (3.7)	2 (3.2)
Hormonal therapy alone	12 (14.8)	10 (15.9)
No therapy	11 (13.6)	10 (15.9)

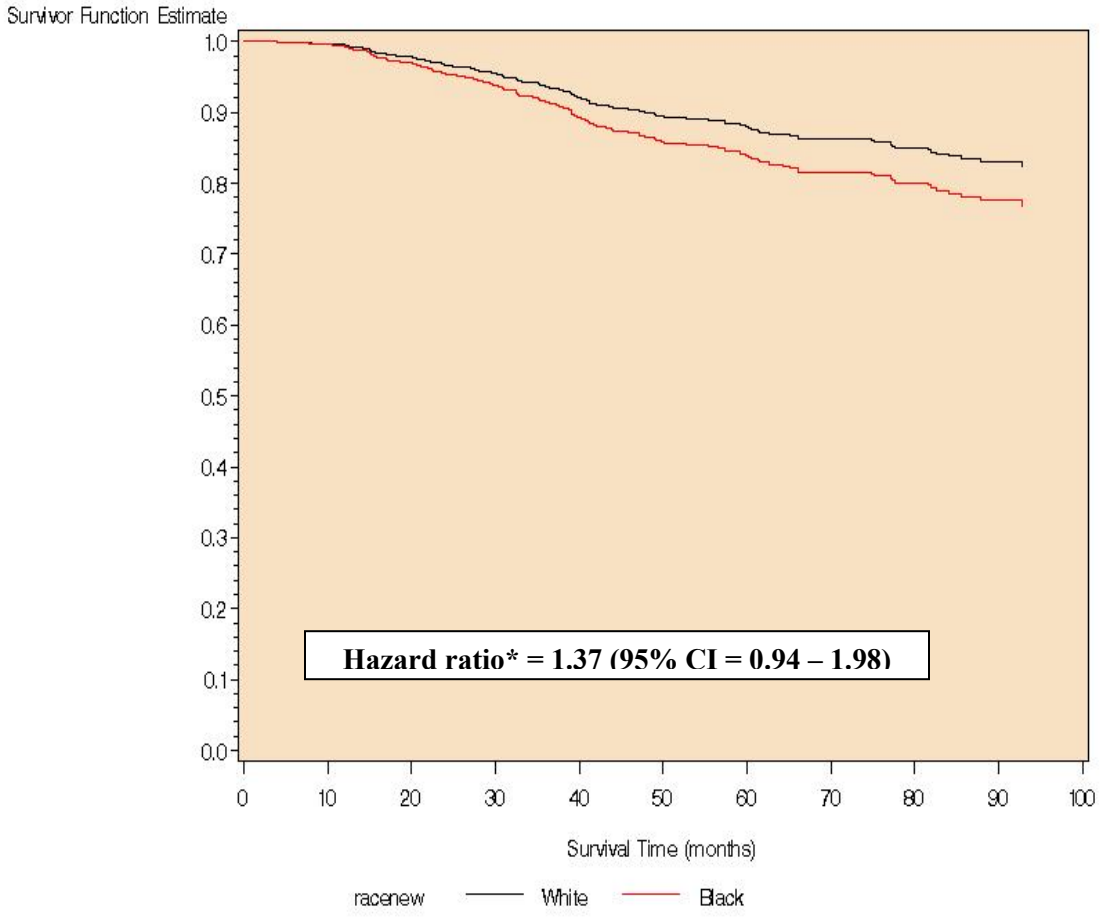
*Standard breast cancer treatment is defined as

Table 4: The odds of standard initial treatment for early breast cancer among blacks as compared to whites.

Treatment Received	**Odds Ratio (95% Confidence Intervals)**	
	Unadjusted	Adjusted
Standard breast cancer treatment	1.09 (0.77, 1.54)	0.95 (0.68, 1.33)
Surgery BCS or mastectomy vs. no surgery	0.83 (0.32, 2.15)	0.70 (0.26, 1.91)
Of those with surgery: BCS vs. mastectomy	1.13 (0.82, 1.55)	1.16 (0.82, 1.65)
Of those with BCS: Radiation vs. no radiation	0.96 (0.62, 1.50)	1.11 (0.69, 1.80)
Adjuvant Therapy ER positive or PR positive Hormonal therapy alone vs. no therapy	1.33 (0.69, 2.58)	1.02 (0.49, 2.10)
Hormonal therapy alone vs. hormonal therapy plus chemotherapy	1.21 (0.58, 2.54)	1.46 (0.61, 3.50)
ER negative and PR negative Chemotherapy alone vs. no therapy	0.82 (0.32, 2.11)	0.62 (0.21, 1.85)

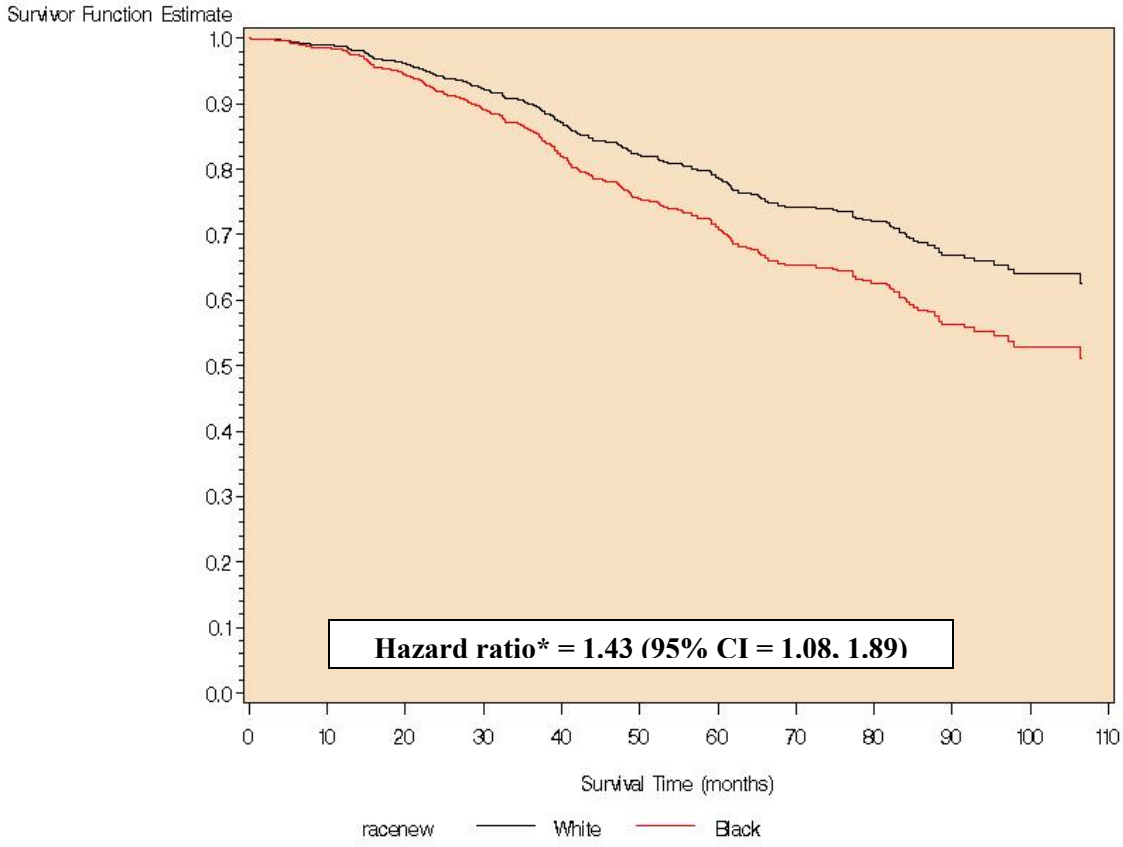
† adjusted for age, marital status, comorbidity, tumor stage, grade and histology
** ER – Estrogen receptor
‡ PR – Progesterone receptor

Figure 1. Breast-cancer specific survival by race, adjusted for age, marital status, stage, histologic type, comorbidity, and receipt of standard treatment for breast cancer.



