RACIAL DISPARITIES IN EARLY STAGE BREAST CANCER TREATMENT

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ABSTRACT OF THE DISSERTATION

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by

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Introduction: Appropriate treatment disparity and delay in receipt of treatment are possible reasons that contribute to shorter survival in African-American (AA) breast cancer patients compared to their White counterparts.

Specific Aims: In early stage breast cancer: 1) determine if racial differences exist in treatment, 2) examine racial disparity of delays in diagnosis and treatment initiation and explore factors that predicted delay in the overall population and by race, 3) examine factors that influenced the choice between mastectomy and breast-conserving surgery (BCS) and whether these factors differed by race.

Methods: Newly diagnosed invasive breast cancer patients during 2005-2010 were identified in seven eastern New Jersey counties through rapid case ascertainment. For each AA woman 18-85 years of age, a white woman was randomly selected (± 5 years of age and from same county). Two data collection methods took place: medical chart review (Aims 1 & 2) and semi-structured interviews (Aim 3). Multivariable binomial and linear regression models were conducted to explore associations between race and outcomes (receipt of standard treatment; diagnosis and treatment delay).

Results: In Aim 1, AAs tended not to receive optimal treatment compared to whites (RR: 1.60; 95% CI: .94, 2.71). Aim 2 demonstrated that AA women experienced longer time to diagnosis and surgical treatment. The geometric mean (95% CI) for whites and AAs in time to diagnosis was 35 (31, 40) and 47 (41, 54); time to surgery was 28 (26, 30) and 33 (30, 35) respectively. Aim 3 demonstrated that health issues that interfered with physical/social activities influenced AAs to receive mastectomy compared to BCS (RR: 1.68; 95% CI: 1.01, 2.77).

Conclusion: We observed racial differences in receipt of optimal treatment (after controlling clinical factors) and took longer time to diagnosis and treatment for early stage breast cancer among AAs compared to white women. These differences could contribute to the observed poor survival in AAs with breast cancer. Also AAs listed previous health issues as an influencing factor in the surgical treatment they received. The findings suggest that interventions are needed to eliminate barriers that contribute to the observed disparity and to help narrow the racial gap in survival rates.

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INTRODUCTION

Breast cancer is one of the most frequently diagnosed cancers in women and is expected to account for 29% of new cancer cases in the US in 2012.[1] Incidence rates for breast cancer has remained relatively stable from 2005 to 2008 after decreasing 2% per year from 1999 to 2005.[1] The 5-year survival for invasive breast cancer increased from 75% during 1975-1977 to 90% in 2002 to 2008.[2]

The improvements in the 5-year survival rates are seen in both Whites and AAs, but the gap in survival rates between the two races has not been shrinking since the early 1980's. The incidence among white women during the period of 2004 to 2008 was 122.3 per 100,000 while the incidence among AA women during the same period was 116.1 per 100,000.[1] Yet, when mortality figures (during the period 2004 to 2008) are compared between the two races, AAs have higher mortality rate 32.0 per 100,000 than white women who experienced a mortality rate of 22.8 per 100.[2] During the period 2002-2008, the 5-year survival rate was higher for White women (91.7%) than for AA women (78.0%).[2]

The National Cancer Institute (NCI) defines "cancer health disparities" as adverse differences in cancer incidence, prevalence, mortality, survivorship, and burden of cancer or related health conditions that exist among specific population groups in the United States.[3] Reasons for the racial disparities are myriad and yet none on its own can fully explain why there is such a drastic difference between the two races.[4] Possible predictors include biologic differences in the nature of the tumor, screening and access to healthcare, socioeconomic factors, and disparity in treatment.

Treatment

One of the reasons for higher mortality among AAs could be due to differences in receipt of cancer treatments. Studies on treatment outcomes where all patients have equal access to treatment documented that similar treatments yield similar outcomes.[5,6] Although the use of treatments seems to be improving overall[7,8], minority women are less likely to receive the appropriate treatments.[9,10] The National Comprehensive Cancer Network (NCCN) outlines detailed recommendations for treatment (local and systemic therapy) of early stage breast cancer based on tumor histology, tumor size, tumor grade, axillary node status, tumor hormone receptor status, human epidermal growth factor receptor 2 (HER2), comorbid conditions, and patient age.[11] Local treatment includes surgery, radiation therapy or both. Systemic therapy contains chemotherapy, hormone therapy, biologic therapy or combinations of the three.[11]

BCS plus radiation. The cumulative incidence of a recurrence in the ipsilateral breast 20 years after surgery was 14.3 percent among the women who underwent irradiation after lumpectomy and 39.2 percent among those who underwent lumpectomy without irradiation ($p < 0.001$).[12] However, multiple studies have reported that AA women who underwent BCS were less likely than white women to receive radiation therapy.[13-16] Elderly AAs have in particular been shown to be at risk of having radiation omitted.[13,17] A study done on Medicare beneficiaries found that AAs more often than whites did not receive radiation, even after accounting socioeconomic status.[13]

Adjuvant Hormonal & Adjuvant Chemotherapy. Recently, large clinical trials have established that dose reductions, delays, or interruptions of chemotherapy for breast cancer can reduce its benefit.[9,18-20] Studies suggest that chemotherapy use and intensity may differ by race.[9,21-23]

In some studies, AA women are offered chemotherapy at similar rates as White women but were more likely to have up-front dose reductions of chemotherapy and to receive lower dose intensity once treatment had started.[21,24] Omission of chemotherapy and dose modifications may explain some of the within-stage survival differences noted between white and AA women with breast cancer. [25-27]

Hassett *et al.*[28] suggest that practice patterns in the delivery of adjuvant chemotherapy that may contribute to disparities in breast cancer survival rates include not providing adjuvant chemotherapy when it is indicated and the delivery of nonstandard chemotherapy regimens or doses.[29] A study on women treated at six New York City hospitals for breast cancer, found that compared to whites, 33% of the AAs did not receive chemotherapy and 29% did not receive hormonal therapy.[10]

On the other hand, Muss *et al.* found no significant differences between AA and White women in the recommended or actual administration of chemotherapy or hormonal therapy in three metropolitan areas.[30] Elledge *et al.* found that among patients with node-positive or locally advanced disease, rates of systemic chemotherapy or hormonal therapy were higher for AA women (81 percent) than for White women (74 percent).[31]

Documenting receipt of systemic therapy can be difficult. Administrative databases and cancer registries do not usually capture detailed information on chemotherapy drugs, doses, or time to completion of treatment, and collecting such information from medical records is labor intensive and challenging.[8]

Treatment Delay

Delay in diagnosis and initiation of treatment are among the reasons considered for widening gap in survival rates for breast cancer between AA women and white

women.   A meta-analysis by Richards *et al.*[32] found that prolonged time of greater than 3 months from symptom recognition to initial treatment (surgery or neo-adjuvant chemotherapy) is associated with lower survival rates.

Delay from abnormal symptoms to diagnostic follow-up.   The National Health Interview Survey (NHIS) data collected from 2000 puts use of mammography at 68% for AAs and 71% for white women in the United States.[33]

Yet, Caplan *et al.* reported that white women had shorter diagnostic intervals (time from abnormal symptom recognition by CBE or mammogram to date of pathologic diagnosis of cancer) than women of other racial or ethnic groups.[34] AA women with prior breast abnormalities or high levels of cancer anxiety were less likely to complete recommended diagnostic tests in a timely fashion.[35] Elmore *et al.* found that the median time to reach a final pathologic diagnosis was 74 days for AA women and 59 days for white women.[36] AA women were more likely than white women to have an incomplete diagnostic evaluation within 30 days (84% versus 60%; $P < 0.01$).[36] These differences may be explained by barriers that prevent patients to reach the medical system for care initially and may continue to promote further delays in care.[36]

One of the barriers that prolong time to diagnostic follow-up is lack of insurance. Uninsured women and women who rely on public assistance to finance their medical care appear to have greater barriers to accessing care for non-emergent problems.[37,38] AAs are more likely to either have Medicaid or have no insurance.[39] Yet, studies have found that AAs have longer time to have a medical consult after abnormal symptom recognition compared to whites even after socioeconomic status was accounted.[38,40] Other factors that could explain longer delays found in AAs include poor patient–provider

communication[41-43]; logistical barriers to access of care[41,44,45]; and negative

mammography experiences[44].

<u>Delay from surgery to adjuvant radiation or chemotherapy</u>. NCCN treatment

guidelines recommend irradiation after mastectomy for women with positive axillary

lymph node dissection[47] and for those who have received BCS[12].   A systematic review of

studies on radiation initiation found breast cancer patients who received radiation more

than eight weeks after surgery were more likely to have increased local recurrence rates.[48]

The few studies that have considered racial differences in radiation delay have

only studied patients older than 65 years of age.[49-52] Hershman *et al.* reported that while

58% of the white patients received radiation less than one month after surgery, only 49%

of the AAs started radiation during the same interval time.[49] But the likelihood of being

delayed longer than 3 months was similar between both races.[49] Gold *et al.* found that

among women with stage 1 breast cancer, AA women were more likely to delay receipt

of radiation therapy by greater than 8 weeks compared to white women after surgery

(OR=1.56; 95% CI 1.17, 2.08).[50]

The National Quality Forum endorsed the start of chemotherapy within 120 days

from diagnosis of breast cancer based on data reporting survival and chemotherapy

initiation.[53-57] The association of chemotherapy delay and race is not well studied. Two

studies have looked at race and delay in receiving chemotherapy but the results are

inconsistent.   A national cohort study on women diagnosed with invasive breast cancer

(stages 1 to 3) report AAs are more likely to delay starting chemotherapy greater than 90

days compared to white women (RR: 1.56; 95% CI: 1.44, 1.69).[58] On the other hand, a

study based on SEER Medicare found no significant racial differences in chemotherapy delay.[53]

AA women have white blood cell (WBC) counts and absolute neutrophile count (ANC) that are on average 25%–40% lower than those of women of European-American ancestry.[59] Therefore, the lower WBC or ANC count would prevent physicians from treating AA women for the prescribed treatment schedule and at the full dose intensity, perhaps contributing to the observed racial disparities in survival between these groups of patients.[22] AA women who have lower ANCs than white women may have larger declines in their WBC counts to below conventionally defined treatment thresholds, hence, leading to reduced doses of chemotherapy regimens or treatment delays.[22]

Therefore, to provide women the best opportunity for survival from breast cancer, it is important to minimize any delays in the diagnosis and treatment of breast cancer.[60] Caplan *et al.*[60] found that more AA women than White women attributed diagnostic delays due to difficulties in scheduling appointments rather than to physician inaction. This seems to indicate that AA women have poorer access to care than white women, making it more difficult to set-up appointments.[60] Gorin *et al.* compared treatment in Medicare enrollees and found that AAs had significantly increased diagnosis and treatment delays by comparison to all other female enrollees.[61] For patients who have medical insurance, system inefficiencies, such as busy clinics, have been implicated in delay differences by ethnic/racial groups.[35,62,63] Other potential sources of delay in diagnosis and treatment include fear, hopelessness,[64] cultural beliefs, or mistrust in the health care system, out-of-pocket costs, and age.[13,36]

Choice of Surgery

An important decision for a patient in the treatment of early breast cancer is choice of the type of surgery: breast conserving surgery (BCS) or mastectomy. BCS followed by radiation has been shown to have similar survival benefits as mastectomy.[12]

Factors influencing choice of surgery. BCS has been characterized by variation in level of use by factors such as race, socioeconomic status, and geographic residence. Prior studies have reported AAs are less likely to receive BCS.[65,66] But recent studies show that there are no racial differences in receipt of BCS or mastectomy.[67-69] Greater use of BCS has been found in more urban areas compared with rural areas,[65,70] in patients residing in the northeastern United States compared with those residing in central and southern states[65,71] and among women of higher socioeconomic status compared with women of lower socioeconomic status.[72]

Barriers like travel distance to a radiation treatment facility may influence the receipt of postoperative breast irradiation and as a result choice of surgery. Radiation therapy that follows BCS typically involves daily treatments (weekends excluded), for a period of 5–6 consecutive weeks.[73] Increased use of BCS is associated with urban residence and with treatment in a hospital with radiotherapy facility.[65,74] Women residing at an increased distance from a hospital with a radiotherapy facility had a decreased likelihood of undergoing BCS.[75] The lower probability of undergoing BCS was statistically significant for women residing 15 miles or more from the nearest hospital with a radiotherapy facility. Celaya *et al.*[76] also found similar results and gave possible reasons for decreased use of radiation therapy to include women's perceived access to care[75], regional practice patterns[73], access to transportation[77], and socioeconomic status[78].

There have been conflicting results with respect to use of BCS by age, with some investigators finding greater use among older women,[79] and others finding greater use among younger women.[80-83] Hiotis *et al*[84] reported decrease utilization of BCS with increased age.[85] A possible explanation is a perceived decrease in the value of breast preservation as women age, either in the eyes of the patient or the physician. Similarly, among women offered a choice of surgery, older women were significantly more likely to choose mastectomy in one study.[86]

Rationale

AA breast cancer patients have shorter survival compared to their white counterparts. The shorter survival among AAs could be due to lack of receiving standard guideline recommended treatments, as well as, delay in receiving appropriate diagnosis and treatment. In the face of similar treatment benefits between AAs and whites, there is some evidence suggesting that AAs are less likely than whites to receive standard treatment.

However, definitive data on this and the reasons for the racial disparity in the treatment of breast cancer are lacking. Studies of racial disparity in breast cancer treatment are more consistent with receipt of adjuvant radiation therapy after breast conservation surgery[17], but there is little population-based information available on racial disparities on the use of adjuvant systemic treatment for breast cancer. The limited data on receipt of systemic treatments are due to the nature of labor intensive data collection that requires collecting treatment data from multiple providers involved in the care of the breast cancer patient. Moreover, the most important limitation of the few studies that have reported disparity in AA and whites is the lack of adjustment for patient mix, in

particular with respect to difference in clinical variables. This dissertation is unique in the at it accounts for patient differences in clinical and other prognostic factors that are relevant in physicians' treatment decisions.

The specific aims of the dissertation were:

1) To determine if racial differences exist in the treatment of early stage breast cancer between AA and white women.

2) To examine racial disparity of delays in diagnosis and treatment initiation for early stage breast cancer and explore factors that predicted delay in the overall population and by race.

3) To examine factors that influenced the choice between mastectomy and breast-conserving surgery (BCS) for women with early stage breast cancer and whether these factors differed between AA and White women.

REFERENCES

1.	Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin. Jan-Feb 2012;62(1):10-29.

2.	Howlader N NA, Krapcho M, Neyman N, Aminou R, Waldron W, Altekruse SF, Kosary CL, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Eisner MP, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). . SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations), National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2009_pops09/, based on November 2011 SEER data submission, posted to the SEER web site, April 2012.

3.	NCI. NCI Fact Sheet: Cancer Health Disparities. http://www.cancer.gov/cancertopics/factsheet/disparities/cancer-health-disparities. Accessed October 12, 2010.

4.	Newman LA, Kuerer HM, Hunt KK, et al. Local recurrence and survival among black women with early-stage breast cancer treated with breast-conservation therapy or mastectomy. Ann Surg Oncol. Apr-May 1999;6(3):241-248.

5.	Brawley OW, Freeman HP. Race and outcomes: is this the end of the beginning for minority health research? J Natl Cancer Inst. Nov 17 1999;91(22):1908-1909.

6.	Dignam JJ. Differences in breast cancer prognosis among African-American and Caucasian women. CA Cancer J Clin. Jan-Feb 2000;50(1):50-64.

7.	Tammemagi CM, Nerenz D, Neslund-Dudas C, Feldkamp C, Nathanson D. Comorbidity and survival disparities among black and white patients with breast cancer. JAMA. Oct 12 2005;294(14):1765-1772.

8.	Malin JL, Schneider EC, Epstein AM, Adams J, Emanuel EJ, Kahn KL. Results of the National Initiative for Cancer Care Quality: how can we improve the quality of cancer care in the United States? J Clin Oncol. Feb 1 2006;24(4):626-634.

9.	Hershman D, McBride R, Jacobson JS, et al. Racial disparities in treatment and survival among women with early-stage breast cancer. J Clin Oncol. Sep 20 2005;23(27):6639-6646.

10.	Bickell NA, Wang JJ, Oluwole S, et al. Missed opportunities: racial disparities in adjuvant breast cancer treatment. J Clin Oncol. Mar 20 2006;24(9):1357-1362.