*Hazard ratio is for blacks as compared to whites

Figure 2. Overall survival by race, adjusted for age, marital status, and comorbidity



*Hazard ratio is for blacks as compared to whites

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ABSTRACT OF MANUSCRIPT 2 OF 3

RACIAL DIFFERENCES IN DELAYS IN TREATMENT OF EARLY BREAST CANCER AMONG MEDICAID BENEFICIARIES

Dissertation Director:

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ABSTRACT

Background: Although white women have higher incidence of breast cancer, black women sustain higher mortality from breast cancer than whites. Delays in initiation of treatment after diagnosis may contribute to the poorer survival among blacks. There is relatively little information on the extent to which racial differences exist in delays in surgical, adjuvant radiation, hormonal, and chemotherapy treatments for early breast cancer.

Methods: We linked the New Jersey Cancer Registry and the Medicaid Research files to obtain diagnostic, prognostic, and treatment information on 237 black and 485 white women 20-64 years of age diagnosed with early stage breast cancer between January 1997 and December 2001. Racial/ethnic groups were compared with respect to delays in initiation of surgical treatment after confirmed diagnosis, in adjuvant radiation therapy after breast conserving surgery, and in adjuvant hormonal and chemotherapy after definitive surgery.

Results: Blacks as compared to whites more often experienced delays of 2 or more months and 3 or more months in initiation of adjuvant chemotherapy after definitive

surgery. Also, delays of 2 or more months in adjuvant radiation therapy after breast conserving surgery were observed more frequently among blacks (76.7%) as compared to whites (63.0%). After controlling for other predictors, compared with white women, black women had 1.9-fold odds (95% confidence interval, 0.92, 3.93) of delay of 3 or more months in adjuvant chemotherapy. No racial differences were observed in delays in initiation of surgical treatment and adjuvant hormonal therapy. In addition, women who experienced delays in radiation and chemotherapy were at higher risk to die from breast cancer than women who did not experience such delays.

Conclusion: The findings of the current study suggest that racial differences exist in adjuvant chemotherapy treatment delays and that breast cancer specific survival is poorer among those with treatment delays. These differences were noted even in a population with similar socioeconomic status and insurance access, suggesting that other patient, physician, and care-process level factors may contribute to the observed differences. More research is needed to identify these factors.

RACIAL DIFFERENCES IN DELAYS IN TREATMENT OF EARLY BREAST CANCER AMONG MEDICAID BENEFICIARIES

Introduction

White women have higher incidences of breast cancer than do black women. However, black women have significantly higher mortality rates due to breast cancer than their white counterparts[1, 2]. This racial difference in the burden of the disease has been attributed to several factors including more advanced stage at diagnosis,[3] socioeconomic status,[4-6] lack of access to care, non optimal treatment,[7-9] or to greater likelihood of being diagnosed with more aggressive tumors.[10-16] The excess death rate among blacks appears to result from differences in access to care and quality of breast cancer treatment rather than biological differences in tumor characteristics or treatment outcomes between the races.[17-20]

Racial differences in delays in the initiation of treatment after definitive diagnosis may contribute to the poorer survival among blacks. A handful of studies have examined such racial inequities in treatment delays for breast cancer.[21-24] Gwyn and colleagues conducted a study in metropolitan Atlanta which showed a 2.3 fold increase in treatment delay ($\geq$ 1 month vs. < 1 month) for blacks compared to whites adjusted for poverty index, insurance status, and marital status. In that study, however, adjuvant hormonal therapy as well as adjuvant radiation after breast conserving surgery was not included in the calculation of treatment delay. Another study conducted at Yale-New Haven Medical Center found that 33% of black women had not started treatment within 30 days of the diagnosis compared with 21% of white women ($p=0.056$). This finding was border line

significant and did not account for confounding factors.[22] A more recent study conducted in an insured population, i.e. Medicare beneficiaries, using the linked SEER-Medicare claims database showed that compared with white women, black women had a 1.64-fold increase odds (95% confidence interval, 1.40-1.91) of treatment delay beyond 1 month.[23] That study also did not include adjuvant hormonal therapy in their definition of treatment delay.

Access to care may contribute to treatment delays and blacks are more likely than whites to be uninsured. Furthermore, a more in-depth examination of racial differences in delays for all possible treatment options for early breast cancer is warranted. We, therefore, conducted a study to examine racial differences in delays in surgical, adjuvant radiation after BCS, adjuvant hormonal, and adjuvant chemotherapy treatment for early stage breast cancer in a similarly insured population, i.e. Medicaid beneficiaries, who were relatively homogeneous with respect to socioeconomic status and access to care as a result of their eligibility into Medicaid.

Methods

Data Sources

We conducted a retrospective cohort study by using data from a linked New Jersey Cancer Registry and New Jersey Medicaid Research file. The New Jersey Cancer Registry database provided information on socio-demographic variables (age, race, marital status) and on characteristics of the tumor (date of diagnosis, histologic type, grade or differentiation, cancer stage, date and type of surgical treatment, dates of initiation of radiation therapy, of adjuvant hormonal therapy, and of adjuvant chemotherapy). Assessment of the accuracy of cancer registry data against other data sources shows that cancer registries have similar quality of information on tumor stage, surgery type, and receipt of radiation. Information on receipt of adjuvant systemic treatment was less accurate from cancer registries.[25]

Encounter data from the New Jersey Medicaid research file was used to supplement information on adjuvant systemic treatment obtained from the cancer registry data. A detailed description of the New Jersey Medicaid claims data files is available in the previous manuscript of this dissertation. In brief, the New Jersey Medicaid database includes all medical encounter claims submitted by providers for the care of Medicaid enrollees.[26, 27] These data are compiled by the Centers for Medicare and Medicaid Services (CMS) which checks the quality and completeness of data received from each state and converts the State Medicaid data to State Medicaid Research Files (SMRF) for the years prior to 1999 or the Medicaid Analytic Extract (MAX) for the years 1999 and later.

The SMRF/MAX has four separate files: (1) the personal summary file, (2) the inpatient file, (3) the other therapy file, and (4) the drug file. Table 1 provides details on the types of information available in each of these files. Each file has a unique identifier for each Medicaid eligible enrollee. This identifier was used to merge these four data files.

Study Participants

Participants in this study were women 20-64 years of age who were diagnosed with early-stage breast cancer (SEER Summary Stage 'localized' and 'regional spread to lymph nodes') between January 1997 and December 2001. This corresponds to the American Joint Commission on Cancer (AJCC) stages I, IIA, IIB or IIIA.[28] We excluded women who were neither white nor black, who were diagnosed with other cancers, and whose breast cancer was not the primary cancer.

Linkage of NJSCR and Medicaid files

Women who met the above criteria were identified from the New Jersey Cancer Registry and linked with the New Jersey Medicaid File for the same years using probabilistic record linkage methodology. This method does not require linkage variables (social security number, date, month, and year of birth, gender, race, zip code of residence) from the two files to match exactly. In order to determine a matched or unmatched pair, each variable contributes some information, i.e., weight. Weights take into account the reliability of the linkage variable and the probability of random agreement of the variable in the two files. The total weight for each linked record was

used to classify records as matched, not matched, or uncertainly matched (clerical pairs) based on whether the statistical probability of a match exceeded a certain threshold.

To accomplish the record linkage duplicate records were first deleted. Linked records that had a higher weight associated with them were accepted as 'matched'. Records that were uncertainly matched were examined manually and evaluated using a set of rules developed by the research team. Records that met these rules were selected as 'matches'. The final linked database included 722 women with early stage breast cancer (485 white and 237 black).

Outcome measures

We examined the following outcomes variables: surgical treatment delay, adjuvant radiation treatment delay, and adjuvant systemic treatment delay. Surgical treatment delay was defined as the time interval from biopsy-proven diagnosis to definitive surgery. Adjuvant radiation treatment delay was defined as the time interval from definitive surgery after diagnosis to adjuvant radiation therapy among those who received breast conserving surgery. Adjuvant hormonal and chemotherapy treatment delay was defined as the time interval from definitive surgery after diagnosis to adjuvant hormonal and/or chemotherapy treatment, as applicable.