11.	(NCCN) NCCN. Clinical Practice Guidelines in Oncology. Breast Cancer. http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf V. 2. , 2010.

12.	Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med. Oct 17 2002;347(16):1233-1241.

13.	Mandelblatt JS, Kerner JF, Hadley J, et al. Variations in breast carcinoma treatment in older medicare beneficiaries: is it black or white. Cancer. Oct 1 2002;95(7):1401-1414.

14.	Ballard-Barbash R, Potosky AL, Harlan LC, Nayfield SG, Kessler LG. Factors associated with surgical and radiation therapy for early stage breast cancer in older women. J Natl Cancer Inst. Jun 5 1996;88(11):716-726.

15.	Riley GF, Potosky AL, Klabunde CN, Warren JL, Ballard-Barbash R. Stage at diagnosis and treatment patterns among older women with breast cancer: an HMO and fee-for-service comparison. JAMA. Feb 24 1999;281(8):720-726.

16.   Shavers VL, Harlan LC, Stevens JL. Racial/ethnic variation in clinical presentation, treatment, and survival among breast cancer patients under age 35. Cancer. Jan 1 2003;97(1):134-147.

17.   Shavers VL, Brown ML. Racial and ethnic disparities in the receipt of cancer treatment. J Natl Cancer Inst. Mar 6 2002;94(5):334-357.

18.   Wood WC, Budman DR, Korzun AH, et al. Dose and dose intensity of adjuvant chemotherapy for stage II, node-positive breast carcinoma. N Engl J Med. May 5 1994;330(18):1253-1259.

19.   Hryniuk W. Importance of chemotherapy scheduling: pieces of the puzzle. Cancer Invest. 1999;17(7):545-546.

20.   Budman DR, Berry DA, Cirrincione CT, et al. Dose and dose intensity as determinants of outcome in the adjuvant treatment of breast cancer. The Cancer and Leukemia Group B. J Natl Cancer Inst. Aug 19 1998;90(16):1205-1211.

21.   Griggs J, Sorbero M. Ethnicity and Age Predict Suboptimal Adjuvant Chemotherapy for Breast Cancer. Academy Health Annual Meeting. Atlanta, GA2001.

22.   Hershman D, Weinberg M, Rosner Z, et al. Ethnic neutropenia and treatment delay in African American women undergoing chemotherapy for early-stage breast cancer. J Natl Cancer Inst. Oct 15 2003;95(20):1545-1548.

23.   Bickell NA, McEvoy MD. Physicians' reasons for failing to deliver effective breast cancer care: a framework for underuse. Med Care. Mar 2003;41(3):442-446.

24.   Sorbero M, Greggs J. Do Physician Prescribing Patterns Differ by Patient Ethnicity in the Treatment of Localized Breast Cancer? Academy Health Annual Meeting. Atlanta, GA2001.

25.   Lash TL, Silliman RA, Guadagnoli E, Mor V. The effect of less than definitive care on breast carcinoma recurrence and mortality. Cancer. Oct 15 2000;89(8):1739-1747.

26.   Eley JW, Hill HA, Chen VW, et al. Racial differences in survival from breast cancer. Results of the National Cancer Institute Black/White Cancer Survival Study. JAMA. Sep 28 1994;272(12):947-954.

27.   Cross CK, Harris J, Recht A. Race, socioeconomic status, and breast carcinoma in the U.S: what have we learned from clinical studies. Cancer. Nov 1 2002;95(9):1988-1999.

28.   Hassett MJ, Griggs JJ. Disparities in breast cancer adjuvant chemotherapy: moving beyond yes or no. J Clin Oncol. May 1 2009;27(13):2120-2121.

29.   Hewitt M, Simone J. Ensuring Quality Cancer Care. Washington, DC: National Academies Press; 1999.

30.   Muss HB, Hunter CP, Wesley M, et al. Treatment plans for black and white women with stage II node-positive breast cancer. The National Cancer Institute Black/White Cancer Survival Study experience. Cancer. Nov 15 1992;70(10):2460-2467.

31.   Elledge RM, Clark GM, Chamness GC, Osborne CK. Tumor biologic factors and breast cancer prognosis among white, Hispanic, and black women in the United States. J Natl Cancer Inst. May 4 1994;86(9):705-712.

32.   Richards MA, Westcombe AM, Love SB, Littlejohns P, Ramirez AJ. Influence of delay on survival in patients with breast cancer: a systematic review. Lancet. Apr 3 1999;353(9159):1119-1126.

33.   Swan J, Breen N, Coates RJ, Rimer BK, Lee NC. Progress in cancer screening practices in the United States: results from the 2000 National Health Interview Survey. Cancer. Mar 15 2003;97(6):1528-1540.

34.   Caplan LS, May DS, Richardson LC. Time to diagnosis and treatment of breast cancer: results from the National Breast and Cervical Cancer Early Detection Program, 1991-1995. Am J Public Health. Jan 2000;90(1):130-134.

35.   Vernon SW, Tilley BC, Neale AV, Steinfeldt L. Ethnicity, survival, and delay in seeking treatment for symptoms of breast cancer. Cancer. Apr 1 1985;55(7):1563-1571.

36.   Elmore JG, Nakano CY, Linden HM, Reisch LM, Ayanian JZ, Larson EB. Racial inequities in the timing of breast cancer detection, diagnosis, and initiation of treatment. Med Care. Feb 2005;43(2):141-148.

37.   Access of Medicaid recipients to outpatient care. N Engl J Med. May 19 1994;330(20):1426-1430.

38.   Moormeier J. Breast cancer in black women. Ann Intern Med. May 15 1996;124(10):897-905.

39.   Denavas-Walt C, Proctor B, Smith J. Income, Poverty, and Health Insurance Coverage in the United States: 2010. U.S. Census Bureau, Washington, DC. 2011.

40.   Coates RJ, Bransfield DD, Wesley M, et al. Differences between black and white women with breast cancer in time from symptom recognition to medical consultation. Black/White Cancer Survival Study Group. J Natl Cancer Inst. Jun 17 1992;84(12):938-950.

41.   Arnsberger P, Fox P, Ryder P, Nussey B, Zhang X, Otero-Sabogal R. Timely follow-up among multicultural women with abnormal mammograms. Am J Health Behav. Jan-Feb 2006;30(1):51-61.

42.   Poon EG, Haas JS, Louise Puopolo A, et al. Communication factors in the follow-up of abnormal mammograms. J Gen Intern Med. Apr 2004;19(4):316-323.

43.   Karliner LS, Patricia Kaplan C, Juarbe T, Pasick R, Perez-Stable EJ. Poor patient comprehension of abnormal mammography results. J Gen Intern Med. May 2005;20(5):432-437.

44.   Jones BA, Dailey A, Calvocoressi L, et al. Inadequate follow-up of abnormal screening mammograms: findings from the race differences in screening mammography process study (United States). Cancer Causes Control. Sep 2005;16(7):809-821.

45.   Kaplan CP, Eisenberg M, Erickson PI, Crane LA, Duffey S. Barriers to breast abnormality follow-up: minority, low-income patients' and their providers' view. Ethn Dis. Autumn 2005;15(4):720-726.

46.   Allen JD, Shelton RC, Harden E, Goldman RE. Follow-up of abnormal screening mammograms among low-income ethnically diverse women: findings from a qualitative study. Patient Educ Couns. Aug 2008;72(2):283-292.

47.   Recht A, Edge SB, Solin LJ, et al. Postmastectomy radiotherapy: clinical practice guidelines of the American Society of Clinical Oncology. J Clin Oncol. Mar 1 2001;19(5):1539-1569.

48.   Huang J, Barbera L, Brouwers M, Browman G, Mackillop WJ. Does delay in starting treatment affect the outcomes of radiotherapy? A systematic review. J Clin Oncol. Feb 1 2003;21(3):555-563.

49.   Hershman DL, Wang X, McBride R, Jacobson JS, Grann VR, Neugut AI. Delay in initiating adjuvant radiotherapy following breast conservation surgery and its impact on survival. Int J Radiat Oncol Biol Phys. Aug 1 2006;65(5):1353-1360.

50.   Gold HT, Do HT, Dick AW. Correlates and effect of suboptimal radiotherapy in women with ductal carcinoma in situ or early invasive breast cancer. Cancer. Dec 1 2008;113(11):3108-3115.

51.   Gold HT, Thwin SS, Buist DS, et al. Delayed radiotherapy for breast cancer patients in integrated delivery systems. Am J Manag Care. Nov 2009;15(11):785-789.

52.   Punglia RS, Saito AM, Neville BA, Earle CC, Weeks JC. Impact of interval from breast conserving surgery to radiotherapy on local recurrence in older women with breast cancer: retrospective cohort analysis. BMJ. 2010;340:c845.

53.   Hershman DL, Wang X, McBride R, Jacobson JS, Grann VR, Neugut AI. Delay of adjuvant chemotherapy initiation following breast cancer surgery among elderly women. Breast Cancer Res Treat. Oct 2006;99(3):313-321.

54.   Buzdar AU, Smith TL, Powell KC, Blumenschein GR, Gehan EA. Effect of timing of initiation of adjuvant chemotherapy on disease-free survival in breast cancer. Breast Cancer Res Treat. 1982;2(2):163-169.

55.   Colleoni M, Bonetti M, Coates AS, et al. Early start of adjuvant chemotherapy may improve treatment outcome for premenopausal breast cancer patients with tumors not expressing estrogen receptors. The International Breast Cancer Study Group. J Clin Oncol. Feb 2000;18(3):584-590.

56.   Desch CE, McNiff KK, Schneider EC, et al. American Society of Clinical Oncology/National Comprehensive Cancer Network Quality Measures. J Clin Oncol. Jul 20 2008;26(21):3631-3637.

57.   Cold S, During M, Ewertz M, Knoop A, Moller S. Does timing of adjuvant chemotherapy influence the prognosis after early breast cancer? Results of the Danish Breast Cancer Cooperative Group (DBCG). Br J Cancer. Sep 19 2005;93(6):627-632.

58.   Fedewa SA, Ward EM, Stewart AK, Edge SB. Delays in adjuvant chemotherapy treatment among patients with breast cancer are more likely in African American and Hispanic populations: a national cohort study 2004-2006. J Clin Oncol. Sep 20 2010;28(27):4135-4141.

59.   Bain BJ. Ethnic and sex differences in the total and differential white cell count and platelet count. J Clin Pathol. Aug 1996;49(8):664-666.

60.   Caplan LS, Helzlsouer KJ, Shapiro S, Wesley MN, Edwards BK. Reasons for delay in breast cancer diagnosis. Prev Med. Mar-Apr 1996;25(2):218-224.

61.   Gorin SS, Heck JE, Cheng B, Smith SJ. Delays in breast cancer diagnosis and treatment by racial/ethnic group. Arch Intern Med. Nov 13 2006;166(20):2244-2252.

62.   Goodson WH, 3rd, Moore DH, 2nd. Causes of physician delay in the diagnosis of breast cancer. Arch Intern Med. Jun 24 2002;162(12):1343-1348.

63.   Struthers R, Nichols LA. Utilization of complementary and alternative medicine among racial and ethnic minority populations: implications for reducing health disparities. Annu Rev Nurs Res. 2004;22:285-313.

64.   Everson SA, Goldberg DE, Kaplan GA, et al. Hopelessness and risk of mortality and incidence of myocardial infarction and cancer. Psychosom Med. Mar-Apr 1996;58(2):113-121.

65.   Nattinger AB, Gottlieb MS, Veum J, Yahnke D, Goodwin JS. Geographic variation in the use of breast-conserving treatment for breast cancer. N Engl J Med. Apr 23 1992;326(17):1102-1107.

66.   Osteen RT, Karnell LH. The National Cancer Data Base report on breast cancer. Cancer. Apr 1 1994;73(7):1994-2000.

67.   Smith GL, Xu Y, Shih YC, et al. Breast-conserving surgery in older patients with invasive breast cancer: current patterns of treatment across the United States. J Am Coll Surg. Oct 2009;209(4):425-433 e422.

68.   Enewold L, Zhou J, McGlynn KA, et al. Racial variation in breast cancer treatment among Department of Defense beneficiaries. Cancer. Feb 1 2012;118(3):812-820.

69.   Banerjee M, George J, Yee C, Hryniuk W, Schwartz K. Disentangling the effects of race on breast cancer treatment. Cancer. Nov 15 2007;110(10):2169-2177.

70.   Johantgen ME, Coffey RM, Harris DR, Levy H, Clinton JJ. Treating early-stage breast cancer: hospital characteristics associated with breast-conserving surgery. Am J Public Health. Oct 1995;85(10):1432-1434.

71.   Farrow DC, Hunt WC, Samet JM. Geographic variation in the treatment of localized breast cancer. N Engl J Med. Apr 23 1992;326(17):1097-1101.

72.   Michalski TA, Nattinger AB. The influence of black race and socioeconomic status on the use of breast-conserving surgery for Medicare beneficiaries. Cancer. Jan 15 1997;79(2):314-319.

73.   Athas WF, Adams-Cameron M, Hunt WC, Amir-Fazli A, Key CR. Travel distance to radiation therapy and receipt of radiotherapy following breast-conserving surgery. J Natl Cancer Inst. Feb 2 2000;92(3):269-271.

74.   Nattinger AB, Gottlieb MS, Hoffman RG, Walker AP, Goodwin JS. Minimal increase in use of breast-conserving surgery from 1986 to 1990. Med Care. May 1996;34(5):479-489.

75.   Nattinger AB, Kneusel RT, Hoffmann RG, Gilligan MA. Relationship of distance from a radiotherapy facility and initial breast cancer treatment. J Natl Cancer Inst. Sep 5 2001;93(17):1344-1346.

76.   Celaya MO, Rees JR, Gibson JJ, Riddle BL, Greenberg ER. Travel distance and season of diagnosis affect treatment choices for women with early-stage breast cancer in a predominantly rural population (United States). Cancer Causes Control. Aug 2006;17(6):851-856.

77.   Goodwin JS, Nattinger AB. Effect of season and climate on choice of therapy for breast cancer in older women. J Am Geriatr Soc. Sep 1995;43(9):962-966.

78.   McGinnis LS, Menck HR, Eyre HJ, et al. National Cancer Data Base survey of breast cancer management for patients from low income zip codes. Cancer. Feb 15 2000;88(4):933-945.

79.   Samet JM, Hunt WC, Farrow DC. Determinants of receiving breast-conserving surgery. The Surveillance, Epidemiology, and End Results Program, 1983-1986. Cancer. May 1 1994;73(9):2344-2351.

80.   Lazovich DA, White E, Thomas DB, Moe RE. Underutilization of breast-conserving surgery and radiation therapy among women with stage I or II breast cancer. JAMA. Dec 25 1991;266(24):3433-3438.

81.   Lazovich D, Solomon CC, Thomas DB, Moe RE, White E. Breast conservation therapy in the United States following the 1990 National Institutes of Health Consensus Development Conference on the treatment of patients with early stage invasive breast carcinoma. Cancer. Aug 15 1999;86(4):628-637.
82.   Lazovich D, White E, Thomas DB, Moe RE, Taplin S. Change in the use of breast-conserving surgery in western Washington after the 1990 NIH Consensus Development Conference. Arch Surg. Apr 1997;132(4):418-423.
83.   Morris CR, Cohen R, Schlag R, Wright WE. Increasing trends in the use of breast-conserving surgery in California. Am J Public Health. Feb 2000;90(2):281-284.
84.   Hiotis K, Ye W, Sposto R, Skinner KA. Predictors of breast conservation therapy: size is not all that matters. Cancer. Mar 1 2005;103(5):892-899.
85.   Vlastos G, Mirza NQ, Meric F, et al. Breast conservation therapy as a treatment option for the elderly. The M. D. Anderson experience. Cancer. Sep 1 2001;92(5):1092-1100.
86.   Ward S, Heidrich S, Wolberg W. Factors women take into account when deciding upon type of surgery for breast cancer. Cancer Nurs. Dec 1989;12(6):344-351.

RACIAL DIFFERENCES IN RECOMMENDATION AND RECEIPT OF OPTIMAL

TREATMENT FOR EARLY STAGE BREAST CANCER

by

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RACIAL DIFFERENCES IN RECOMMENDATION AND RECEIPT OF OPTIMAL

TREATMENT FOR EARLY STAGE BREAST CANCER

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ABSTRACT

Introduction: African-American women with invasive breast cancer have shorter survival when compared to white women. Though improvements in the 5 year survival rates are seen in both White and AAs, the gap between the two races has not been shrinking.