Surgical treatment delay was computed by subtracting the date of definitive surgery from the date of diagnosis. For the calculation of adjuvant radiation treatment delay, the date of initiation of adjuvant radiation therapy was subtracted from the date of definitive surgery, while adjuvant systemic treatment delay was calculated as date of the date of initiation of adjuvant hormonal therapy and/or chemotherapy minus the date of

definitive surgery. We categorized treatment delays into less than 1 month, 1-2 months, 2-3 months, 3-6 months, and greater than 6 months except for adjuvant radiation treatment delay, which was categorized into less than 2 months, 2-3 months, 3-6 months, and greater than 6 months because there were very few women who received adjuvant radiation therapy within a month after breast conserving surgery. These definitions of treatment delays also confer with existing treatment guidelines[29] and with other studies.[21-24]

The dates of diagnosis, definitive surgery, and the initiation of radiation therapy were obtained from the NJSCR files. On the other hand, the dates of initiation of chemotherapy and hormonal therapy were ascertained from both the NJSCR file and the Medicaid drug and other therapy encounter records. Standard polychemotherapy regimens include a combination of doxorubicin, cyclophosphamide and 5-fluorouracil or epirubicin, cyclphosphamide, and 5-fluorouracil. Hormonal therapy includes any of the following most commonly prescribed drugs; tamoxifen or raloxifene, anastrozole or letrozole, and goserelin or leuprolide. These drugs are listed in the Medicaid data either as National Drug Codes (NDC) or as Healthcare Common Procedure Coding Systems (HCPCS) J-codes. The Food and Drug Administration requires that drug manufacturers identify and report all drug products using a unique, three-segment number, called the National Drug Code (NDC), which is a universal product identifier for human drugs.[30] The HCPCS is a standardized coding system developed by the Centers for Medicare and Medicaid Services to identify medical services and procedures furnished by physicians and other health care professionals.[31] We used the Lexicon database[32] to identify all possible NDC and HCPCS J-codes for adjuvant hormonal therapy and adjuvant

chemotherapy. This database includes several relational databases of drug names, drug product information, disease names and coding systems (NDC, HCPCS, and others).[32] Drugs can be identified from this database using the drug name, brand description, or active ingredients. Each drug name is associated with a unique drug identifier, which was used to identify the relevant codes. We then, linked the codes identified from Lexicon to NDC and J-codes available in encounter records of the Medicaid files. This enabled us to identify all encounters for adjuvant hormonal and chemotherapy treatments from the Medicaid claims files.

To ascertain the initiation of hormonal or chemotherapy treatments, we used the date of the first encounter filed for these drugs or the date of initiation of these treatments from the NJSCR files, whichever was earlier.

Main predictor variable

Patient's race/ethnicity was the main independent variable of interest. Race and ethnicity information was obtained from the NJSCR files and was categorized into blacks and whites irrespective of Hispanic ethnicity.

Secondary predictor variables

We included patient characteristics (age and marital status at diagnosis) and tumor characteristics (stage of cancer at diagnosis, tumor histology, grade, and receptor status) in our analyses as these factors may be associated with treatment delay and also determine the choice of treatment. Comorbid conditions were identified from the Medicaid inpatient and other therapy files using ICD-9 codes. Comorbidity was classified by computing the Charlson's comorbidity index;[33] which is a weighted measure

of number and severity of comorbid conditions. This index was originally developed and tested in a cohort of breast cancer patients to assess the effect of comorbidity on breast cancer mortality.[33]

This study was approved by the Institutional Review Boards of the University of Medicine and Dentistry of New Jersey and the New Jersey Department of Health and Senior Services.

Statistical Analysis

We first compared the distribution of patient characteristics (age at diagnosis, marital status, comorbidity) and tumor characteristics (histology, grade, ER and PR status) between blacks and whites. We then examined the cumulative percentage of blacks and whites who experienced greater than 1 month, 1-2 months, 2-3 months, 3-6 months, and over 6 months delay in surgical, radiation, and adjuvant hormonal and chemotherapy treatment. We estimated the odds of black women experiencing delays in receipt of treatment compared to whites using logistic regression models. For this analysis, treatment delays were categorized into three cumulative time intervals; ≥ 1 month vs. < 1 month, ≥ 2 months vs. < 2 months, and ≥ 3 months vs. < 3 months.

For treatment delays that were significantly different between blacks and whites, we constructed sequential logistic regression models to evaluate the contribution of each predictor variable. We started with an unadjusted model and then included covariates one at a time. We compared the unadjusted odds of treatment delay for blacks compared to whites with the odds after adding one covariate at a time into the model until a fully adjusted model was constructed. In addition, we conducted survival analysis using the Kaplan-Meier method to evaluate if delays in treatment initiation were related to poorer breast cancer specific survival. Survival time was computed as the difference between the date of diagnosis and date of death for decedents or the date of last follow-up for survivors. All analyses were completed with the use of SAS software, version 9.1.

Results

Table 2 provides the distribution of patient and tumor characteristics between blacks and whites. Blacks were more likely than whites to have characteristics that indicated a poor prognosis. Blacks were younger, never married (single), and were diagnosed more frequently with tumors that had spread to lymph nodes, were receptor negative, and were poorly differentiated or anaplastic.

Most women, irrespective of race, received their surgical treatment within 3 months of diagnosis (Figure 1A). The median treatment delay for both blacks and whites was 7 days. On the other hand only 32% of the women received adjuvant radiation treatment within 2 months of their BCS and even 6 months post BCS, only 71% of the women overall had received radiation. In addition, black women were less likely to be treated with radiation within 2 months of their BCS than their white counterparts [median delay of 3.8 months (blacks) and 3.0 months (whites)]. Figure 2 shows the cumulative percentages of black and white women who experienced delays in adjuvant hormonal and chemotherapy treatments by race. Overall only about 31% of women, regardless of race, received adjuvant hormonal or chemotherapy within a month of definitive surgery. There were no racial differences in adjuvant hormonal therapy delays for any of the time periods studied [median delays of 2.7 months (blacks) and 2.5 months (whites)]. On the other hand, black women were more likely to experience delays of 1 to 3 months in initiation of adjuvant chemotherapy [median delays of 1.5 months (blacks) and 1.3 months (whites)].

Tables 3 and 4 describe differences in treatment delays between black and white breast cancer patients. We did not find any differences between blacks and whites for

surgical treatment delay as well as for adjuvant hormonal treatment delay. However, black women were more likely to experience adjuvant radiation treatment delays of 2 months or more compared to white women [Odds Ratio (OR)=1.93; 95% confidence interval (95% CI)=0.95, 3.90]. Blacks also experienced adjuvant chemotherapy delays of ≥ 2 months (OR=1.73; 95% CI=1.08, 2.78) and ≥ 3 months (OR=1.92; 95% CI=1.01, 3.64) more often than did whites.

We constructed sequential logistic regression models to assess the significance of several potential predictor variables for treatments where bivariate analyses demonstrated that blacks were more likely to have delays than whites. . The results of this analysis are presented in Table 5. None of the potential predictor variables substantially changed the odds for delays in radiation therapy or for delays in adjuvant chemotherapy for blacks compared to whites.

Figures 1 and 2 show Kaplan Meier survival curves to compare breast cancer specific survival among women with and without delays in initiation of radiation treatment after BCS and in initiation of adjuvant chemotherapy after definitive surgery. This analysis showed that women with delays in initiation of these treatments had poorer survival as compared to those without delays. Specifically, women with delay of 2 months or more in initiation of radiation therapy and chemotherapy after definitive surgery were 2-fold and 1.29-fold more likely to die of breast cancer respectively than women who did not experience such delays. However, these hazard ratios were not statistically significant at the 0.05 level.

Discussion

Delays in initiation of treatment after confirmed breast cancer diagnosis may contribute to disparate outcomes among blacks and whites. In this study, we found that blacks were more likely than whites to experience delays of 2 or more and 3 or more months in initiation of adjuvant chemotherapy after definitive surgery. Also, blacks were almost 2 times more likely to have delays in initiation of adjuvant radiation therapy after BCS, although this finding was marginally significant. However, we did not find any racial differences in surgical and adjuvant hormonal therapy delays.

The strength of our study is that we examined racial differences in delays in surgical, adjuvant radiation, hormonal, and chemotherapy separately. Studies examining racial differences in treatment delays for breast cancer have defined treatment as initiation of definitive surgery, neoadjuvant chemotherapy or radiation, or the initiation of chemotherapy or hormonal therapy only for metastatic disease, whichever came first.[22-24] Most women diagnosed with breast cancer are treated surgically first. Therefore, the above definition of treatment initiation is likely to include mostly surgical treatment delays. In addition, to our knowledge, this is the first study to examine racial differences in hormonal treatment delays.

The few studies that have examined racial differences in treatment delays (as defined above) have found that blacks are more likely than whites to have delayed initiation of treatment after definitive diagnosis.[22-24] It was not clear from these studies, however, the treatments that contributed to this racial difference. In our study, we found no racial differences in surgical and adjuvant hormonal therapy delays. On the other hand, blacks were more likely to experience delays in initiation of adjuvant

chemotherapy after definitive surgery as well as in initiation of adjuvant radiation therapy after BCS. This difference may be a reflection of social barriers to care such as availability of transportation and assistance from friends or family to coordinate several outpatient visits that are required for adjuvant chemotherapy and radiation therapy.

There is evidence that racial differences in breast cancer care are significantly reduced or disappear when factors such as socioeconomic status and health insurance are taken into account.[34-37] We studied Medicaid beneficiaries who are relatively homogeneous with respect to socioeconomic status as all enrollees have incomes below the federal poverty line. In addition, Medicaid enrollees are also likely to have similar access to care as they can avail of inpatient and outpatient services through their enrolment in Medicaid. Therefore, by studying this population, we were able to minimize the effect of socioeconomic status and lack of access on the receipt of breast cancer treatment and consequently on delays in treatment initiation. The use of Medicaid encounter data also enabled us to obtain information on adjuvant hormonal and chemotherapy treatments which are frequently administered in outpatient settings.

Several cultural and psychosocial factors may play a role in the increased delays observed among blacks in our study. Although these factors were not measured in this study, there is evidence that factors such as a sense of fatalism, a perception that surgery and medicines are not effective, certain religious and folk beliefs, body image, and social norms may contribute to delays in treatment initiation.[22, 38]

Racial differences in delays in treatment initiation observed in this study are not trivial because delays in treatment initiation in our study were found to be associated with an increased risk of death due to breast cancer. A systematic review of studies has shown

reduced survival among women who experienced delays in diagnosis after presentation of symptoms.[39] Another recent study that examined the impact of radiation delays after lumpectomy on survival also found that delays of 3 months or more were associated with poorer survival.[40] Thus, racial differences in treatment delays observed in this study are likely to contribute to the poorer survival among black women.

In conclusion, this study found that blacks experienced delays in initiation of adjuvant chemotherapy and radiation therapy more often than whites, but the two racial groups were comparable with respect to surgical and adjuvant hormonal therapy delays. This finding is more imperative as we also found that treatment delays were associated with poorer survival in our study. The reasons for such disparities are likely to be complex and pervasive throughout the health care system. More research is needed to fully understand the mechanisms by which patient, physician, and care-process factors lead to racial differences in treatment delays.

Table 1: Description of data available from the New Jersey State Medicaid files

Filename (description)	Variables extracted
Personal summary file (patient-level)	Date of birth Date of death Gender Race/ethnicity County code Zip code Social security number
Inpatient file (claims-level)	Date of admission Primary and secondary diagnoses codes Procedure dates Procedure codes
Drug file (claims-level)	Type of drug Number of days supplied Date of prescription Date filled Quantity of drug National Drug Code (NDC) number
Other therapy file (claims-level) Outpatient and emergency services	Date of service Type of service Primary and secondary diagnoses codes Procedure code Drug codes for injections

Table 2: Descriptive characteristics of the study sample, by race

Characteristics	White (n=485)	Black (n=237)
Patient Characteristics		
Age in years, n (%)		
< 40	85 (17.5)	52 (21.9)
40-44	84 (17.3)	40 (16.9)
45-49	79 (16.3)	30 (12.7)
50-54	84 (17.3)	33 (13.9)
55-59	70 (14.4)	36 (15.2)
60-64	83 (17.1)	46 (19.4)
Marital status, n (%)		
Single	133 (27.4)	111 (46.8)
Married	173 (35.7)	39 (16.5)
Widowed/Separated/Divorced	158 (32.6)	73 (30.8)
Unknown	21 (4.3)	14 (5.9)
Charlson's Comorbidity Index, n (%)		
0	329 (67.8)	152 (64.1)
1-2	114 (23.5)	59 (24.9)
3 or greater	42 (8.7)	26 (11.0)
Tumor Characteristics		
SEER summary stage, n (%)		
Localized	275 (56.7)	126 (53.2)
Regional spread to lymph nodes alone	210 (43.3)	111 (46.8)
Receptor status, n (%)		
ER or PR positive	247 (50.9)	98 (41.3)
ER and PR negative	81 (16.7)	63 (26.6)
ER and PR not done	32 (6.6)	14 (5.9)
ER and/or PR unknown	125 (25.8)	62 (26.2)
Tumor grade, n (%)		
Well differentiated	45 (9.3)	16 (6.8)
Moderately differentiated	146 (30.1)	61 (25.7)
Poorly differentiated	205 (42.3)	126 (53.2)
Anaplastic	6 (1.2)	6 (2.5)
Unknown/unstaged	83 (17.1)	28 (11.8)
Tumor histology, n (%)		
Infiltrating ductal	391 (80.6)	196 (82.7)
Lobular	34 (7.0)	6 (2.5)
Adenocarcinoma	11 (2.3)	1 (0.4)
Mucinous adenocarcinoma	7 (1.4)	4 (1.7)
Other	42 (8.7)	30 (12.7)

Figure 1: Cumulative percentages of black and white women receiving surgical treatment within specified time interval after diagnosis.

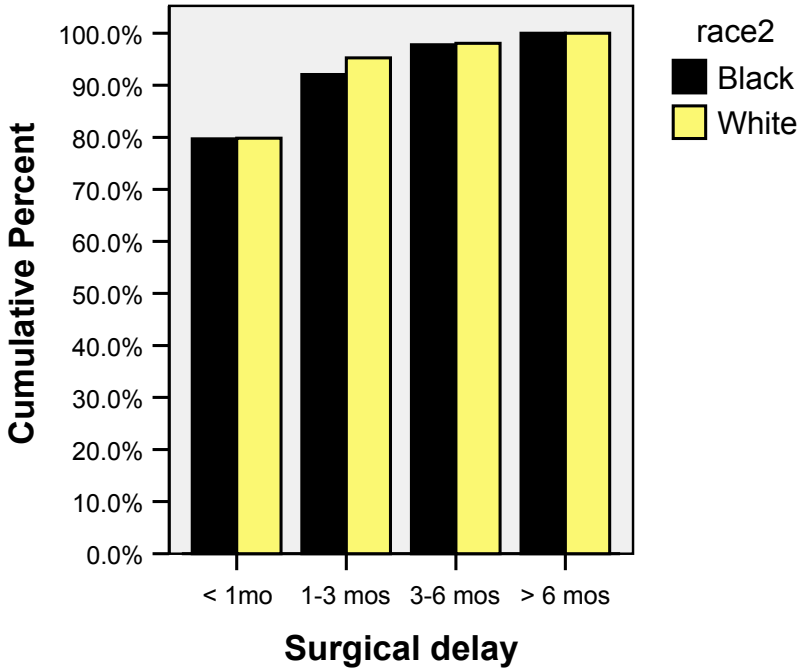


Figure 2: Cumulative percentages of black and white women receiving adjuvant radiation treatment within specified time interval after breast conserving surgery.