Methods: A retrospective cohort study was conducted using newly-diagnosed early stage invasive breast cancer patients. Subjects diagnosed with breast cancer during 2006-2010 from all major hospitals in eastern New Jersey were identified through rapid case ascertainment methodology. Detailed medical record data on 626 subjects (329 White women and 297 Black women) were collected from both doctors' offices and hospitals. Optimal treatment was defined using the National Comprehensive Cancer Network (NCCN) guidelines for surgery, and adjuvant treatments (radiation, chemotherapy, hormonal and monoclonal therapy). We evaluated both physician recommendation and patient receipt of optimal treatments.

Results: The overall physician recommendation of optimal treatment was similar between AAs and whites (83%). About 78% of the white women and 73% of the AA women received optimal treatment. No significant differences in optimal treatment were

seen between AAs and whites; physician not recommending optimal treatment (RR: 0.89 (0.56, 1.43)) and patients not receiving optimal treatments (RR: 1.03 (0.75, 1.40)).

Conclusions: No significant racial differences were found in recommendation of optimal treatment by physicians or in patient receipt of optimal treatment according to NCCN treatment guidelines.

RACIAL DIFFERENCES IN OPTIMAL TREATMENT OF EARLY STAGE BREAST

CANCER

Introduction

    Treatment improvements in the past two decades have significantly

increased survival for early stage breast cancer patients.[1,2] Despite similar treatment

benefits[3,4], African-American (AA) women are reported to have poor outcomes compared

to white women.[5] Past studies have reported that there are racial differences in surgical

treatment[6,7], and adjuvant therapy (radiation and chemotherapy)[8,9] when comparing AAs

and whites. However, appropriate adjuvant treatments are centered on prognostic and

predictive factors[10] and the lack of availability of these factors for most population based

studies is a major limitation when interpreting differences in receipt of appropriate

treatment.

    The National Comprehensive Cancer Network (NCCN) treatment guidelines are

widely used and accepted in oncology practices in the United States. NCCN articulates

that treatment decisions should be based on clinical factors such as nodal involvement,

tumor histology, estrogen/progesterone receptor status, tumor size, tumor grade, surgical

margin status and human epidermal growth factor receptor 2 (HER2) status.

    The limitation of the few studies that have compared receipt of treatment between

AAs and whites is that they did not make the two races similar in terms of clinical

characteristics nor adjust for them. Therefore, the examination of racial disparity in

breast cancer treatment is incomplete. Most of the existing literature relies on state cancer

registry data that neither provides detailed information on the different treatments that a

patient receives across the stages of breast cancer care nor the detailed clinical and

laboratory information needed to determine appropriate treatment. Additionally, the

extensive efforts required to conduct in-depth medical record review poses a barrier to

capturing details on treatment received. The objective of this study is to examine racial

differences in the receipt of optimal treatment as defined by the NCCN guidelines for

local-regional invasive breast cancer after taking into account detailed clinical factors.

Materials and Methods

Study population

A 1:1 (AA to white) matched retrospective cohort study among patients diagnosed with stage I, II, and $T_3N_1M_0$ breast cancer and residing in northern and central New Jersey (NJ) was conducted.

Subject recruitment

Subjects who participated in the Women's Circle of Health Study (WCHS) and who consented to participate in this study, the Breast Cancer Treatment Disparity Study (BCTDS) were recruited. Details on the WCHS study have been reported elsewhere.[11] For each year from 2005 to 2010, all female patients who were newly diagnosed with early stage breast cancer were identified from Passaic, Bergen, Hudson, Essex, Union, Middlesex, and Mercer counties using rapid case ascertainment methodology. Public health representatives from the New Jersey State Cancer Registry (NJSCR) actively visited major hospitals in the aforementioned counties to identify subjects close to the time of their diagnosis. The proportion of AAs in these counties was much higher than the rest of the state which allowed for their oversampling in the study.

Subjects were excluded if they were neither AA nor white, non-residents of NJ, diagnosed with inflammatory breast cancer, diagnosed with breast cancer with histologic features other than adenocarcinoma, or were diagnosed with any other cancer besides non-melanoma skin cancer. After identification of potentially eligible subjects for the study, all AA subjects who were 18 to 85 years of age at the time of diagnosis were selected. For each AA subject, a white woman with breast cancer was randomly selected

from those who matched on age at diagnosis (± 5 years) and county of residence. A white subject was not matched more than once.

A letter was sent to the physicians of potential participants by the NJSCR staff notifying them about the study and that their patients will be contacted to participate in BCTDS. In the letter the physicians were asked to provide any reason their patients should not be contacted. If no response was received within three weeks, the state assumed agreement (passive consent). Eligible women were then telephoned by the NJSCR staff to obtain a verbal consent.

Women aged ≤ 75 years of age were contacted by the WCHS staff to schedule in-person interviews. At the time of the interview they obtained: consent to participate in the current study, names and address (if available) of providers involved in the breast care of the patient (the R form), and permission to release their medical records. Women older than 75 years of age were directly contacted by the BCTDS staff (as they were not eligible for participation in the WCHS study) and the same three forms and consents were mailed to them. Consent was first obtained for the AA patient in a matched pair and then the white patient was approached. In the event that an AA patient's first white match refused, the NJSCR had two back-up matches to contact. Medical records for a total of 626 subjects (297 AAs and 329 whites) were obtained and abstracted.

The study was approved by Institutional Review Boards (IRB) at both the University of Medicine and Dentistry of New Jersey (UMDNJ) and New Jersey Department of Health and Senior Services (for NJSCR).

Medical Record Review

At the time of consent, patients were also asked to provide names and addresses (if available) of providers who were involved in their breast cancer care.   All health care providers listed by the participants were contacted to obtain medical records. Addresses and phone numbers of each hospital and physician were identified by searching several databases (including American Medical Association, NJ Physicians maintained by the Division of Consumer Affairs, American Board of Medical Specialties, American College of Surgeons, American College of Radiology, web sources such as webmd.com, and web based yellow pages). In situations where physicians switched group practice, the original group practice office was contacted to obtain the forwarding address of the provider.

A letter was sent to all providers requesting a copy of the patient's medical records along with a copy of patient's consent to release their medical records. Providers were also asked to identify the name of other physician(s) involved in the care of the participant. Specifically, records were received for initial diagnostic information, biopsy reports, breast surgery, and adjuvant treatment(s). As most adjuvant treatments are provided in an outpatient setting, outpatient records were obtained for the period covering a year prior through a year after the initial diagnosis of breast cancer from hospitals, the primary physician, surgical oncologist, medical oncologist(s) and radiation oncologist (as applicable). The operating reports, pathology reports and discharge summary were also obtained for hospitalizations either for surgery or chemotherapy.

From the medical records trained personnel abstracted detailed information on prior history of breast disease, comorbidity, missed appointments, long-term medications, tests performed during diagnostic and metastatic work-up, all surgeries related to

treatment, clinical characteristics of the tumor, nodal involvement; margin status, and any adjuvant treatments planned or administered.

NCCN Recommendations: "Standard" versus "Standard with additional"

Treatment information was ascertained from both in-patient and out-patient medical records using a standard abstraction form. Optimal treatment includes surgery (mastectomy or BCS) and adjuvant treatments when applicable (radiation, chemotherapy, hormonal, and trastuzumab therapy) as defined by the National Comprehensive Cancer Network (NCCN). [12] NCCN provides "decision trees" as a method of determining treatments. These "decision trees" were utilized to develop an algorithm for defining optimal treatment based on uniform consensus of the NCCN panel members. Therefore, treatments identified as category 1 (high level of evidence with uniform consensus) or category 2A (lower level of evidence with uniform consensus) were taken as basis for the algorithm recommendations. If a recommended treatment was preceded by "±", then it was considered as an additional treatment given to the patient at the discretion of the physician. Any treatments before "±" was considered as recommendation that is NCCN "standard" and the inclusion of any treatment after the "±" was considered as recommendation that is NCCN "standard with additional".

For example, in the NCCN 2010 version 2 guidelines, a patient with the following factors: ER/PR positive, HER2 positive, unfavorable histology, tumor size between 0.6cm to 1.0 cm with moderately or poorly differentiated tumor grade, is recommended by NCCN to receive endocrine therapy ± adjuvant chemotherapy (category 1). For the standard treatment definition, chemotherapy will not be included as a NCCN

recommended treatment. On the other hand, for the standard with additional treatment definition both endocrine therapy and chemotherapy will be NCCN recommended for the patient.

Since NCCN guidelines are updated at least annually, the appropriate guideline recommendations corresponding to the patients' year of diagnosis were used in the definition of optimal treatment. When more than one guideline version was available for a diagnosis year then the guideline with the earliest date of publication for that year was used.

Table 1 describes in a flow chart the NCCN guideline recommendations (category 1 and 2A), as well as racial distribution by clinical factors. This represents the possible treatments recommended for patients depending on their diagnosed tumor/clinical characteristics. All patients must receive either breast conserving surgery (BCS) or total mastectomy. BCS is to be followed by radiation treatments; on the other hand, radiation treatment after mastectomy depends on the tumor size, node status, and margin status. NCCN has suggested omitting radiation after BCS for those over 70 years of age with hormone positive receptors, negative nodes, and tumor size $\leq$ 2cm who receive endocrine therapy.

Systemic treatments follow any of the 4 pathways shown. These pathways depend on a combination of the tumor's estrogen receptor (ER), progesterone receptor (PR) , and HER2 status. Pathway 1 shows the first combination of hormone receptor positive and HER2 status positive, pathway 2 is for a patient who is hormone receptor negative and HER2 status positive, pathway 3 is for a patient who is hormone receptor positive and HER2 status negative and finally pathway 4 shows the last combination which is for a

patient who is both hormone receptor and HER2 negative. Each pathway then displays

further classification of a patient's tumor/clinical characteristics (tumor histology, tumor

size, tumor grade and node status) which identifies the appropriate systemic treatments.

Therefore, optimal treatment is defined comprehensively by surgery, radiation,

chemotherapy, endocrine and monoclonal treatment. For example, if patient "A"

receives mastectomy as the primary surgery and is identified with negative lymph nodes

and positive margin status then she should receive adjuvant radiation to the chest wall. If

her tumor receptors are hormone receptor positive and HER2 positive then she will

follow pathway 1. Her tumor histology, size, grade and negative lymph node status then

determine what systemic treatments she should receive.

Outcome Variable: Overall Optimal Treatment

We considered the optimal treatment definition from two different approaches: 1) Did

physicians recommend the optimal treatment according to NCCN guidelines (Yes or No).

2) If physicians did recommend according to NCCN guidelines, did patients receive the

optimal treatment (Yes or No). These two approaches were further broken down to

consider recommendations from NCCN as either "standard" or "standard with

additional".

     Physician Recommendation of overall optimal treatment definition

If the physician recommended all of the treatments according to guideline, then the

physician recommendation of optimal treatment was "Yes". This category also contained

patients who were part of clinical trials regardless of treatment received. If the treating

physician did not recommend an NCCN treatment that was listed then the physician recommendation of optimal treatment was "No".

Patient Receipt of overall optimal treatment definition

If the patient received all treatments that their physicians recommended according to guidelines, then the receipt of optimal treatment was "Yes". This category also contained patients who were part of clinical trials. Surgery was considered as received if patient had either BCS or mastectomy as their primary surgery. Primary surgery was defined as BCS or total mastectomy. For receipt of radiation, the sites recommended by NCCN must be irradiated for the patient to be included in the receipt "yes" category. For chemotherapy the receipt of treatment was defined as yes if the patient completed the cycles planned by the treating oncologist. Patients who switched to alternative chemotherapy regimens due to side effects were considered as received yes if they completed the alternative cycles that the oncologist recommended. For both hormonal and trastuzumab treatment, receipt was established as "yes" if the patient started treatment and not necessarily completed them. If the patient did not receive the NCCN recommended treatments then they were categorized as "No". If medical records for a patient were not received, then treatments were set as missing.

Explanatory Variable: Race

Self-reported race is the explanatory variable of interest and was categorized as white (W) or African-American (AA).

Variables of clinical importance

Clinical indicators for the invasive cancer were abstracted in meticulous detail from the

pathology reports. Tumor size was recorded as the largest invasive tumor size in

centimeters given by pathology reports. If the size was not available through pathology

due to neo-adjuvant chemotherapy, then a clinical size established by the treating

physicians were noted.   Tumor histology reflected the histology from the primary

surgery. It was categorized as unfavorable (ductal, lobular, mixed, metaplastic,

medullary, papillary, micro-invasive) and favorable (tubular/ cribiform,

mucinous/colloid). Two patients were identified as positive lymph nodes with an in-situ

tumor (no invasive tumor found). These two were placed in the unfavorable category.

ER and PR status, as well as, HER2 status was recorded as positive or negative.

If a patient had a final report of borderline status then they were categorized as positive

for the study. Tumor grade that reflected the most severe level from any recorded

surgery was taken as the final grade (poorly differentiated, moderately differentiated, or

well differentiated).

The lymph nodes were recorded as negative (zero lymph nodes positive),

micrometastases, or positive (1 to 3 nodes macrometastases positive) through sentinel

node biopsy and/or axillary node dissection. Patient's margin status after the primary

surgery was defined as positive (tumor involves the inked surgical margin), close (tumor-

free margin width of ≤ 1 mm for invasive tumor and ≤ 2mm for in-situ tumor), or

negative (tumor-free margin width of > 1mm for invasive tumor and > 2 mm for in-situ

tumor)[13,14]. Margin definition is controversial and we chose definitions that were more

conservative.

Other covariates

The total number of comorbidities for a patient was based on how many of the following morbidity categories were documented in the hospital records: cerebro-vascular accident, congestive heart failure, diabetes mellitus, gastro-intestinal disease, hypertension, ischemic heart disease, malignancies, organic heart disease, peripheral vascular disease, primary arrhythmias/conduction problems, renal disease, respiratory problems, neurologic disorders, immunologic/connective tissue disorders, endocrine disorders (other than diabetes), and moderate/severe liver disease.

Also included were age in years at breast cancer diagnosis, first or second degree family history of breast cancer (yes or no), total household income, and primary insurance (Medicaid, Medicare, private, no insurance (includes charity care)). Type of treatment facility was categorized as the hospital where the patients received their surgery as either a teaching hospital or community-based hospital.   The hospital designation was based on the American College of Surgeons website (http://www.facs.org).

Statistical Analysis

We compared distribution by race for demographics (age at diagnosis, marital status, income, education, type of insurance), clinical (menopausal status, comorbidity count, method of initial tumor discovery), and tumor characteristics (histology, grade, ER and/or PR status, HER2 status, triple negative status, AJCC stage) by using chi-square tests. Then distribution by race was separately compared for each category of optimal treatment (*i.e.* optimal surgery, optimal radiation, optimal chemotherapy, optimal endocrine therapy, and optimal monoclonal therapy).

The rate of a physician not recommending the optimal treatment or the rate of a patient not receiving the optimal treatment (according to NCCN "standard" recommendation) was compared between AA and white using multivariable binomial regression. The same analysis and comparison method was then applied to each response category of optimal treatment (surgery, radiation, chemotherapy, endocrine, and monoclonal) separately. Clinical variables were inherently adjusted by way of outcome definition. Out of those where physicians recommended the optimal treatment, a sub-analysis was conducted to explore racial differences in patient receipt of optimal treatment.

All analyses were controlled for the confounding effects of age, income, insurance, and comorbidity. To account for the within-physician correlation, the between race comparison of physician not recommending or patient not receiving treatment at average population-level was assessed with a marginal model with GEE (generalized estimating equation) inference procedure with compound symmetry working correlation. We repeated the above analyses for the NCCN "standard with additional" recommendation.

Analyses were performed using SAS software, version 9.2 (SAS Institute Inc., Cary, NC).

Results

Of the 2,679 eligible breast cancer patients identified in 2005-2010 by the

NJSCR, n=1,391 (AA: 859, W: 532) did not participate (refusal either by physician or

patient) and n=1,288 (AA: 584, W: 704) agreed to participate. Seventy-three percent of

those who agreed to participate had their medical records released for abstraction and

were included in our study.

Table 1 represents the racial distribution of the study subjects (n=626) by clinical

factors commonly used to decide upon adjuvant treatments. The subjects do not add up

to 626 due to medical records missing for either clinical factors or treatments for some

patients. A majority of the patients were hormone receptor status positive and HER2

status negative with unfavorable histology (58% AA and 73% White).

Tables 2-4 shows the demographic, clinical and tumor characteristics of the study

subjects by race which included 626 early stage invasive breast cancer patients

(White:329; AA:297). Most AA were either under 40 years of age or between 55 to 64

years of age, have had some college education (24%), categorized in income of less than

$35,000 (33%). Compared to whites, more AAs have either government primary

insurance or no insurance. In both races, screening mammography and patient self-

discovery were the most frequent methods of breast cancer detection. AAs were more

likely to have an increased number of comorbidities compared to whites at diagnosis

(36% versus 23%) (Table 3). More AAs were diagnosed with poorly differentiated tumor

grade and have triple negative tumors (Table 4).

Optimal treatment recommendation by physician and receipt of optimal treatment
(following the "standard" treatment guidelines)

Table 5 shows the proportion of optimal treatment recommendation by physicians stratified by patient race. The overall physician recommendation of optimal treatment was similar between AAs and whites (83%). Optimal surgery was recommended for all patients. Optimal radiation was recommended for 87% of the women. Optimal chemotherapy was recommended for 96% of the white women and 93% of the AA women. Recommendation for optimal endocrine treatment and trastuzumab treatment showed some differences among the women by race. About 4% more AAs than white were not recommended the optimal endocrine treatment and about 3% more AAs were not recommended optimal trastuzumab treatment. Table 6 shows the proportion of patient receipt after physicians recommended optimal treatments based on NCCN guidelines. Out of 523 patients whose physicians recommended NCCN treatments, 8% of the white women and 8% of the AA women did not receive optimal treatment.   Receipt of chemotherapy treatment showed the most differences between the races with almost 7% fewer AAs receiving chemotherapy compared to white women.

Table 7 shows details of the variables used for the overall physician not recommending optimal treatment and the overall patient not receiving optimal treatment models. Though borderline significant, AAs tended not to receive optimal treatment after adjusting for clinical factors (RR: 1.60 (0.94, 2.71). No racial differences were found in physicians not recommending optimal treatment (adjusted RR: .89 (0.56, 1.43). Compared to those with private insurance, those with no insurance were more likely not to have optimal treatment recommended (adjusted RR: 2.01 (1.29, 3.13)). Type of

treatment facility (community-based hospitals versus teaching hospitals) was considered in the model as a covariate of interest and was found to be not significant (p-value=0.5563). The inclusion of this variable did not result in any meaningful interpretation and was removed from the final model.

Tables 8 and 9 shows the risk of physician not recommending or patient not receiving optimal treatment for AAs compared to whites for each category of optimal treatment. Optimal surgery alone was not modeled since there was no difference in receipt and recommendation of the outcome by both races. No significant results were seen for physician not recommending according to NCCN guidelines for each category of treatment. AAs for more likely not to receive chemotherapy after adjustment of clinical factors (RR: 1.95 (1.00, 3.78)).

Optimal treatment recommendations by physicians and Receipt of optimal treatment (following the "standard with additional" guidelines)

Mostly chemotherapy was the treatment that was preceded by "±" in the NCCN guidelines and was the main difference between "standard" and "standard with additional" treatment. Table 10 shows the proportion of optimal treatment recommendation by physicians stratified by patient race. Optimal chemotherapy was more recommended to AAs than compared to whites (82.2% versus 77.5%). Optimal endocrine (93.3% versus 97%) and trastuzumab treatments (96.3% versus 99.1%) were recommended in AAs less. Table 11 shows the proportion of optimal treatment received by race after physicians recommended optimal treatments according to NCCN guidelines. Out of the 429 patients whose physicians recommended treatments according to NCCN,

12% of the white women and 21% of the AA women did not receive optimal treatment. Receipt of optimal chemotherapy was seen in 78.7% of the AAs and 89.4% of the white women. Optimal endocrine treatment was less likely to be received by AAs compared to whites (90% versus 96.8%).

Table 12 shows the association of physician not recommending optimal treatment and patient not receiving optimal treatment according to NCCN "standard with additional" guidelines. No significant racial differences were seen in physician not recommending. On the other hand, AAs were more likely not to receive optimal treatment after adjusting for clinical factors (adjusted RR: 1.79 (1.15, 2.79)). Those who are in the older age groups were more likely not to receive the optimal treatment (adjusted RR for those $\geq$ 65 years of age: 1.11 (1.00, 1.24)) with borderline significance adjusted for race, income, insurance, and comorbidities. When each type of optimal treatment was looked at separately, physicians were more likely to recommend chemotherapy to AAs compared to whites (adjusted RR: .62; 95% CI: .42, .90)) (Table 13). AAs for more likely not to receive chemotherapy after adjustment of clinical factors (RR: 1.92 (1.15, 3.20)) (Table 14).

Discussion

This unique study considered a comprehensive approach at gathering clinical data which allowed a more informative view on racial disparity and treatment differences in local-regional invasive breast cancer. No previous studies to the authors' knowledge have considered physician recommendation of treatments by an established guideline or to have examined patient receipt of all modality of treatments that is currently available to breast cancer patients. Therefore, the primary aim of this study was to examine racial differences in treatment of invasive breast cancer in both physician recommendation and patient receipt of optimal treatment according to the NCCN guidelines.

Our study showed borderline statistical differences in race for overall optimal treatment receipt after adjusting for detailed clinical factors. We identified primary insurance to be an independent predictor of treatment recommendation. Patients who were categorized as having no insurance compared to those with private insurance were more at risk of not having the optimal treatment recommended to them. These findings are similar to a recent paper by Freedman *et al.* which showed that uninsured breast cancer patients were less likely to receive definitive loco-regional therapy, adjuvant hormonal therapy and adjuvant chemotherapy.[15] Other studies have shown Medicaid receipts to be less likely to receive the systemic treatment when compared to women with private insurance.[15,16] We did not see statistically significant results for Medicaid patients mostly due to our small sample size for this category. Though we did not see significant differences with individual income-based SES, results of lower use of guideline recommended treatments have been shown with area-based SES.[17]

Studies have shown inconclusive results in racial disparity and receipt of treatments.[17-22] Bickell *et al.* found evidence of racial disparity among receipt of chemotherapy in a sample of patients across six New York City hospitals. Their report shows that AAs are more likely to underuse efficacious adjuvant systemic treatments compared to whites after adjusting for tumor stage, comorbidity, age, insurance, and referral to medical oncologist.[22] But, their study did not consider individual or area-based SES in the analysis. Freedman *et al.* found racial differences in receipt of radiation treatment and adjuvant systemic treatments in AAs compared to white women.[15] On the other hand, a recent paper by Wu *et al.* did not find racial differences in the receipt of chemotherapy after adjusting for age, area-based SES, tumor characteristics, clinical factors, hospital accreditation with the commission of cancer and cancer registry.[17] Though we did not observe racial disparity in receipt of chemotherapy, we did observe that when the standard plus additional treatment guidelines were considered, chemotherapy was more likely to be recommended by physicians to AAs as compared to whites. Since more AAs in the sample had triple negative tumor characteristics this is not unexpected.

Nevertheless, no other study has undertaken to examine the receipt of treatment from a comprehensive point, considering surgery, radiation, chemotherapy, hormonal and monoclonal into one definition. A few studies that have attempted to consider all treatments for local-regional invasive cancer has been limited by the availability of tumor characteristics and treatment information from population based cancer registries. A study by Balasubramanian *et al.* studied racial differences among Medicaid beneficiaries using the National Institutes of Health (NIH) consensus report definition for standard

treatment (surgery, radiation, hormonal therapy, and chemotherapy). They reported that when considering women with similar access to insurance, no racial differences were found across surgical treatments, radiation after BCS, and adjuvant systemic therapy after adjusting for age, marital status, comorbidity, and tumor characteristics.[18] Using patients from the Alabama statewide cancer registry, Worthington *et al.* found that AAs and whites received comparable overall standard treatment with the NCCN guidelines. But this study was limited by not including socio-economic factors and insurance as part of their analysis.[20]

Omitting a vital part of treatment in the care for breast cancer has been shown to adversely impact survival.[23-25] Our study indicates the importance of insurance as an access to quality of care for the treatment that is recommended to the patient as well as received by the patient. Several studies have noted the effect of insurance on preventive care treatment receipt. Though they caution their sample size is small, another study by Bickell *et al.* reported an increased risk of not receiving radiation and systemic treatments among women with Medicaid or no insurance. [26] Breen *et al.* noted in the National Cancer Institute Black-White Cancer Survival Study that older women and women without insurance were significantly less likely to receive minimum expected therapy. [27] A Metropolitan Detroit SEER registry linked to Medicaid showed Medicaid insured women were more likely to be diagnosed at a later stage disease, and less likely to have received BCS or BCS post-radiation.[28]

Our study strengths included using NCCN appropriate guidelines according to patient's diagnosis year, availability of comprehensive clinical factors and treatment information from hospital and out-patient records, and use of individual based SES data.

Our study has recognized limitations. First, our study is geographically limited to women who resided in New Jersey and may not be generalizable to women who live elsewhere. Second, even though treatments can be recommended by NCCN, it can still be individualized for each patient. Additionally, more physicians are using gene-expression tests such as Oncotype Dx to assess treatments decisions. Because there was not uniform consensus among the NCCN panel members for Oncotype Dx, we did not include it as part of the recommendation definition.

In conclusion, racial differences were found in receipt of overall optimal treatment definitions for patients diagnosed with local-regional invasive breast cancer. Current statistics show the incidence of breast cancer as being stable among the races, and that the death rates decreased slightly from 1992 to 2007 for AAs, the gap in the rate in mortality between AAs and whites does not show a decline.[29] Patient navigation programs should target women not starting treatments recommended by physicians with patient education. Interventions such as patient reminders, improving physician-patient communication and decision aids can address attitudes and beliefs that are barriers to treatments for breast cancer. .

Tables and Figures

Table 1. Racial distribution of clinical factors represented in the NCCN 2010 guidelines for early stage breast cancer

SURGERY	Size	Margin Status	Node	Radiation Sites Recommended	White (n)	AA (n)
Lumpectomy	N/A	N/A	P	Whole breast	35	36
			N	Whole breast	164	134
Mastectomy	N/A	N/A	P	Chest Wall + Supraclavicular	47	41
	> 5cm	N/A	N	Chest Wall	2	3
	N/A	P	N	Chest Wall	3	2
	≤ 5 cm	C	N	Chest Wall	6	8
	≤ 5 cm	N	N	No Radiation	70	67

HER2 Status	ER/PR Status	Histology	Tumor Size	Grade	Node Status	Systemic Treatments Recommended	White (n)	AA (n)
P	P	Unfavorable	≤ 0.5cm	N/A	N	No	9	8
			≤ 0.5cm	N/A	M	E	1	1
			> 0.5 cm to 1.0cm	1	N	No	2	0
			> 0.5 cm to 1.0cm	1	M	E	0	0
			> 0.5 cm to 1.0cm	2 or 3	N or M	E ± C	1	2
			>1.0 cm	N/A	N or M	E +C +Trastuzumab	18	18
			N/A	N/A	P	E +C +Trastuzumab	5	10
		Favorable	< 1.0 cm	N/A	N or M	No	0	0
			≥ 1.0cm	N/A	N or M	E	1	0
			N/A	N/A	P	E	0	0
P	N	Unfavorable	≤ 0.5cm	N/A	N	No	2	2
			≤ 0.5cm	N/A	M	C	2	0
			> 0.5 cm to 1.0cm	N/A	N or M	C	2	1
			>1.0 cm	N/A	N or M	C+Trastuzumab	10	10
			N/A	N/A	P	C+Trastuzumab	3	3
		Favorable	≤ 0.5cm	N/A	N	No	0	0
			≤ 0.5cm	N/A	M	C	0	0
			> 0.5 cm to 1.0cm	N/A	N or M	C	0	0
			>1.0 cm	N/A	N or M	C	0	0
			N/A	N/A	P	C	0	0

Pathway 1 *or*

Pathway 2 *or*

ER: Estrogen Receptor; PR: Progesterone receptor; HER2: Human Epidermal Growth Factor Receptor 2; N/A: Not applicable; P: Positive; N: Negative; C: Close; M: Micrometastasis;
Unfavorable (U): Ductal, Lobular, Mixed, Metaplastic, Medullary; Favorable (F): Tubular, Colloid; E: Endocrine Therapy; C: Chemotherapy;
NCCN: National Comprehensive Cancer Network

Table 1 (contd). Racial distribution of clinical factors represented in the NCCN 2010 guidelines for early stage breast cancer

	HER2 Status	ER/PR Status	Histology	Tumor Size	Grade	Node Status	Systemic Treatments Recommended	White (n)	AA (n)
Pathway 3 *or*	N	P	Unfavorable	≤ 0.5cm	N/A	N	No	33	26
				≤ 0.5cm	N/A	M	E	3	1
				> 0.5 cm to 1.0cm	1	N	No	37	6
				> 0.5 cm to 1.0cm	1	M	E	1	0
				> 0.5 cm to 1.0cm	2 or 3	N or M	E ± C	37	16
				>1.0 cm	N/A	N or M	E ± C	86	78
				N/A	N/A	P	E +C	45	33
			Favorable	< 1.0 cm	N/A	N or M	No	0	0
				≥ 1.0cm	N/A	N or M	E	3	2
				N/A	N/A	P	E ± C	0	1
Pathway 4	N	N	Unfavorable	≤ 0.5cm	N/A	N	No	2	4
				≤ 0.5cm	N/A	M	C	0	0
				> 0.5 cm to 1.0cm	N/A	N or M	C	4	2
				>1.0 cm	N/A	N or M	C	17	37
				N/A	N/A	P	C	6	15
			Favorable	≤ 0.5cm	N/A	N	No	0	0
				≤ 0.5cm	N/A	M	C	0	0
				> 0.5 cm to 1.0cm	N/A	N or M	C	0	0
				≥ 1.0cm	N/A	N or M	C	0	0
				N/A	N/A	P	C	0	0

ER: Estrogen Receptor; PR: Progesterone receptor; HER2: Human Epidermal Growth Factor Receptor 2; N/A: Not applicable; P: Positive; N: Negative; C: Close; M: Micrometastasis

Unfavorable (U): Ductal, Lobular, Mixed, Metaplastic, Medullary; Favorable (F): Tubular, Colloid; E: Endocrine Therapy; C: Chemotherapy; NCCN: National Comprehensive Cancer Network

Table 2. Demographic characteristics of participants by race

Characteristic, %	White (N=329)	AA (N=297)
Age at Diagnosis in years		
<40 years	8.5	11.1
40-44	10.6	9.1
45-49	16.7	10.8
50-54	16.4	15.2
55-59	13.7	20.5
60-64	14.6	17.2
65-69	9.4	4.4
≥ 70 years	10.0	11.8
Marital Status		
Married/Living as married	66.6	37.7
Single/Widowed	21.6	28.6
Separated/Divorced	7.6	24.2
Unknown	4.3	9.4
Education		
High School/GED graduate or less	1.8	10.1
Technical/Vocational School	18.8	28.6
Some College	22.5	24.2
College Graduate	29.8	17.2
Post Graduate Degree	22.8	10.4
Unknown	4.3	9.4
Annual Income		
<$35,000	7.9	33.3
$35,000-$69,999	17.9	24.6
≥ $70,000	62.9	24.2
Unknown	11.2	17.8
Primary Health Insurance		
Medicaid	2.1	4.7
Medicare	15.5	18.5
Private	78.1	63.3
No Insurance/Charity	2.7	10.4
Unknown	1.5	3.0
Type of Hospital Facility		
Non-teaching (community-based)	35.6	43.1
Teaching	59.3	51.2
Unknown	5.2	5.7

Table 3. Clinical characteristics of participants by race

Characteristic, %	White (N=329)	AA (N=297)
Mode of Detection		
Patient finding	35.6	48.8
Physician finding	6.1	3.7
Screening Mammography	56.5	45.8
Other	1.8	1.7
Menopause		
Pre	34.7	28.3
Peri	12.2	13.5
Post	53.2	58.2
Family History		
Yes	44.7	36.4
No	55.3	63.6
Prior Benign Breast Disease History		
Yes	35.3	33.0
No	64.7	67.0
Count of Comorbity		
0	29.8	14.5
1 to 2	47.1	49.8
≥ 3	23.1	35.7