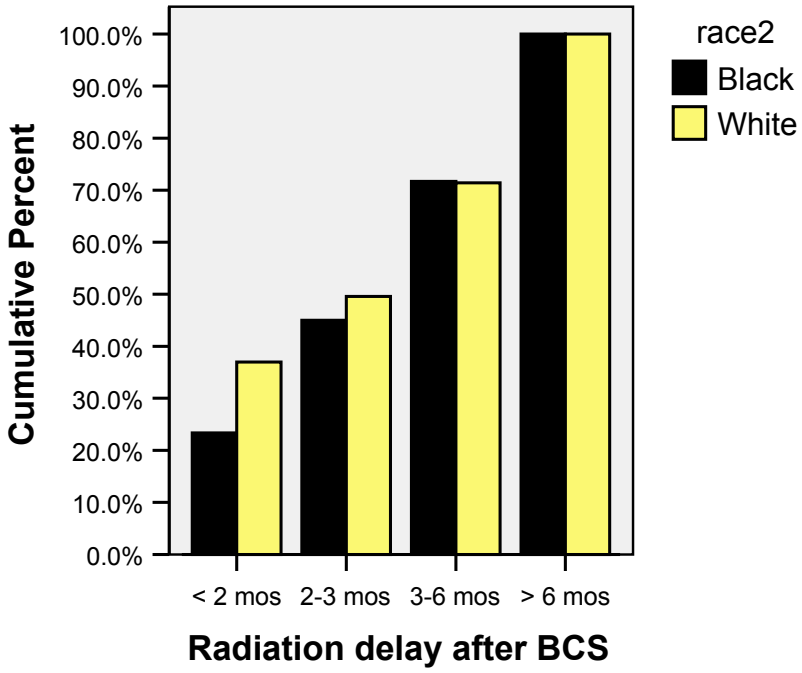
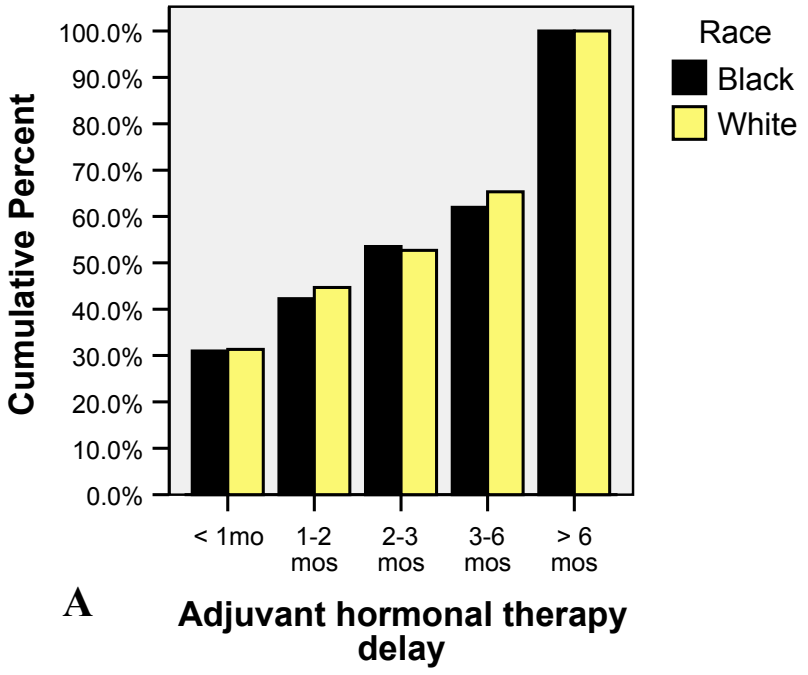


Figure 3: Cumulative percentages of black and white women receiving adjuvant hormonal and chemotherapy treatment within specified time intervals following definitive surgery.



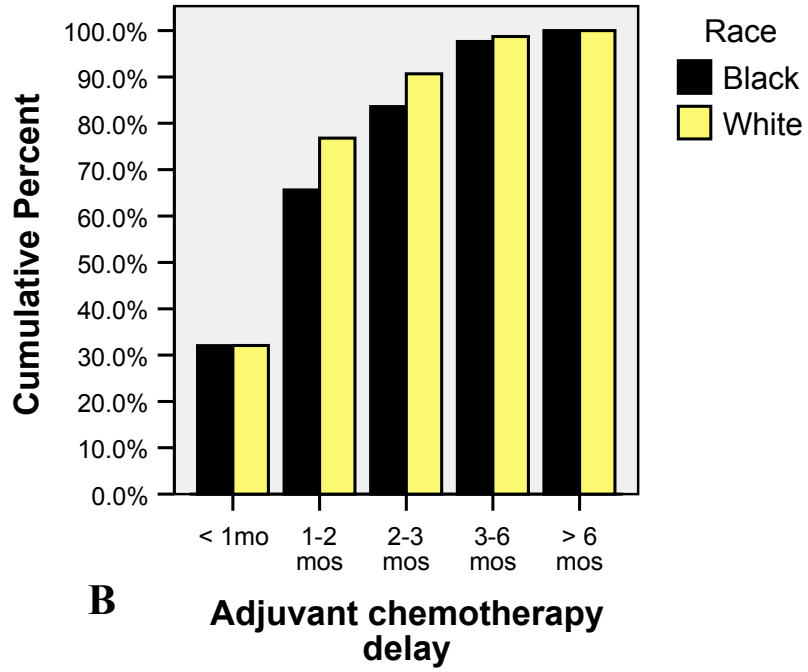


Table 3: Surgical, adjuvant radiation, and adjuvant systemic treatment delays in blacks and whites.

	Blacks	**Whites**
Surgical treatment delay[a] (n=693)		
< 1 month	181 (79.7)	372 (79.8)
≥ 1 month	46 (20.3)	94 (20.2)
Adjuvant radiation treatment delay[b] (n=179)		
< 2 months	14 (23.3)	44 (37.0)
≥ 2 months	46 (76.7)	75 (63.0)
< 3 months	27 (45.0)	59 (49.6)
≥ 3 months	33 (55.0)	60 (50.4)
Adjuvant hormonal treatment delay[c] (n=221)		
< 1 month	22 (31.0)	47 (31.3)
≥ 1 month	49 (69.0)	103 (68.7)
< 2 months	30 (42.2)	67 (44.7)
≥ 2 months	41 (57.8)	83 (55.3)
< 3 months	38 (53.5)	79 (52.7)
≥ 3 months	33 (46.5)	71 (47.3)
Adjuvant chemotherapy delay[d] (n=365)		
< 1 month	41 (32.0)	76 (32.1)
≥ 1 month	87 (68.0)	161 (67.9)
< 2 months	84 (65.6)	182 (76.8)
≥ 2 months	44 (34.4)	55 (23.2)
< 3 months	107 (83.6)	215 (90.7)
≥ 3 months	21 (16.4)	22 (9.3)

Table 4: Differences in surgical, adjuvant radiation, hormonal, and chemotherapy treatment delay for African American women relative to white women

	Odds ratio (95% CI)
Surgical treatment delay[a] (n=693)	
≥ 1 mo vs. < 1 mo	1.01 (0.68, 1.49)
Adjuvant radiation treatment delay[b] (n=179)	
≥ 2 mos vs. < 2 mos	1.93 (0.95, 3.90)
≥ 3 mos vs. < 3 mos	1.20 (0.64. 2.24)
Adjuvant hormonal treatment delay[c] (n=221)	
≥ 1 mo vs. < 1 mo	1.02 (0.55, 1.87)
≥ 2 mos vs. < 2 mos	1.10 (0.62, 1.95)
≥ 3 mos vs. < 3 mos	0.97 (0.55, 1.70)
Adjuvant chemotherapy delay[d] (n=365)	
≥ 1 mo vs. < 1 mo	1.00 (0.63, 1.59)
≥ 2 mos vs. < 2 mos	1.73 (1.08, 2.78)
≥ 3 mos vs. < 3 mos	1.92 (1.01, 3.64)

[a] Surgical treatment delay was defined as the time interval from biopsy-proven diagnosis to definitive surgery

[b] Adjuvant radiation treatment delay was defined as the time interval from definitive surgery after diagnosis to adjuvant radiation therapy among those who received breast conserving surgery

[c] Adjuvant hormonal treatment delay was defined as the time interval from definitive surgery after diagnosis to initiation of adjuvant hormonal therapy