Table 4. Tumor characteristics of participants by race

Characteristic, %	White (N=329)	AA (N=297)
Tumor Grade		
Well differentiated	25.2	11.8
Moderately differentiated	41.6	40.4
Poorly differentiated	28.3	42.1
Unknown	4.9	5.7
Estrogen & Progesterone Receptor Status		
One positive	9.1	16.2
Both positive	76.0	55.6
Both negative	14.9	27.3
Not Available	0.0	1.0
HER2 Receptor Status		
Positive	14.6	18.2
Negative	82.7	77.1
Not Available	2.7	4.7
Triple Negative	9.1	20.2
AJCC stage		
Stage 1	63.2	46.8
Stage IIA	24.0	35.0
Stage IIB	10.0	14.1
T3N1M0	1.8	2.0
Unknown	0.9	2.0
Tumor Size		
$\leq .5$cm	14.0	15.2
$> .5$ to ≤ 1.0cm	28.6	13.8
> 1.0cm to ≤ 2.0 cm	35.0	31.3
> 2.0 cm to ≤ 5.0 cm	19.8	36.0
> 5cm	2.7	3.7
Node Status		
Negative	74.5	71.7
Micrometastasis	7.0	3.7
Positive	17.9	22.9
Unknown	0.6	1.7
Margin Status		
Positive	3.6	3.7
Close	10.3	12.5
Negative	85.7	83.2
Unknown	0.3	0.7
Tumor Histology		
Ductal/lobular/mixed/medullary	98.5	99.0
Tubular/colloid	1.5	1.0

Table 5. Physician Recommendation of Optimal Treatments by Race based on NCCN "standard" treatment guidelines

Optimal Treatment Recommended, %	White (N=329)	AA (N=297)	*P-value**
SURGERY	99.7	100.0	*0.3417*
ADJUVANT RADIATION THERAPY	88.4	86.5	*0.4777*
CHEMOTHERAPY	96.0	94.3	*0.1855*
ENDOCRINE TREATMENT	97.0	93.3	*0.0704*
MONOCLONAL TREATMENT	99.1	96.3	*0.0171*
OVERALL OPTIMAL TREATMENT	83.9	83.2	*0.6023*

P-values from χ^2 test of indicated race

Table 6. Patient receipt after physicians recommended optimal treatments based on NCCN "standard" treatment guidelines, by race

Optimal Treatment Received, %	White (N=276)	AA (N=247)	*P-value**
SURGERY	100	99	*0.1342*
ADJUVANT RADIATION THERAPY	97	96	*0.0496*
CHEMOTHERAPY	94	87	*0.0125*
ENDOCRINE TREATMENT	97	91	*0.0128*
MONOCLONAL TREATMENT	100	97	*0.0107*
OVERALL OPTIMAL TREATMENT	92	88	*0.0808*

P-values from χ^2 test of indicated race

Table 7. Relative Risks and 95% CI for physician not recommending and patient not receiving overall optimal treatment according to NCCN guidelines

Variables	"Standard" Treatment Plan			
	Physician Not Recommending		Patient Not Receiving	
	Unadjusted RR (95% CI)	Adjusted RR (95% CI)*	Unadjusted RR (95% CI)	Adjusted RR (95% CI)*
Race				
White	1.00	1.00	1.00	1.00
AA	1.06 (0.74, 1.52)	0.89 (0.56, 1.43)	1.60 (0.94, 2.71)	.94 (0.88, 1.01)
Age at Diagnosis				
<45 years	0.81 (0.51, 1.29)	0.81 (0.55, 1.21)	1.25 (0.52, 3.03)	1.00 (0.91, 1.09)
45-54 years	0.58 (0.35, 0.96)	0.55 (0.36, 0.83)	1.24 (0.55, 2.79)	0.98 (0.89, 1.08)
55-64 years	0.70 (0.40, 1.24)	0.49 (0.19, 1.27)	1.12 (0.50, 2.50)	1.01 (0.96, 1.06)
≥ 65 years	1.00	1.00	1.00	1.00
Income				
<$50,000	1.35 (0.92, 1.98)	1.21 (0.79, 1.85)	1.65 (.92, 2.96)	.96 (0.90, 1.02)
≥ $50,000	1.00	1.00	1.00	1.00
Primary Insurance				
Private	1.00	1.00	1.00	1.00
Medicaid	1.35 (0.55, 3.34)	1.22 (0.48, 3.05)	3.10 (1.39, 6.89)	0.91 (0.67, 1.23)
Medicare	1.14 (0.70, 1.85)	1.47 (0.63, 3.46)	0.72 (0.31, 1.65)	1.04 (0.99, 1.09)
No Insurance/Charity	2.19 (1.31, 3.67)	2.01 (1.29, 3.13)	1.56 (0.60, 4.06)	0.95 (0.79, 1.14)
Count of Comorbidity				
0	1.00	1.00	1.00	1.00
≥ 1	0.86 (0.57, 1.30)	1.04 (0.64, 1.67)	1.30 (.65, 2.59)	1.02 (0.94, 1.10)

* RRs adjusted for all variables in the table

Table 8. **Relative Risks and 95% CI for physician not recommending optimal treatments for early stage breast cancer among AA compared to whites based on NCCN "standard" treatment guidelines**

Category of optimal treatments	Relative Risk (95% Confidence Intervals)
Optimal Radiation	1.09 (0.70, 1.69)
Optimal Chemotherapy	0.94 (0.35, 2.48)
Optimal Endocrine Therapy	1.53 (0.41, 5.63)
Optimal Monoclonal Therapy	1.61 (0.36, 7.13)

Table 9. **Relative risk of patients not receiving treatments after physicians recommended optimal treatments for early breast cancer among AA compared to whites based NCCN "standard" treatment guidelines**

Category of optimal treatments	Relative Risk (95% Confidence Intervals)
Optimal Radiation	0.71 (0.24, 2.15)
Optimal Chemotherapy	1.95 (1.00, 3.78)
Optimal Endocrine Therapy	2.93 (0.57, 15.00)
Optimal Monoclonal Therapy	---

Table 10. Physician Recommendation of Optimal Treatments by Race based on NCCN "standard with additional" treatment guidelines

Optimal Treatment Recommended, %	White (N=329)	AA (N=297)	P-value*
SURGERY	99.7	100.0	*0.3417*
ADJUVANT RADIATION THERAPY	88.4	86.5	*0.4777*
CHEMOTHERAPY	77.5	82.2	*0.0392*
ENDOCRINE TREATMENT	97.0	93.3	*0.0704*
MONOCLONAL TREATMENT	99.1	96.3	*0.0171*
OVERALL OPTIMAL TREATMENT	66.3	71.0	*0.2977*

*P-values from χ^2 test of indicated race

Table 11. Patient receipt after physicians recommended optimal treatments based on NCCN "standard with additional" treatment guidelines, by race

Optimal Treatment Received, %	White (N=218)	AA (N=211)	P-value*
SURGERY	100.0	99.1	*0.1496*
ADJUVANT RADIATION THERAPY	96.8	94.8	*0.0721*
CHEMOTHERAPY	89.4	78.7	*0.0075*
ENDOCRINE TREATMENT	96.8	90.0	*0.0166*
MONOCLONAL TREATMENT	100.0	96.7	*0.0253*
OVERALL OPTIMAL TREATMENT	88.1	78.7	*0.0088*

*P-values from χ^2 test of indicated race

Table 12. Relative Risks and 95% CI for physician not recommending and patient not receiving overall optimal treatment according to NCCN guidelines

| | "Standard with additional" Treatment Plan | | | |
| | Physician Not Recommending | | Patient Not Receiving | |
Variables	Unadjusted RR (95% CI)	Adjusted RR (95% CI)*	Unadjusted RR (95% CI)	Adjusted RR (95% CI)*
Race				
White	1.00	1.00	1.00	1.00
AA	0.86 (0.68, 1.10)	0.80 (0.61, 1.07)	1.79 (1.15, 2.79)	0.93 (0.84, 1.03)
Age at Diagnosis				
<45 years	1.00	1.00	1.00	1.00
45-54 years	1.03 (0.71, 1.51)	1.02 (0.73, 1.42)	0.97 (0.51, 1.86)	1.02 (0.92, 1.14)
55-64 years	1.06 (0.73, 1.53)	1.03 (0.71, 1.49)	1.07 (0.57, 2.01)	1.01 (0.89, 1.13)
≥ 65 years	1.82 (1.28, 2.60)	1.26 (0.74, 2.13)	1.86 (0.97, 3.57)	1.11 (1.00, 1.24)
Income				
<$50,000	1.29 (1.00, 1.68)	1.22 (0.91, 1.65)	2.38 (1.48, 3.83)	0.90 (0.78, 1.03)
≥ $50,000	1.00	1.00	1.00	1.00
Primary Insurance				
Private	1.00	1.00	1.00	1.00
Medicaid	1.11 (0.56, 2.20)	1.05 (0.56, 1.97)	2.40 (1.12, 5.16)	0.99 (0.70, 1.40)
Medicare	1.79 (1.39, 2.31)	1.36 (0.88, 2.12)	1.80 (1.06, 3.05)	0.87 (0.72, 1.05)
No Insurance/Charity	1.30 (0.82, 2.06)	1.28 (0.86, 1.92)	1.38 (0.60, 3.19)	0.96 (0.77, 1.19)
Count of Comorbidity				
0	1.00	1.00	1.00	1.00
≥1	1.12 (0.83, 1.50)	1.03 (0.71, 1.47)	1.34 (0.77, 2.34)	0.98 (0.89, 1.08)

* RRs adjusted for all variables in the table

Table 13. Relative Risks and 95% CI for physician not recommending optimal treatments for early breast cancer among AA compared to whites based on NCCN "standard with additional" treatment guidelines

Category of optimal treatments	Relative Risk (95% Confidence Intervals)
Optimal Radiation	1.09 (0.70, 1.69)
Optimal Chemotherapy	0.71 (0.50, 1.01)
Optimal Endocrine Therapy	1.53 (0.41, 5.63)
Optimal Monoclonal Therapy	1.61 (0.36, 7.13)

Table 14. Relative risk of patients not receiving treatments after physicians recommended optimal treatments for early breast cancer among AA compared to whites based NCCN "standard with additional" treatment guidelines

Category of optimal treatments	Relative Risk (95% Confidence Intervals)
Optimal Radiation	0.91 (0.31, 2.65)
Optimal Chemotherapy	1.92 (1.15, 3.20)
Optimal Endocrine Therapy	5.44 (0.64, 46.10)
Optimal Monoclonal Therapy	---

References

1.   Tammemagi CM, Nerenz D, Neslund-Dudas C, Feldkamp C, Nathanson D. Comorbidity and survival disparities among black and white patients with breast cancer. JAMA 2005;294:1765-72.

2.   Malin JL, Schneider EC, Epstein AM, Adams J, Emanuel EJ, Kahn KL. Results of the National Initiative for Cancer Care Quality: how can we improve the quality of cancer care in the United States? J Clin Oncol 2006;24:626-34.

3.   Dignam JJ. Efficacy of systemic adjuvant therapy for breast cancer in African-American and Caucasian women. J Natl Cancer Inst Monogr 2001:36-43.

4.   Dignam JJ, Redmond CK, Fisher B, Costantino JP, Edwards BK. Prognosis among African-American women and white women with lymph node negative breast carcinoma: findings from two randomized clinical trials of the National Surgical Adjuvant Breast and Bowel Project (NSABP). Cancer 1997;80:80-90.

5.   Altekruse S, Kosary C, Krapcho M, *et al.* SEER Cancer Statistics Review, 1975-2007, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2007/, based on November 2009 SEER data submission, posted to the SEER web site, 2010.

6.   Muss HB, Hunter CP, Wesley M, *et al.* Treatment plans for black and white women with stage II node-positive breast cancer. The National Cancer Institute Black/White Cancer Survival Study experience. Cancer 1992;70:2460-7.

7.   Dunmore C, Plummer P, Regan G, Mattingly D, Jackson S, Millikan R. Re: race and differences in breast cancer survival in a managed care population. J Natl Cancer Inst 2000;92:1690-1.

8.   Mandelblatt JS, Kerner JF, Hadley J, *et al.* Variations in breast carcinoma treatment in older medicare beneficiaries: is it black or white. Cancer 2002;95:1401-14.

9.   Hershman D, McBride R, Jacobson JS, *et al.* Racial disparities in treatment and survival among women with early-stage breast cancer. J Clin Oncol 2005;23:6639-46.

10.   Cianfrocca M, Goldstein LJ. Prognostic and predictive factors in early-stage breast cancer. Oncologist 2004;9:606-16.

11.   Ambrosone CB, Ciupak GL, Bandera EV, *et al.* Conducting Molecular Epidemiological Research in the Age of HIPAA: A Multi-Institutional Case-Control Study of Breast Cancer in African-American and European-American Women. J Oncol 2009;2009:871250.

12.   Clinical Practice Guidelines in Oncology. Breast Cancer. (Accessed 2010, at http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf V. 2. .)

13.   Dunne C, Burke JP, Morrow M, Kell MR. Effect of margin status on local recurrence after breast conservation and radiation therapy for ductal carcinoma in situ. J Clin Oncol 2009;27:1615-20.

14.   Singletary SE. Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. Am J Surg 2002;184:383-93.

15.   Freedman RA, Virgo KS, He Y, *et al.* The association of race/ethnicity, insurance status, and socioeconomic factors with breast cancer care. Cancer 2011;117:180-9.

16.   Harlan LC, Greene AL, Clegg LX, Mooney M, Stevens JL, Brown ML. Insurance status and the use of guideline therapy in the treatment of selected cancers. J Clin Oncol 2005;23:9079-88.

17. Wu XC, Lund MJ, Kimmick GG, *et al.* Influence of race, insurance, socioeconomic status, and hospital type on receipt of guideline-concordant adjuvant systemic therapy for locoregional breast cancers. J Clin Oncol 2012;30:142-50.

18. Balasubramanian BA, Demissie K, Crabtree BF, Ohman Strickland PA, Kohler B, Rhoads GG. Racial differences in adjuvant systemic therapy for early breast cancer among Medicaid beneficiaries. Breast J 2010;16:162-8.

19. Freedman RA, Virgo KS, He Y, *et al.* The association of race/ethnicity, insurance status, and socioeconomic factors with breast cancer care. Cancer 2010:n/a-n/a.

20. Worthington J, Waterbor JW, Funkhouser E, Falkson C, Cofield S, Fouad M. Receipt of standard breast cancer treatment by African American and White women. Int J Med Sci 2008;5:181-8.

21. Shavers VL, Harlan LC, Stevens JL. Racial/ethnic variation in clinical presentation, treatment, and survival among breast cancer patients under age 35. Cancer 2003;97:134-47.

22. Bickell NA, Wang JJ, Oluwole S, *et al.* Missed opportunities: racial disparities in adjuvant breast cancer treatment. J Clin Oncol 2006;24:1357-62.

23. Early BCTCG. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;365:1687-717.

24. Nielsen HM, Overgaard M, Grau C, Jensen AR, Overgaard J. Study of failure pattern among high-risk breast cancer patients with or without postmastectomy radiotherapy in addition to adjuvant systemic therapy: long-term results from the Danish Breast Cancer Cooperative Group DBCG 82 b and c randomized studies. J Clin Oncol 2006;24:2268-75.

25. Clarke M, Collins R, Darby S, *et al.* Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;366:2087-106.

26. Bickell NA, Aufses AH, Jr., Chassin MR. The quality of early-stage breast cancer care. Ann Surg 2000;232:220-4.

27. Breen N, Wesley MN, Merrill RM, Johnson K. The relationship of socio-economic status and access to minimum expected therapy among female breast cancer patients in the National Cancer Institute Black-White Cancer Survival Study. Ethn Dis 1999;9:111-25.

28. Bradley CJ, Given CW, Roberts C. Race, socioeconomic status, and breast cancer treatment and survival. J Natl Cancer Inst 2002;94:490-6.

29. DeSantis C, Siegel R, Bandi P, Jemal A. Breast cancer statistics, 2011. CA Cancer J Clin 2011;61:409-18.

RACIAL DIFFERENCES IN TIME TO DIAGNOSIS AND TREATMENT

INITIATION FOR EARLY STAGE BREAST CANCER

by

PRETHIBHA GEORGE

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Written under the direction of

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ABSTRACT OF MANUSCRIPT 2 OF 3

RACIAL DIFFERENCES IN TIME TO DIAGNOSIS AND TREATMENT

INITIATION FOR EARLY STAGE BREAST CANCER

Dissertation Director:

Kitaw Demissie, MD, PhD

ABSTRACT

Introduction/Background: Delays in diagnosis and treatment may contribute to excess deaths among African-American (AA) breast cancer patients. The objective was to examine racial differences in time to diagnosis and treatment initiation for early stage breast cancer and examine predictors associated with increased time to diagnosis and treatment.

Methods: This is a retrospective cohort study of 626 women who were newly diagnosed with invasive breast cancer during the period 2005-2010. They were identified from seven counties of eastern New Jersey through rapid case ascertainment methodology. For each AA woman age 18-85 years, a white woman within 5 years of age who resided in the same county was randomly selected. Time intervals were defined as days from symptom recognition to diagnosis (time to diagnosis), from biopsy-proven diagnosis to initial surgical treatment (time to surgery), from the end of the last chemotherapy cycle or after last surgery to initiation of radiation (time to radiation) and from last surgery to

initiation of chemotherapy (time to chemotherapy). Using linear regression, geometric

mean times (in days) were estimated.

Results: AA women experienced longer time to diagnosis and surgical treatment.   The

geometric mean days (95%CI) for whites and AAs in time to diagnosis was 35 (31, 40)

and 47 (41, 54); time to surgery was 28 (26, 30) and 33 (30, 35) respectively. No racial

differences were seen in time to chemotherapy or time to radiation treatment. Important

predictors of increased time included age at diagnosis, income, insurance, tumor

characteristics, and type of treatment facilities.

Conclusions: AA breast cancer patients experience longer time intervals in receiving

diagnosis and surgical treatment for breast cancer; interventions to reduce the time may

help narrow the racial gap in mortality between the races.

RACIAL DIFFERENCES IN TIME TO DIAGNOSIS AND TREATMENT

INITIATION FOR EARLY STAGE BREAST CANCER

Introduction

White women are diagnosed with breast cancer more often than African-American (AA) women (126.5 per 100,000 versus 118.3 in AA during 2003 to 2007)[1], but the mortality rates are higher in AA women. Since the 1980's the mortality gap between the two races has widened.[2] The age-adjusted mortality rate from 2003-2007 was 32.4 per 100,000 for AAs versus 23.4 per 100,000 for Whites.[2] During the period 1999-2006, the 5-year survival was higher for White women (90.5%) than for AA women (77.2%).[1,3] Possible reasons for these differences include the biological nature of the tumor[4-6], access to healthcare, socioeconomic factors[7-9], and disparity in treatment[10]. A potential mechanism that may also contribute to the racial disparity is delay in receipt of care.

Time to diagnosis and time to receipt of appropriate treatment has been used as a measure of quality of care[11] with a demonstrated (significant) impact on survival. A systematic review by Richards *et al.*, reports that a delay greater than 3 months from onset of symptoms to diagnosis or treatment has an adverse impact on survival.[12] Few studies have explored racial inequalities in delay of diagnosis and treatment[13-17] and most do not differentiate the time between the different treatments that are given to patients, and instead only look at treatment delay by first treatment given (surgery or neo-adjuvant chemotherapy or radiation). Gwyn *et al.* showed that AAs are more likely to have an increase in treatment delay (≥ 1month) compared to whites.[15] Hoffman *et al.* conducted a

study in the District of Columbia examining the effect of race and insurance on time to diagnosis. They found privately insured AAs have significantly longer diagnosis times compared to privately insured whites.[13] Most recently, studies have looked specifically at racial differences in delay of time to adjuvant chemotherapy and adjuvant radiation but results are not consistent.[17-19]

Access to care and socioeconomic status are important factors in studying the relationship between race and treatment delays. A more in-depth examination of time to diagnosis and treatment for loco-regional breast cancer is warranted as a possible explanation for mortality differences seen by race. This study takes advantage of the detailed records abstracted from both hospitals and outpatient clinics to examine this issue. The primary objective of this study is to explore racial differences in the time to receive a biopsy-proven diagnosis, initial surgical treatment, adjuvant chemotherapy and radiation. We also explored how various predictors of time differed between AAs and whites.

Materials and Methods

Study Population

Subjects who participated in the Women's Circle of Health Study (WCHS) and who consented to participate in this study the Breast Cancer Treatment Disparity Study (BCTDS) were recruited. The general methodology of subject recruitment for the WCHS study has been reported elsewhere.[20] In brief, the study is a 1:1 matched retrospective cohort study (AA to White). Patients residing in northern and central New Jersey who were diagnosed with stage I, II, and $T_3N_1M_0$ breast cancer during 2005-2010 were identified through rapid case ascertainment by the New Jersey State Department of Health and Senior Services (NJDHSS). Subjects were excluded if they were neither AA nor white, non-residents of NJ, diagnosed with inflammatory breast cancer, diagnosed with breast cancer with histologic features other than adenocarcinoma, were diagnosed with any other cancer besides non-melanoma skin cancer.

All African-American women who were younger than 85 years of age and diagnosed with invasive breast cancer were first identified. For each AA woman with breast cancer, a white woman within ($\pm$ 5 years of age) and who resided in the same county was randomly selected from the pool of potential white breast cancer patients. Subjects who agree to be contacted were then telephoned by WCHS research staff to arrange schedules for an in-person interview at home. During the home interview, trained WCHS interviewers administered questionnaires. At the same time, they also requested, participation of study subjects in BCTDS. Patients who agreed to participate gave consent for the release of their medical records and also agreed to be contacted by

BCTDS staff for a follow-up telephone interview. A total of 626 women have been

included in the BCTDS study thus far (297 AAs and 329 whites).

Medical records were obtained from each patient's primary physician, surgical

oncologist, medical oncologist and radiation oncologist. Trained personnel abstracted

socio-demographic and health related characteristics (age at diagnosis, comorbidities,

mode of symptom recognition), and tumor characteristics (hormone receptor status, her-

2-neu status, tumor grade, size, lymph node status). Dates were documented at the

following points: symptom recognition and/or abnormal mammogram, initial consult

with primary physician, date of surgery and/or first day of chemotherapy, hormonal

therapy or radiation therapy. Patient data such as race, income, education, and

menopause status were collected through patient interviews conducted by WHCS.

Additionally, a semi-structured interview was conducted on 360 of the women

who participated in the BCTDS (AA: 175; White: 185). The aim of the interview was to

examine factors that influenced their surgical treatment choice (BCS versus mastectomy).

Factors such as surgeon's recommendation, family's advice, job related demands and

situational barriers such as caring for a dependent and issues with transportation to the

treatment facility were explored with the patients. The study was approved by

Institutional Review Boards (IRB) at both the University of Medicine and Dentistry of

New Jersey (UMDNJ) and New Jersey Department of Health and Senior Services (for

NJSCR).

Outcome variables

The four outcomes examined include (Figure 1):

1) Time to diagnosis: defined as the time interval in days from date of abnormal symptom recognition to the date of biopsy-proven diagnosis.   Mode of discovery of first symptom of breast cancer was recorded if found by patient, physician, or screening mammography. If the exact date or the abnormal finding was not documented, but the month and year were known then the 15th of the month was used as a proxy.

2) Time to surgical treatment: defined as the time interval in days from date of biopsy proven diagnosis to date of first surgical procedure (BCS or total mastectomy). Since time to treatment was the goal of the study, further restrictions for this variable were taken: patients were excluded if the first surgery was on the same date as their biopsy (n=3) or their biopsy was an excisional biopsy with no other subsequent surgical treatments (n=22).

3) Time to adjuvant chemotherapy: defined as the time interval in days from date of the last surgery (either the first surgery or, when appropriate, the last re-excision) to date of administration of the first dose of adjuvant chemotherapy.

4) Time to adjuvant radiation treatment: defined as either the time interval in days from date of the last surgery (either BCS or the last re-excision after BCS) or date of the last dose of chemotherapy administered to the start date of radiation treatment.

All four of the outcome measures were investigated as continuous variables as well as in a categorical manner (initiation of diagnosis and treatment in 30 days or greater, 60 days or greater, and 90 days or greater). Patients who either received chemotherapy before surgery (n= 35) or patients who received radiation before adjuvant chemotherapy (n=12) were excluded from this study as they were not representative of the rest of the study population.

Main explanatory variable

Self-reported race was the explanatory variable of interest, categorized as non-Hispanic white (W) or non-Hispanic African-American (AA).

Predictors of delay

1. Patient/demographic characteristics: These variables included age at diagnosis, annual income, education, and primary health insurance (private and non-private which includes Medicaid, Medicare, charity, or no insurance).

2. Competing priorities: The following three predictors were collected from the semi-structured interviews: caring for dependents ("At the start of your treatment for breast cancer, was anyone dependent on you for their everyday care?") was noted as yes or no, problem with transportation to treatment facilities ("Was getting to and from the treatment facility a factor in your surgery decision?") recorded as yes or no, and job related demands ("If employed: Did your job influence your choice of treatment?") were categorized as yes or no.

3. Clinical/tumor characteristics: Clinical variables included mode of tumor discovery, family history of breast cancer, menopausal status (yes or no), type of surgery (breast conserving surgery or mastectomy) and radiation sequence (radiation after chemotherapy or radiation after surgery). The total number of co-morbidities for a patient was based on how many of the following morbidity categories were documented in the hospital records: cerebral vascular accident, congestive heart failure, diabetes mellitus, gastro-intestinal

disease, hypertension, ischemic heart disease, malignancies, organic heart

disease, peripheral vascular disease, primary arrhythmias/conduction

problems, renal disease, respiratory problems, neurologic disorders,

immunologic/connective tissue disorders, endocrine disorders (other than

diabetes), and moderate/severe liver disease. Tumor variables of interest

included tumor size, tumor grade, estrogen/progesterone status, and lymph

node status (negative: zero lymph nodes positive; positive: one to three

positive nodes).

4. <u>Health service factors:</u> Hospital facility

type (facility where patient underwent surgery) or radiation facility type

(facility where patient received radiation) was categorized as either a teaching

hospital or community-based hospital. The designation was based on the

American College of Surgeons Commission on Cancer accreditation criteria

(website http://www.facs.org).

Statistical Analysis

The data was analyzed with linear and binomial regression models to find racial

differences for each outcome variable (time to diagnosis, time to surgical treatment, time

to chemotherapy, and time to radiation treatment). Log transformations of time (in days)

were used to satisfy the normality and constant variance assumption of the residuals.

Any values lower than one was changed to one to calculate geometric mean days. The

relationship between each outcome variable and race were also modeled by using a

binomial regression model to find the risk of delay at three different cut-off days: delay

of ≥ 30 days versus < 30 days, delay of ≥ 60 days versus < 60 days, and delay of ≥ 90

days versus < 90 days. A multivariable linear regression model was used to identify the overall predictors of delay for diagnosis and treatments, as well as stratified by race.

The following predictors were examined for time to diagnosis: age at diagnosis, income, education, insurance, mode of detection, family history of breast cancer, comorbidity, tumor size, tumor grade, lymph node status, demand of caring for a dependent, transportation difficulties, and job-related demands.

The following predictors were examined for time to surgery, chemotherapy and/or radiation: age at diagnosis, income, education, insurance, family history of breast cancer, comorbidity, tumor size, tumor grade, lymph node status, type of surgery received, type of treatment facility, demand of caring for a dependent, transportation difficulties, and job-related demands.

Analyses were performed using SAS software, version 9.2 (SAS Institute Inc., Cary, NC).

Results

The study sample consisted of 582 women (AA: 273, White: 309) after excluding patients who received neo-adjuvant chemotherapy or radiation before adjuvant chemotherapy. Tables 1 and 2 show the demographic characteristics of the participants and clinical and tumor characteristics by race. Most AA did not have a college degree (62%), had non-private insurance (35%) and were categorized in annual income bracket of less than $70,000 (57%). In both races, screening mammography was the most frequent method of breast cancer detection (Table 2). More AAs were diagnosed with larger tumor sizes (> 2 cm) and had either moderately or poorly differentiated tumor grade. They were also more likely to be estrogen receptor, progesterone receptor and Her-2/neu negative amplification negative ("triple negative").

Table 3 shows the unadjusted geometric mean days for the overall study population and by race for time to diagnosis and treatment. Dates for abnormal symptom recognition were missing for 6 white women and 14 AA women. Time to receiving a biopsy-proven diagnosis was longer for AAs compared to whites (p=0.0018). AAs took a geometric mean of 47 days (95% CI: 41, 54) compared to whites who took 35 days (95% CI: 31, 40). Time to first surgical treatment was also longer for AAs (p =0.0047). AAs took an average (in terms of geometric means) 33 days compared to whites (28 days) to surgery from a diagnostic biopsy. About 291 women received chemotherapy in this study after their last surgical treatment (AA: 147; W: 144). No statistically significant differences were seen between the races. The overall median time was 42 days to receiving the first dose of chemotherapy. Among 389 women who underwent BCS for definitive surgery, 328 received radiation treatment either after their last surgery

or after their last dose of chemotherapy (AA: 148; W: 180). Similar to results in time to

chemotherapy, the geometric mean days were not significantly different by race for

adjuvant radiation treatment (p=0.2416).

Table 4 depicts time to diagnosis and treatment categorized by three cumulative

cut-off time periods. Similar to the results seen in Table 3, significant racial differences

are seen for time to diagnosis at all three time periods. AAs are 43% more likely to

undergo a diagnostic biopsy $\geq$ 90 days after abnormal symptoms are detected for invasive

cancer (RR: 1.43 (95% CI: 1.03, 1.99)).   Racial differences were observed for time to

surgical treatment for $\geq$ 60 days and for $\geq$ 90 days. AAs are 2.5 times more likely than

whites to take more than 60 days between diagnostic biopsy and first surgical treatment

(RR: 2.49 (95% CI: 1.57, 3.97)). Nevertheless, 93% of AAs and 99% of whites in the

study sample underwent their surgical treatment within 90 days from diagnostic biopsy.

No statistically significant differences were seen for time to chemotherapy or for time to

adjuvant radiation treatment when time was categorized into cumulative time periods.

Table 5 shows the adjusted geometric mean days between predictors of time to

diagnosis and treatment. Important predictors of increased time to diagnosis were low

income, patient detection of abnormal symptoms, and small tumor sizes. Time to

diagnosis in patients categorized with < $70,000 annual income was 46 days (95% CI:

36.8, 58.1) compared to those with $\geq$ $70,000 annual income at 37 days (95% CI: 29.5,

46.9). When abnormal symptoms of breast cancer were patient-detected a geometric

mean of 46 days (95% CI: 36.5, 59.1) was observed as compared to detection by clinical

breast exam or screening mammography (37 days; 95% CI: 30, 46)). Those with smaller

tumor size (≤ 1cm) took longer time (46 days) compared to those with larger tumor sizes (37 days).

An overall predictor of increased time to surgical treatment was the type of initial surgical treatment received. Patients underwent mastectomy 41 geometric mean days after their biopsy compared to those who received BCS (28 days; p < 0.001). For time to chemotherapy, those with non-private insurance had a geometric mean of 51 days when compared to those with private insurance (45 days; p=0.0805).

Significant predictors of increased time to radiation treatment were age at diagnosis under 50 years (41 days; 95% CI: 34, 49) compared to greater than 65 years of age (27 days; 95% CI: 21, 34); tumor size (those with sizes > 1 cm took 39 days compared to those with ≤ 1cm (31 days)); type of radiation facility (those who received radiation in a community based facility took 38 days compared to those who got treated at teaching facilities took 31 days); and the sequence of radiation (those who received radiation after chemotherapy were in 29 days as compared to those treated subsequent to last surgical procedure (42 days)).