[d] Adjuvant chemotherapy treatment delay was defined as the time interval from definitive surgery after diagnosis to initiation of adjuvant chemotherapy

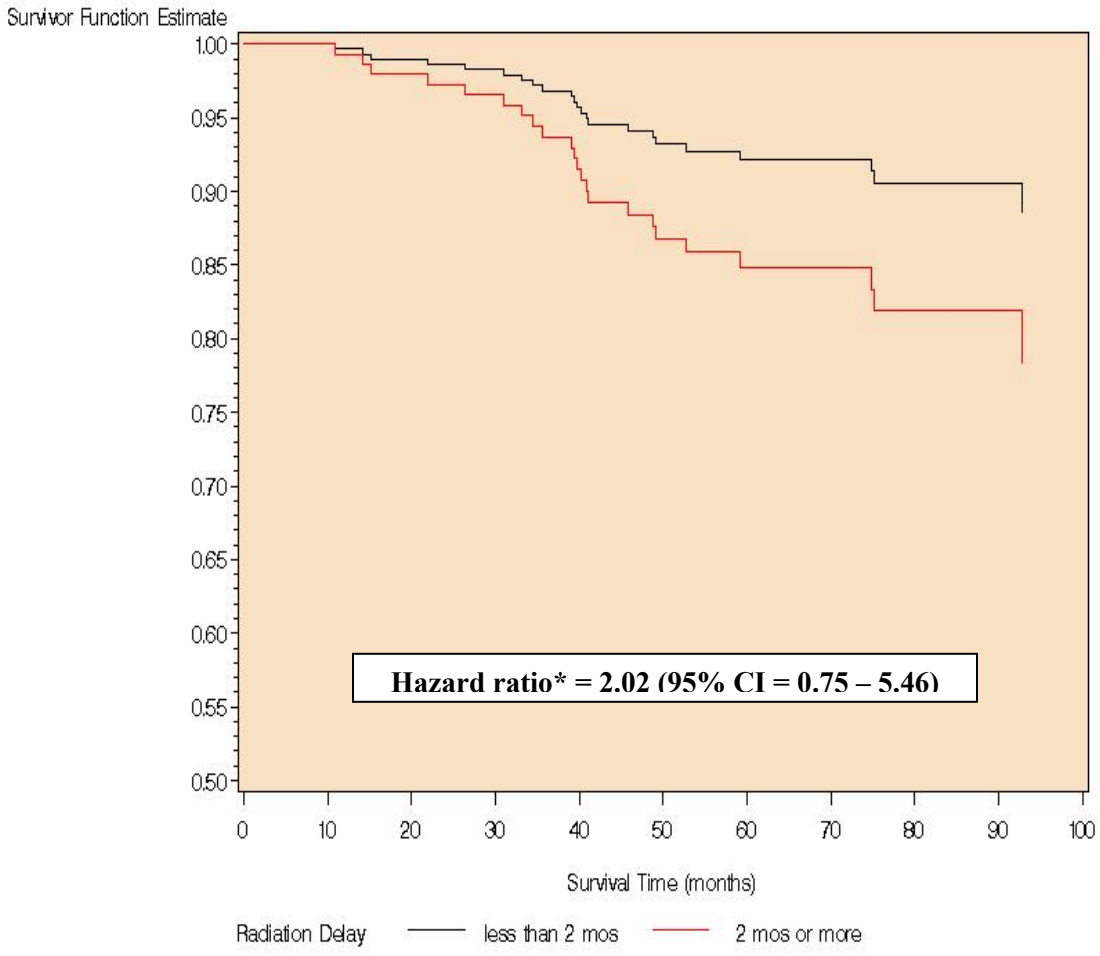
Table 5: Sequential logistic regression models for delays in adjuvant radiation and adjuvant chemotherapy to evaluate the contribution of each predictor variable in the observed differences between blacks and whites

Model	Adjuvant radiation delay†	Adjuvant chemotherapy delay†	
	≥ 2 vs. < 2 mos	≥ 2 vs. < 2 mos	≥ 3 vs. < 3 mos
Unadjusted	1.93 (0.95, 3.90)	1.73 (1.08, 2.78)	1.92 (1.01, 3.64)
Plus age	1.84 (0.89, 3.80)	1.75 (1.08, 2.82)	1.85 (0.96, 3.55)
Plus marital status	1.90 (0.88, 4.12)	1.69 (1.03, 2.77)	2.03 (1.03, 4.00)
Plus cancer stage	2.00 (0.92, 4.37)	1.70 (1.03, 2.79)	2.02 (1.02, 3.99)
Plus tumor grade	1.90 (0.85, 4.22)	1.53 (0.92, 2.54)	1.76 (0.87, 3.55)
Plus histologic type	2.02 (0.89, 4.57)	1.50 (0.90, 2.50)	1.79 (0.88, 3.62)
Plus receptor status	1.92 (0.84, 4.39)	1.49 (0.90, 2.50)	1.91 (0.93, 3.91)
Plus comorbid score*	1.91 (0.83, 4.37)	1.49 (0.89, 2.50)	1.90 (0.92, 3.93)

* Fully adjusted model includes patient's age, marital status, Charlson's comorbidity index, stage of cancer, tumor grade, histologic type, and receptor status.

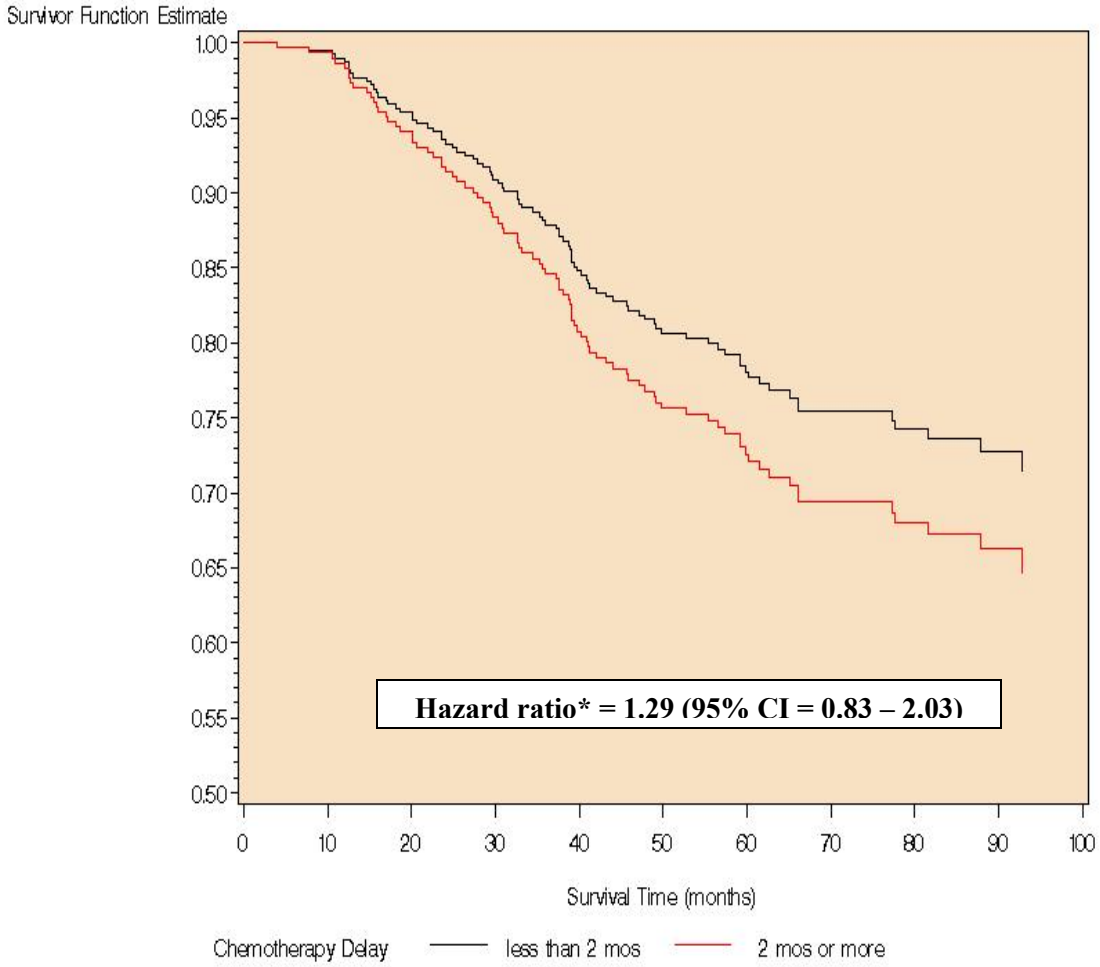
†Numbers presented are odds ratios (95% confidence intervals) for blacks as compared to whites

Figure 4: Kaplan Meier curves of breast cancer specific survival by time interval from breast conserving surgery to initiation of radiation therapy.



*Hazard ratio is for delay in initiation of radiation therapy after BCS of 2 months or more compared to less than 2 months

Figure 5: Kaplan Meier curve of breast cancer specific survival by time interval from initial definitive surgery to adjuvant chemotherapy.



*Hazard ratio is for delay in initiation of adjuvant chemotherapy after initial definitive surgery of 2 months or more compared to less than 2 months

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CONCLUSION

Age and race disparities in breast cancer treatment may contribute to the disparate outcomes observed among the elderly and among racial/ethnic minorities. The aims of this dissertation were to (1) determine the frequency of use of adjuvant systemic treatment for early breast cancer among women 65 years of age and older, (2) examine differences in receipt of standard treatment for early breast cancer between blacks and whites, and (3) examine differences in delays in treatment for early breast cancer between blacks and whites. The findings of this dissertation confirm that the utilization of adjuvant systemic treatment for early breast cancer in the elderly is non-optimal and that racial disparities exist in delays in initiation of adjuvant chemotherapy. These findings are consistent with other research studies. However, we found no racial differences in standard treatment for early breast cancer in a population with similar socioeconomic status and access to care. The challenge now is to move forward and identify the mechanisms by which these disparities occur and identify ways to reduce or even eliminate them from society.

Data obtained from primary care physicians and oncologists of elderly women diagnosed with early stage breast cancer in New Jersey revealed that less than 50% of women with receptor negative tumors received adjuvant chemotherapy alone or in combination with hormonal therapy. In addition, adjuvant therapy was not prescribed to 30% of the elderly women in this study.

Extensive research has been done in the area of racial disparities in breast cancer treatment. However, it is unclear the extent to which socioeconomics status and access to care play a role in the observed racial differences. In this dissertation that studied

Medicaid beneficiaries who are relatively homogeneous with respect to those characteristics, there were no differences between black and white women in receipt of standard treatment for early breast cancer. In addition, blacks and whites had similar breast cancer specific survival. However, overall survival favored whites.

Although no racial differences were observed in receipt of standard treatment, blacks were 73% more likely than whites to experience a delay of 2 months or more and almost 2 times more likely than whites to have a delay of 3 months or more in initiation of adjuvant chemotherapy. Blacks were also 2 times more likely than whites to have delay in initiation of adjuvant radiation after breast conserving, although this result was borderline significant. In conclusion, the frequency of use of adjuvant systemic treatment among elderly women with early breast cancer in New Jersey is low. Although receipt of standard treatment for early breast cancer was similar between black and white New Jersey Medicaid beneficiaries with early breast cancer, blacks experienced delays in initiation of adjuvant radiation and chemotherapy more often than their white counterparts.

The findings of this dissertation have important implications. Because of the rapid growth of the elderly population and the higher mortality due to breast cancer in this age group, breast cancer in the elderly is a major public health problem. Although clinical trials have conclusively demonstrated a substantial survival benefit with the use of adjuvant chemotherapy in middle aged women, comparable data are not available on women older than 70 years of age as older women are frequently underrepresented in clinical trials. Therefore, decisions to prescribe adjuvant chemotherapy in the elderly are made by clinicians on a case-by-case basis. There is evidence that elderly women are

less likely to receive efficacious treatment because of concerns of poor tolerability and toxicity. However, women older than 65 years of age who have few concomitant illnesses may be able to tolerate chemotherapy as well as younger women. Efforts to reduce this age bias and to increase the frequency of use of adjuvant systemic therapy may help to reduce the occurrence of poor outcomes among these women. In addition, efforts to include older women in clinical trials of cancer drugs may help to generate clinical guidelines that can help oncologists treat their older patients more appropriately.

In addition to the elderly, racial/ethnic minorities also suffer disproportionately from breast cancer. Although several studies have shown that minorities receive breast cancer treatment less often than do whites, there is evidence to suggest that differences in treatment and survival may be more attributable to socioeconomic status and access to care rather than to race. Aim 2 of this dissertation demonstrated that racial differences in standard treatment for breast cancer and breast cancer specific survival are not evident when socioeconomic status and health care access factors are similar. This implies that people with similar access to care and similar social status are likely to receive similar treatment.

Although there were no differences in receipt of standard treatment for early breast cancer between blacks and whites, another mechanism by which racial disparity may exist in treatment utilization is through timeliness of providing appropriate therapy. Aim 3 of this dissertation showed that blacks were more likely to experience delays in initiation of adjuvant chemotherapy and to a lesser extent, adjuvant radiation therapy. This suggests that even in settings where socioeconomic status and access to care are similar, treatment delays among blacks may contribute to their poorer outcomes from

breast cancer. Identifying the reasons for this difference requires a more in-depth look at the role of several patient, physician, and care-process level factors involved in the complex management of patients with breast cancer. The Institute of Medicine calls for a robust research agenda to better understand how the process and structure of care may vary by race. Such research must consider the range of influences on patients' and providers' attitudes and expectations in the clinical encounter, clinical decision making employed by providers and the influence of patient race in these processes, the nature and quality of communication between patients and providers, and the environments and settings in which care is delivered.

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APPENDIX

APPENDIX I

LINKAGE OF THE NEW JERSEY CANCER REGISTRY AND MEDICAID FILES

Data for manuscripts 2 and 3 of this dissertation were compiled by linking the New Jersey State Cancer Registry (NJSCR) files with the New Jersey Medicaid files for the years 1997 through 2001. We utilized a stepwise probabilistic strategy to link the NJSCR and Medicaid data files. The record linkage was performed using a program called Automatch. This program performs a probabilistic record linkage by identifying a match between records based on a formal statistical model.[1] The advantage of probabilistic record linkage is that it uses all available identifiers to establish a match (e.g., gender, date of birth, social security number, race, address, phone number) and does not require identifiers to match exactly. This method uses the concept of 'blocking' to efficiently compare large number of records. Blocking variables define the set of records that are examined for matches. If the set is too large, then the matching program has to perform many comparisons, since every record in the set on file A is compared to every record in the set in file B. Therefore, blocks should be as small as possible. For instance, variables with the most number of values and highest reliability are the best blocking variables. Social security number, month, day, and year of birth are examples of good blocking variables. Once blocks are selected, comparisons are made between all record pairs in the block. In order to determine a matched or unmatched pair, each variable contributes some information, i.e., weight. Weights take into account two properties of the variables; the reliability of the variable (m-probability) and the probability of a random agreement of the variable (u-probability). Each identifier is assigned a weight

and the total weighted comparison yields a score, which is used to classify records as matched, not matched, or uncertainly matched (clerical pairs) based on whether the statistical probability of a match exceeds a certain threshold.

The record linkage was accomplished in consultation and assistance from Ms. Pamela Agovino at the New Jersey Department of Health and Senior Services. The process was conducted in 3 stages.