Table 6 displays the important independent predictors of time to diagnosis and treatment when stratified by race (see appendix for complete list of predictors). AAs took longer time to receiving diagnostic biopsy when tumor size ≤ 1cm compared to > 1 cm (p=0.0493). Though not significant, time to biopsy for AA's ≥ 65 years of age was (37 days versus 56 days; p=0.4086) as compared to those < 50 years of age. This pattern was also seen for time to radiation treatment; time was shorter for older AAs took less time (16 days; 95% CI: 10, 27; p=0.0058) as compared to those under 50 years of age (38 days; 95% CI: 27, 52). White women who received surgical treatments at community-

based hospitals had shorter time to surgery compared to teaching-based facilities (p= 0.0282). Primary insurance was another predictor of significance, especially for AAs. Those with non-private insurance took longer geometric mean days in time to chemotherapy (p =0.0692) and radiation (p=0.0067).   Another predictor for time to chemotherapy for AAs was the demand on a patient in caring for dependents. AAs without this demand had longer time to chemotherapy as compared to those with this demand (p=0.0508).   Other predictors of radiation by race included family history and type of radiation facility. AAs who had a family history of breast cancer took less time (24 days) to radiation compared to those without any history (31 days; p=0.0517). In both races, those who received radiation at community-based hospitals had increased time to radiation compared to teaching hospital facilities. AAs and whites receiving radiation after their last dose of chemotherapy had shorter time as compared to those receiving radiation after their last surgery (p < 0.10).

Discussion

The purpose of this study was to determine if racial disparity exists in delaying diagnosis and/or treatment in loco-regional invasive breast cancer patients and to determine the predictors that are significantly associated with these delays. In our study, AAs were more likely to experience diagnostic delay and surgical treatment delay greater than 60 days or 90 days as compared to their white cohorts. However, AAs were comparable with white women in receiving radiation treatment and chemotherapy within 60 days. The predictors of delay included socioeconomic status, tumor characteristics and the type of facility for treatment.

Other studies have shown similar racial differences in time to receiving a diagnostic biopsy.[13-15,21] Early detection of cancer can lead to effective treatment and thus, better survival. Yet, AAs are more likely to present with late stage cancer that is a contributing factor to the high mortality found in this group.[22,23] Racial differences in treatment delay have been reported though the results are not consistent.[14,17-19,21,24-26] In our study, AAs were more likely to undergo surgery more than 60 days (RR: 2.49; 95% CI: 1.57, 3.97) or 90 days (RR: 10.1; 95% CI: 2.37, 43.2) after their biopsy. Gorin *et al.* reported overall treatment delay in AAs after adjustment of clinical and socioeconomic status. Though their definition of treatment included surgery, radiation or chemotherapy, the results were similar to the current study in that more AAs experienced clinical delays compared to white women.[14] Another study, though not statistically significant, found white women experienced longer delay in treatment compared to AAs (20.9% versus 11.3%, p-value=.0890).[21]

Barriers that lead to delay in diagnosis in AAs are multi-faceted and include access to care issues. AAs in this study were more likely to have lower education, be in lower income bracket, and have non-private insurance (government insurance or no insurance). Consistently, literature has shown that medically underserved women, who include minorities, are more disadvantaged in regard to diagnosis, treatment and survival.[8,27] In this study, patients with an annual income of less than $70,000 or those with non-private insurance took longer time to undergo biopsy.

Other patient factors such as cultural beliefs/perception have been shown to adversely influence screening behavior but were not factors explored for the current study.[28] A study performed at East Carolina University demonstrated that psychosocial and cultural influences in combination with socioeconomic factors were related to the late stage presentation of breast cancer in AAs.[29] Forty-eight percent of AAs found the abnormality themselves and were less likely to have it detected by a physician or by screening mammography. Gwyn *et al.* also found mode of detection to be a factor in predicting diagnosis delay diagnosis in AAs.[15] Though our results were not significant, we found that when a patient detected their cancer themselves, time to diagnosis was longer as compared to detection through clinical breast exam or screening mammography. Also, our current study showed that patients with smaller tumor sizes ($\leq$ 1 cm) were more likely to have longer time to diagnosis. AAs were significantly more likely to have almost two months longer time to diagnosis when they had smaller tumor sizes compared to larger tumors. It could be that with larger tumors, biopsies can be performed in an office by the surgeon rather than needing to schedule with radiology or coordinate operation room time.

A consistent predictor of delay in treatment in our study was health insurance. The role of insurance has been shown to play a role in receipt of breast cancer treatment in other studies.[7,30,31] We found that AAs with non-private insurance were more likely to take longer time to obtain treatment. Barriers such as transportation availability and communication with physicians are possible additional reasons for delay.[32] During the semi-structured interviews, the majority of patients (>85%) in both whites and AAs, stated that transportation was not an issue in receiving treatment and was not a significant factor in predicting increased time to treatment. Patients diagnosed at younger age (< 65 years) in our study tended to have longer time to surgery and time to adjuvant radiation treatment as compared to those ≥ 65 years of age. In the older age group, a possible explanation is that fewer participants have the demands of a dependent; more than 90% of this age group reported that having a dependent to care for did not influence their treatment choices.

For white women, those who had their first surgical treatment at a teaching facility were more likely to take have an increased time to surgery. A finding by the Task Force on Academic Health Centers states that proportion of uninsured patients served by academic health centers is increasing.[33] This explanation does not clarify the results since most white women in our study with private insurance went to teaching hospitals for their surgery. On the other hand, a national study done by Fedewa *et al.* reported that delays in treatment were more common in teaching facilities compared to community cancer centers.[19] A significant predictor of delay in surgery in this study and others has been the type of surgical treatment. Time to mastectomy was more than a month longer as compared to those who underwent BCS. [34,35] This could be due to additional time for

patient decisions, the consultation time for reconstructive surgery after mastectomy, and coordination time between two surgeons.

Significant predictors of time to radiation included type of radiation facility, tumor size and the sequence of radiation. Different communication methods may explain the difference in time seen in community-based hospitals versus teaching hospitals. Physicians at teaching hospitals may have their offices physically located within the building and therefore, more easily participate in same-day consultations via multidisciplinary clinics. Those who received radiation after the last surgery took two weeks longer to initiate radiation as compared to those who started radiation treatment after the last dose of chemotherapy. This is likely because after receiving the chemotherapy, no additional healing time at the surgical site is needed.[36]

Studies have shown mixed results in treatment delay and breast cancer outcome. A systematic review by Richards *et al.* indicated that a delay of greater than three months from onset of symptom recognition to diagnosis or treatment had significant effect on survival (OR: 1.24 (95% CI: 1.17, 1.30).[12] Hershman *et al.* reported that mortality increased in a sample of women older than 65 years when chemotherapy was delayed greater than 3 months.[25] A systematic review on delay in radiation treatment by Huang *et al.* found delay in initiating radiation treatment greater than 8 weeks is associated with higher 5 year local recurrence rate in breast cancer patients.[37] However, Brazda *et al.* found that treatment delay of greater than three months did not have an effect on overall breast cancer survival.[16] But the small sample size in the delayed (greater than three months) group may not have allowed for detection of survival impact.

Efforts to measure treatment quality include evaluating duration of time to deliver appropriate treatments. The American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) have established guidelines that adjuvant chemotherapy should begin within 120 days of diagnosis which allows for surgery and consultation of treatment options.[38] ASCO and NCCN have also suggested that adjuvant radiation should be started within one year of diagnosis which allows for surgical complications and/or prolonged chemotherapy treatment.[38] Two studies have reported that there is no improved survival among women who began chemotherapy within 90 days of surgery.[25,39]

Our study demonstrates racial disparity in delays to diagnosis as well as in undergoing first surgical treatment. But no differences were seen in the time to starting radiation or chemotherapy. Therefore, once a patient has started their initial surgical treatment they are more likely to continue in a timely manner to their next sequential treatments.

To help vulnerable patients receive appropriate and timely care, patient education must be implemented by physicians serving these populations through follow-up calls that encourage open-communications regarding health care. Patient navigation programs should target women who come in for initial screening or breast cancer biopsies and those more likely not to keep regular appointments for preventive care by providing education to reduce misconceptions about breast cancer screening and treatment. Holding community meetings/programs that invite community residents to meet with health educators, primary care physicians, and oncologists can increase greater awareness of programs such as National Breast and Cervical Cancer Early Detection Program

(NBCCEDP), and Breast and Cervical Care Prevention Act of 2000 that can impact timely care of these targeted women. Research has shown that it is vital that patients receive breast cancer diagnosis and treatment in a timely manner which can impact their survival, especially when greater than 90 days are taken before treatment is received. Future efforts should focus on elucidating and eliminating the multitude of barriers which may contribute to this disparity.

Tables and Figures

Figure 1. Defining Time to Diagnosis and Treatment Variables

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┌─────────────────────┐
│ Date of Abnormal    │
│ Symptom Recognition │
└─────────────────────┘
         │ Time to Diagnosis
         ▼
┌─────────────────────┐
│ Date of Biopsy Proven│
│ Diagnosis           │
└─────────────────────┘
         │ Time to Surgical treatment
         ▼
┌─────────────────────┐        Time to Chemotherapy*      ┌─────────────────────┐
│ Date of First       │ ──────────────────────────────▶  │ Start Date of       │
│ Definitive          │                                  │ Chemotherapy        │
│ Surgical Treatment  │        Time to Radiation Therapy* └─────────────────────┘
└─────────────────────┘ ──────────────────────────────▶           │ Time to Radiation Therapy**
                                                                    ▼
                                                          ┌─────────────────────┐
                                                          │ Start Date of       │
                                                          │ Radiation Therapy   │
                                                          └─────────────────────┘
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 *From last surgery
**From last dose of chemotherapy
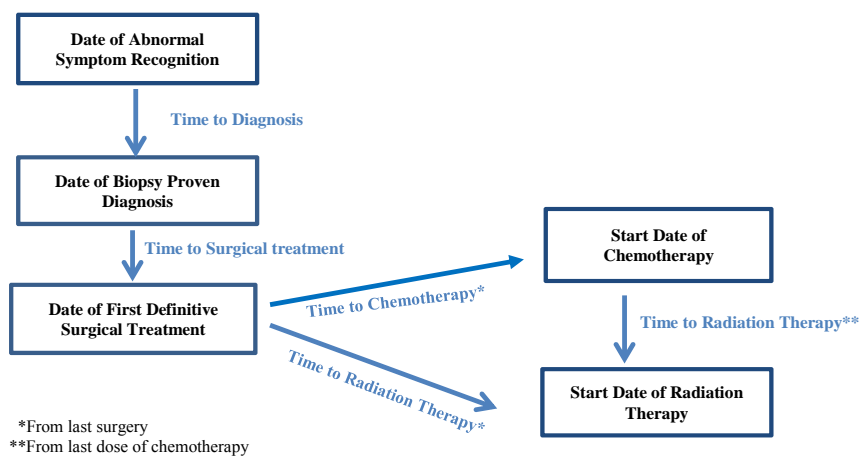
Table 1. Demographic characteristics of participants by race		
Characteristic, %	White (N=309)	AA (N=273)
Age at Diagnosis in years		
< 50	35.6	29.7
50-64	44.7	53.5
≥ 65	19.7	16.8
Marital Status	.	.
Married/Living as married	66.3	37.4
Single/Widowed	21.4	29.3
Separated/Divorced	7.8	23.1
Unknown	4.5	10.3
Education		
< 4 year College Education	42.4	62.3
≥ 4 year College Education	53.1	27.5
Unknown	4.5	10.3
Annual Income		
< $70,000	25.2	56.8
≥ $70,000	63.1	24.9
Unknown	11.7	18.3
Primary Health Insurance		
Private Insurance	78.0	62.3
Non-private	20.4	34.8
Unknown	1.6	2.9

AA: African-American

Table 2 Clinical and tumor characteristics of participants by race		
Characteristic, %	White (N=309)	AA (N=273)
Mode of Detection		
Patient finding	33.7	45.8
Doctor Finding /Screening	66.3	54.2
Menopause		
Pre	34.6	26.7
Peri	12.3	13.9
Post	53.1	59.3
Family History		
Yes	46.3	36.3
No	53.7	63.7
Count of Comorbidity		
0	29.4	14.3
≥ 1	70.6	85.7
Tumor Grade		
Well differentiated	26.5	12.8
Moderately or Poorly differentiated	68.3	81.7
Unknown	5.2	5.5
ER & PR Status		
One positive	9.1	16.5
Both positive	78.6	56.8
Both negative	12.3	26.0
Not Available	0.0	0.7
Her2 Status		
Positive	13.6	16.1
Negative	83.5	79.1
Not Available	2.9	4.8
Triple Negative	7.4	19.4
Tumor Size		
≤ 0.5cm	14.6	16.1
> 0.5 to ≤ 1.0cm	30.4	14.3
> 1.0cm to ≤ 2.0 cm	35.3	32.6
> 2.0 cm to ≤ 5.0 cm	18.1	34.1
> 5cm	1.6	2.9
Node Status		
Negative	75.7	73.6
Positive	23.6	24.5
Missing	0.6	1.8

AA: African-American; ER: Estrogen Receptor; PR: Progesterone Receptor

Table 3. Mean, median and geometric mean (95% CI) in days by race for time to diagnosis and treatment

Outcome	Overall	White	AA
Time to Diagnosis			
Number of Subjects	557	299	258
Mean (SD) in Days	72 (89.9)	65 (87.4)	79 (92.3)
Median in Days	41	36	48
Unadjusted Geometric Mean Days (95%CI)		35 (31, 40)	47 (41, 54)
		p=0.0018	
Time to Surgery			
Number of Subjects	555	297	258
Mean (SD) in Days	37 (24.2)	33 (17.6)	41 (29.5)
Median in Days	31	30	32
Unadjusted Geometric Mean Days (95%CI)		28 (26, 30)	33 (30, 35)
		p=0.0047	
Time to Chemotherapy			
Number of Subjects	291	144	147
Mean (SD) in Days	47 (19.2)	46 (19.1)	48 (19.4)
Median in Days	42	41	43
Unadjusted Geometric Mean Days (95%CI)		42 (40, 45)	45 (42, 48)
		p=0.1564	
Time to Radiation Treatment			
Number of Subjects	328	180	148
Mean (SD) in Days	44 (24.8)	42 (20.7)	47 (28.7)
Median in Days	39	37	41
Unadjusted Geometric Mean Days (95%CI)		37 (34, 40)	40 (36, 44)
		p=0.2416	

SD: Standard Deviation; CI: Confidence Interval

Table 4. Unadjusted RR (95% CI) for time to diagnosis and treatment in African-American women compared to White women	
Time to Diagnosis	RR (95% CI)
≥ 30 days versus < 30 days	1.15 (1.02, 1.30)
≥ 60 days versus < 60 days	1.49 (1.16, 1.91)
≥ 90 days versus < 90 days	1.43 (1.03, 1.99)
Time to Surgery	
≥ 30 days versus < 30 days	1.16 (0.99, 1.37)
≥ 60 days versus < 60 days	2.54 (1.60, 4.04)
≥ 90 days versus < 90 days	10.3 (2.42, 44.10)
Time to Chemotherapy	
≥ 30 days versus < 30 days	1.04 (0.81, 1.33)
≥ 60 days versus < 60 days	1.01 (0.61, 1.69)
≥ 90 days versus < 90 days	1.76 (0.59, 5.26)
Time to Radiation	
≥ 30 days versus < 30 days	1.06 (0.92, 1.22)
≥ 60 days versus < 60 days	1.25 (0.84, 1.84)
≥ 90 days versus < 90 days	4.86 (1.40, 16.90)