1. Prepare the source data files

   a. <u>The NJSCR file</u>

      A NJSCR subset of data was created using the following criteria:

      Behavior = 3 (invasive cases)

      Race = 1 or 2 (white and black)

      Sequence = '00' or '01' (primary cancers only)

      Sex = 2 (female)

      Date of diagnosis = 1997 – 2001

      Age at diagnosis = 20 – 64 years

      Cancer site = C500-C509 (breast)

      Stage of the cancer was not used as a restricting criterion. This was done to provide flexibility with choosing one of several stage variables available in the NJSCR data while selecting the cases for the final analyses. After applying the above criteria, the NJSCR subset included 19,583 records.

   b. <u>The Medicaid file</u>

      The New Jersey Medicaid data has 4 files. These files are: (1) the personal summary file, (2) the inpatient file, (3) the other therapy file, and (4) the

drug file. The personal summary file includes person-level demographic and eligibility information. This was the file primarily used to accomplish the linkage. A dataset with the following variables from the personal summary file was created; a unique identification number used to identify a Medicaid eligible in the Medicaid statistical information system (MSIS ID), subjects' social security number, race, date of birth, gender, and zip code. The personal summary file for the years 1997 through 2001 included 1,391,774 beneficiaries.

In addition, we identified records of female patients with a diagnosis of breast cancer (ICD9 codes 174-174.9) were identified from the Medicaid inpatient file and an indicator variable 'bc' with a value of 1 for those with breast cancer and 0 for those without a diagnosis of breast cancer was created. In the NJSCR file, all patients had a value of 1 for this variable as they all had breast cancer.

2. Define and execute the matching algorithm

The following strategy was used to write the matching algorithm in Automatch.

Pass 1: Block (indicates exact match) on social security number and year of birth. Match on month of birth, day of birth, and sex.

Pass 2: Block on social security number. Match on month of birth, day of birth, year of birth, sex, race, and zip code.

Pass 3: Block on date of birth (month, day, and year). Match on social security number, sex, race, zip code, indicator variable for breast cancer.

The Automatch program to run the above matching algorithm is provided below.

```
program MATCH
dicta MEDdic (defines the Medicaid data dictionary)
dictb RMdic (defines the NJSCR data dictionary)
```

```
block1 CHAR  SSN SSN
block1 char YR_OB YR_OB
MATCH1 CHAR MN_OB MN_OB .95 (m-prob) .0769 (u-prob)
MATCH1 CHAR SEX SEX     .95 .5
match1 CHAR DAY_OB DAY_OB  .95  0.0312
match1 char bc bc .95 .5

BLOCK2 CHAR SSN SSN
MATCH2 CHAR   MN_OB MN_OB    .95 .0769
MATCH2 CHAR  DAY_OB DAY_OB    .95 .0312
MATCH2 char YR_OB YR_OB  .95  .0001
MATCH2 CHAR SEX SEX  .95 .5
MATCH2 CHAR RACE RACE .95 .1667
match2 char zip zip .95 .05

BLOCK3 CHAR  YR_OB YR_OB
BLOCK3 CHAR MN_OB MN_OB
BLOCK3 CHAR  DAY_OB DAY_OB
MATCH3 UNCERT SSN SSN  .95 .0001  700
MATCH3 CHAR RACE RACE .95 .1667
match3 char bc bc .95 .5
match3 char sex sex .95 .5
match3 char zip zip .95 .0001

CUTOFF1    5 -10 (refers to cutoff weights to declare a match or a clerical review respectively)
CUTOFF2    2 -10
CUTOFF3    18 11
```

Several iterations of the above matching program were run to determine the appropriate m- and u-probabilities for each identifying variable. In addition, histograms of the weights were examined to determine the most efficient cutoff values to declare a match, clerical review, or no match.

The results from the 3 passes are summarized below.

Pass 1:

```
*********************************************************************
 *  OUTPUT STATISTICS FOR MATCH: bredis
 *  PASS: 1
 *
 *  1391774  Records on file A (Medicaid)
 *    19583  Records on file B (NJSCR)
```

```
 *  1391774  A records read
 *    19583  B records read
 *     1258  Blocks processed
*      1222  Matched pairs
 *      351  EXACT matched pairs
 *       36  Clerical pairs
 *        0  A duplicates
 *        0  EXACT A duplicates
 *        1  B duplicates
 *        0  EXACT B duplicates
 *  1390516  A residuals (including SKIPS & MISSING)
 *    18324  B residuals (including SKIPS & MISSING)
*****************************************************************
```

Pass 2:

```
*****************************************************************
 *
 *  OUTPUT STATISTICS FOR MATCH: bredis
 *  PASS: 2
 *
 *  1391774  Records on file A
 *    19583  Records on file B
 *  1390516  A residuals from previous pass
 *    18324  B residuals from previous pass
 *  1390516  A records read
 *    18324  B records read
 *       66  Blocks processed
*       17  Matched pairs
 *        0  EXACT matched pairs
 *       19  Clerical pairs
 *        0  A duplicates
 *        0  EXACT A duplicates
 *        0  B duplicates
 *        0  EXACT B duplicates
 *  1390480  A residuals (including SKIPS & MISSING)
 *    18288  B residuals (including SKIPS & MISSING)
 *
 *****************************************************************
```

Pass 3:

```
*****************************************************************
 *
 *  OUTPUT STATISTICS FOR MATCH: bredis
 *  PASS: 3
 *
```

```
 *  1391774  Records on file A
 *    19583  Records on file B
 *  1390480  A residuals from previous pass
 *    18288  B residuals from previous pass
 *  1390480  A records read
 *    18288  B records read
 *     9466  Blocks processed
*       23  Matched pairs
 *        0  EXACT matched pairs
 *       93  Clerical pairs
 *        2  A duplicates
 *        0  EXACT A duplicates
 *        2  B duplicates
 *        0  EXACT B duplicates
 *  1390362  A residuals (including SKIPS & MISSING)
 *    18170  B residuals (including SKIPS & MISSING)
****************************************************************
```

All records that matched from each of the three passes were included. Clerical pairs were manually reviewed and decisions were made based on the following rules developed in consultation with Dr. Kitaw Demissie.

Table 1: Decision rules for clerical pairs from Pass 2 of record linkage

Pass 2: Block on SSN, match on month, day, year of birth, race, sex, and zip code

Accept if weight ≥ 2

If exact match on	Weight	Match
2 of 4 matching variables and SSN differs by 1 digit or SSN is missing (999999999)	> 14.4	Yes (match if race is missing (99) or hispanic (05) in Medicaid data)*
All variables and SSN differs by 2 digits	> 13	Yes

* most Hispanics report as white

Table 2: Decision rules for clerical pairs from Pass 3 of record linkage

Pass 3: Block on date of birth, match on SSN, race, sex, zip code, and indicator variable for breast cancer

Accept match if weight ≥ 18

Do not accept match if weight is 11.73 as this weight referred to a potential match on all identifying variables, but with completely different SSN.

If exact match on	Weight	Match
2 of 4 matching variables and SSN differs by 1 digit or if SSN is missing (999999999)	> 14.4	Yes (match if race is missing (99) or hispanic (05) in Medicaid data)*
All variables and SSN differs by 2 digits	> 13	Yes

* most Hispanics report as white

This probabilistic record linkage procedure yielded 1,416 records that matched from the NJSCR and New Jersey Medicaid files.

3. Creating the linked data file

   The NJSCR unique identification number from the linked records was used to reconstruct the cancer registry data. On the other hand, the Medicaid unique identification number (MSIS ID) was used to merge the inpatient, drug, and other files. Thus, a linked dataset with information on each matched patient was available from the NJSCR as well as the Medicaid claims data.

Determining the success of the matching

The success of the matching algorithm that was employed to link the NJSCR and Medicaid data files depends on what percentage of Medicaid beneficiaries who were known to have been diagnosed with breast cancer were linked with the NJSCR records. In order to do this, all Medicaid enrollees who had a claim for a diagnosis of primary breast cancer (ICD-9 codes 174.-174.9) were identified from the inpatient file (n=1346

individual cases). The probabilistic record linkage procedure included all of the above 1346 individuals.

The Medicaid claims data also has diagnosis codes in the other therapy files which include outpatient claims. 3,125 individual cases of breast cancer were identified from this file. However, it is likely that many of these cases were not diagnosed during the study period. On the other hand, the inpatient claims that have a primary diagnosis of breast cancer are more likely directly related to management of newly diagnosed cancer. We, therefore, decided to use claims from the inpatient file to assess the success rate of our matching.

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PUBLICATIONS

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