Table 5. Adjusted geometric mean days (95% CI)^ for predictors associated with time to diagnosis and treatment				
Predictors	Time to Diagnosis	Time to Surgery	Time to Chemotherapy	Time to Radiation
Age at Diagnosis				
< 50	45.6 (36.2, 57.6)	33.7 (29.6, 38.4)	45.1 (40.3, 50.5)	40.7 (33.8, 48.9)
50-64	44.8 (35.1, 57.2)	35.3 (30.7, 40.4)	46.6 (41.1, 52.7)	37.7 (31.9, 44.6)
≥ 65	35.2 (24.4, 50.8)	32.6 (26.5, 40.2)	51.2 (41.4, 63.4)	26.9 (21.2, 34.1)
	p=0.4656	*p=0.6987*	*p=0.5067*	*p=0.0208*
Annual Income				
< $70,000	46.8 (37.5, 58.4)	35.1 (30.9, 39.7)	46.3 (40.9, 52.5)	37.1 (32, 43.1)
≥ $70,000	37 (29.4, 46.5)	32.7 (28.7, 37.2)	48.8 (43.2, 55.2)	32.2 (27.3, 38)
	p=0.0546	*p=0.3007*	*p=0.3235*	*p=0.0890*
Health Insurance				
Private Insurance	36.7 (29.2, 46.1)	31.5 (27.7, 35.8)	44.6 (39.4, 50.5)	31.6 (27, 37)
Non-private	47.2 (35.7, 62.3)	36.4 (31.1, 42.6)	50.7 (43.9, 58.5)	37.8 (30.9, 46.2)
	p=0.1485	*p=0.1351*	*p=0.0805*	*p=0.1462*
Mode of Detection				
Patient finding	46.4 (36.5, 59.1)	---	---	---
Doctor Finding/Screening	37.3 (30.1, 46.1)	---	---	---
	p=0.0824	---	---	---
Family History of Breast Cancer				
Yes	42.4 (34.1, 52.9)	33.5 (29.6, 37.9)	46.2 (40.9, 52.1)	32.9 (28.1, 38.5)
No	40.8 (32.8, 50.7)	34.2 (30.2, 38.7)	49 (43.3, 55.5)	36.3 (31.3, 42.3)
	p=0.7148	*p=0.7272*	*p=0.2290*	*p=0.1912*
Comorbidity Count				
0	39.5 (29.8, 52.2)	33.8 (28.8, 39.6)	47 (40.7, 54.4)	34.5 (28.2, 42.2)
≥ 1	43.9 (36.7, 52.4)	33.9 (30.7, 37.5)	48.1 (43.2, 53.4)	34.7 (30.6, 39.3)
	p=0.4551	*p=0.9502*	*p=0.7189*	*p=0.9657*
Tumor Size				
≤ 1 cm	46.4 (36.6, 58.7)	34.5 (30.3, 39.4)	50.4 (43.2, 58.8)	31.3 (26.4, 37.1)
> 1 cm	37.3 (30.1, 46.3)	33.2 (29.4, 37.5)	44.9 (40.4, 49.9)	38.2 (32.7, 44.5)
	p=0.0818	*p=0.5545*	*p=0.0993*	*p=0.0317*
Tumor Grade				
Well differentiated	40 (30.2, 53)	35.5 (30.4, 41.6)	47.3 (40, 56)	33.9 (28.1, 41)
Moderately or Poorly differentiated	43.3 (36.1, 51.8)	32.2 (29.1, 35.7)	47.8 (43.3, 52.7)	35.2 (30.9, 40.2)
	p=0.5789	*p=0.2113*	*p=0.8981*	*p=0.6932*

^Adjusted for all variables within the column

Predictors	Time to Diagnosis	Time to Surgery	Time to Chemotherapy	Time to Radiation
Table 5 (contd). Adjusted geometric mean days (95% CI)^ for predictors associated with time to diagnosis and treatment				
Node Status				
Negative	40.5 (33.7, 48.8)	34.4 (31, 38.2)	48.9 (43.2, 55.4)	34.7 (30.5, 39.5)
Positive	42.7 (32.8, 55.6)	33.3 (28.7, 38.6)	46.2 (40.9, 52.2)	34.4 (28.2, 42)
	p=0.6901	*p=0.6426*	*p=0.2503*	*p=0.9383*
Type of Surgical Hospital				
Community Based	---	32.9 (28.8, 37.6)	---	---
Teaching Facility	---	34.8 (31, 39.1)	---	---
	---	*p=0.3894*	---	---
Type of Surgery				
BCS	---	28.3 (25.2, 31.8)	46.9 (41.4, 53.1)	---
Mastectomy	---	40.5 (35.4, 46.3)	48.2 (42.7, 54.5)	---
	---	*p=0<.0001*	*p=0.5633*	---
Type of Radiation Facility				
Community Based	---	---	---	38.4 (33.3, 44.3)
Teaching Facility	---	---	---	31.1 (26.4, 36.7)
	---	---	---	*p=0.0068*
Radiation Sequence				
After Chemotherapy	---	---	---	28.8 (24.2, 34.2)
After Surgery	---	---	---	41.5 (35.4, 48.7)
	---	---	---	*p=0.0003*
Caring Demand				
Yes	40.2 (28.8, 56.2)	29.8 (22.3, 39.7)	44.7 (37.3, 53.6)	44.3 (34.4, 56.9)
No	47.1 (34.3, 64.8)	26.6 (20.2, 34.9)	49.3 (40.9, 59.5)	39 (31.3, 48.6)
	p=0.2951	*p=0.3861*	*p=0.1459*	*p=0.2504*
Transportation Issues				
Yes	42.9 (27.6, 66.7)	32.2 (22.1, 47)	50.4 (39.3, 64.7)	44.9 (33.2, 60.8)
No	44.1 (33.8, 57.7)	24.6 (19.5, 30.9)	43.7 (37.6, 50.9)	38.4 (31.5, 46.8)
	p=0.9012	*p=0.1591*	*p=0.2155*	*p=0.2886*
Job related demands				
Yes	52.3 (31.8, 85.9)	27.9 (18.2, 42.8)	48.7 (36, 65.9)	46.2 (32, 66.6)
No	36.2 (28.8, 45.6)	28.3 (23.3, 34.4)	45.3 (40.4, 50.7)	37.4 (32, 43.6)
	p=0.1594	*p=0.9512*	*p=0.6305*	*p=0.2631*

^Adjusted for all variables within the column

Table 6. Adjusted geometric mean days (95% CI)^ for predictors associated with time to diagnosis and treatment, by race

Predictors	Time to Diagnosis		Time to Surgery		Time to Chemotherapy		Time to Radiation	
	White	AA	White	AA	White	AA	White	AA
Age at Diagnosis								
< 50	40.8 (28.7, 58)	56.2 (38.6, 82.1)	---	---	---	---	38 (29.1, 49.6)	37.5 (26.8, 52.3)
50-64	40.2 (27.7, 58.2)	52.7 (36, 77.1)	---	---	---	---	32 (25.1, 40.7)	33.2 (24.2, 45.5)
≥ 65	40.2 (24.5, 65.9)	36.7 (20, 67.4)	---	---	---	---	32.2 (24, 43.3)	16.2 (9.9, 26.7)
	p=0.9965	*p=0.4086*					*p=0.4210*	*p=0.0058*
Health Insurance								
Private Insurance	---	---	---	---	45.3 (38.5, 53.4)	49 (38.8, 61.9)	35.9 (29.4, 43.8)	21.3 (15.4, 29.5)
Non-private	---	---	---	---	44.5 (35.4, 55.9)	57.8 (46.3, 72.2)	32.1 (23.9, 43.2)	34.8 (24.3, 49.8)
					p=0.8820	*p=0.0692*	*p=0.5631*	*p=0.0067*
Family History of Breast Cancer								
Yes	---	---	---	---	---	---	35 (28.7, 42.8)	23.9 (16.8, 33.8)
No	---	---	---	---	---	---	32.9 (27, 40)	31.1 (23.1, 41.8)
							p=0.5538	*p=0.0517*
Tumor Size								
≤ 1 cm	43.8 (32.1, 59.7)	57.4 (37.7, 87.4)	---	---	---	---	---	---
> 1 cm	37.3 (27.5, 50.5)	39.7 (27.6, 57)	---	---	---	---	---	---
	p=0.3512	*p=0.0493*						
Type of Surgical Hospital								
Community Based	---	---	27.9 (23.8, 32.6)	42 (32.7, 53.9)	---	---	---	---
Teaching Facility	---	---	33 (29, 37.5)	40.5 (31.4, 52.2)	---	---	---	---
			p=0.0282	*p=0.7295*				
Type of Radiation Facility								
Community Based	---	---	---	---	---	---	37.7 (31.6, 44.8)	30.8 (22.5, 42.3)
Teaching Facility	---	---	---	---	---	---	30.6 (24.3, 38.5)	24 (17.4, 33.3)
							p=0.0788	*p=0.0494*
Radiation Sequence								
After Chemo	---	---	---	---	---	---	26 (20.8, 32.6)	23.7 (16.5, 34)
After Surgery	---	---	---	---	---	---	44.2 (36, 54.5)	31.3 (23, 42.6)
							p=0.0002	*p=0.0928*

References

1.   Altekruse S, Kosary C, Krapcho M, *et al.* SEER Cancer Statistics Review, 1975-2007, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2007/, based on November 2009 SEER data submission, posted to the SEER web site, 2010.
2.   ACS. American Cancer Society. Breast Cancer Facts & Figures 2009-2010. Atlanta: American Cancer Society, 2010.
3.   Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. CA Cancer J Clin. Sep-Oct 2010;60(5):277-300.
4.   Elledge RM, Clark GM, Chamness GC, Osborne CK. Tumor biologic factors and breast cancer prognosis among white, Hispanic, and black women in the United States. J Natl Cancer Inst. May 4 1994;86(9):705-712.
5.   Elmore JG, Moceri VM, Carter D, Larson EB. Breast carcinoma tumor characteristics in black and white women. Cancer. Dec 15 1998;83(12):2509-2515.
6.   Middleton LP, Chen V, Perkins GH, Pinn V, Page D. Histopathology of breast cancer among African-American women. Cancer. Jan 1 2003;97(1 Suppl):253-257.
7.   Ayanian JZ, Kohler BA, Abe T, Epstein AM. The relation between health insurance coverage and clinical outcomes among women with breast cancer. N Engl J Med. Jul 29 1993;329(5):326-331.
8.   Bradley CJ, Given CW, Roberts C. Race, socioeconomic status, and breast cancer treatment and survival. J Natl Cancer Inst. Apr 3 2002;94(7):490-496.
9.   Gordon NH, Crowe JP, Brumberg DJ, Berger NA. Socioeconomic factors and race in breast cancer recurrence and survival. Am J Epidemiol. Mar 15 1992;135(6):609-618.
10.   Shavers VL, Brown ML. Racial and ethnic disparities in the receipt of cancer treatment. J Natl Cancer Inst. Mar 6 2002;94(5):334-357.
11.   Kaufman CS, Shockney L, Rabinowitz B, *et al.* National Quality Measures for Breast Centers (NQMBC): a robust quality tool: breast center quality measures. Ann Surg Oncol. Feb 2010;17(2):377-385.
12.   Richards MA, Westcombe AM, Love SB, Littlejohns P, Ramirez AJ. Influence of delay on survival in patients with breast cancer: a systematic review. Lancet. Apr 3 1999;353(9159):1119-1126.
13.   Hoffman HJ, LaVerda NL, Levine PH, Young HA, Alexander LM, Patierno SR. Having health insurance does not eliminate race/ethnicity-associated delays in breast cancer diagnosis in the District of Columbia. Cancer. Aug 15 2011;117(16):3824-3832.
14.   Gorin SS, Heck JE, Cheng B, Smith SJ. Delays in breast cancer diagnosis and treatment by racial/ethnic group. Arch Intern Med. Nov 13 2006;166(20):2244-2252.
15.   Gwyn K, Bondy ML, Cohen DS, *et al.* Racial differences in diagnosis, treatment, and clinical delays in a population-based study of patients with newly diagnosed breast carcinoma. Cancer. Apr 15 2004;100(8):1595-1604.
16.   Brazda A, Estroff J, Euhus D, *et al.* Delays in time to treatment and survival impact in breast cancer. Ann Surg Oncol. Oct 2010;17 Suppl 3:291-296.
17.   Fedewa SA, Ward EM, Stewart AK, Edge SB. Delays in adjuvant chemotherapy treatment among patients with breast cancer are more likely in African American and

Hispanic populations: a national cohort study 2004-2006. J Clin Oncol. Sep 20 2010;28(27):4135-4141.

18.   Hershman DL, Wang X, McBride R, Jacobson JS, Grann VR, Neugut AI. Delay in initiating adjuvant radiotherapy following breast conservation surgery and its impact on survival. Int J Radiat Oncol Biol Phys. Aug 1 2006;65(5):1353-1360.

19.   Fedewa SA, Edge SB, Stewart AK, Halpern MT, Marlow NM, Ward EM. Race and ethnicity are associated with delays in breast cancer treatment (2003-2006). J Health Care Poor Underserved. 2011;22(1):128-141.

20.   Ambrosone CB, Ciupak GL, Bandera EV, et al. Conducting Molecular Epidemiological Research in the Age of HIPAA: A Multi-Institutional Case-Control Study of Breast Cancer in African-American and European-American Women. J Oncol. 2009;2009:871250.

21.   Williams DL, Tortu S, Thomson J. Factors associated with delays to diagnosis and treatment of breast cancer in women in a Louisiana urban safety net hospital. Women Health. Dec 2010;50(8):705-718.

22.   Komenaka IK, Martinez ME, Pennington RE, Jr., et al. Race and ethnicity and breast cancer outcomes in an underinsured population. J Natl Cancer Inst. Aug 4 2010;102(15):1178-1187.

23.   Howlader N, Noone AM KM, Neyman N, Aminou R, Waldron W, Altekruse SF, Kosary CL, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Eisner MP, Lewis DR, Chen HS, Feuer EJ, Cronin KA, Edwards BK (eds). . SEER Cancer Statistics Review, 1975-2008, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2008/, based on November 2010 SEER data submission, posted to the SEER web site, 2011.

24.   Caplan LS, May DS, Richardson LC. Time to diagnosis and treatment of breast cancer: results from the National Breast and Cervical Cancer Early Detection Program, 1991-1995. Am J Public Health. Jan 2000;90(1):130-134.

25.   Hershman DL, Wang X, McBride R, Jacobson JS, Grann VR, Neugut AI. Delay of adjuvant chemotherapy initiation following breast cancer surgery among elderly women. Breast Cancer Res Treat. Oct 2006;99(3):313-321.

26.   Gold HT, Do HT, Dick AW. Correlates and effect of suboptimal radiotherapy in women with ductal carcinoma in situ or early invasive breast cancer. Cancer. Dec 1 2008;113(11):3108-3115.

27.   Richardson LC. Treatment of breast cancer in medically underserved women: a review. Breast J. Jan-Feb 2004;10(1):2-5.

28.   Banning M. Black women and breast health: a review of the literature. Eur J Oncol Nurs. Feb 2011;15(1):16-22.

29.   Lannin DR, Mathews HF, Mitchell J, Swanson MS, Swanson FH, Edwards MS. Influence of socioeconomic and cultural factors on racial differences in late-stage presentation of breast cancer. JAMA. Jun 10 1998;279(22):1801-1807.

30.   Breen N, Wesley MN, Merrill RM, Johnson K. The relationship of socio-economic status and access to minimum expected therapy among female breast cancer patients in the National Cancer Institute Black-White Cancer Survival Study. Ethn Dis. Winter 1999;9(1):111-125.

31.   Roetzheim RG, Gonzalez EC, Ferrante JM, Pal N, Van Durme DJ, Krischer JP. Effects of health insurance and race on breast carcinoma treatments and outcomes. Cancer. Dec 1 2000;89(11):2202-2213.

32.   Asplin BR, Rhodes KV, Levy H, *et al.* Insurance status and access to urgent ambulatory care follow-up appointments. JAMA. Sep 14 2005;294(10):1248-1254.

33.   A Shared Responsibility: Academic Health Centers and the Provision of Care to the Poor and Uninsured, The Commonwealth Fund, April 2001. www.commonwealthfund.org. Accessed April 3, 2012.

34.   Wagner JL, Warneke CL, Mittendorf EA, *et al.* Delays in primary surgical treatment are not associated with significant tumor size progression in breast cancer patients. Ann Surg. Jul 2011;254(1):119-124.

35.   Morris CR, Cohen R, Schlag R, Wright WE. Increasing trends in the use of breast-conserving surgery in California. Am J Public Health. Feb 2000;90(2):281-284.

36.   Gabel M, Hilton NE, Nathanson SD. Multidisciplinary breast cancer clinics. Do they work? Cancer. Jun 15 1997;79(12):2380-2384.

37.   Huang J, Barbera L, Brouwers M, Browman G, Mackillop WJ. Does delay in starting treatment affect the outcomes of radiotherapy? A systematic review. J Clin Oncol. Feb 1 2003;21(3):555-563.

38.   Desch CE, McNiff KK, Schneider EC, *et al.* American Society of Clinical Oncology/National Comprehensive Cancer Network Quality Measures. J Clin Oncol. Jul 20 2008;26(21):3631-3637.

39.   Cold S, During M, Ewertz M, Knoop A, Moller S. Does timing of adjuvant chemotherapy influence the prognosis after early breast cancer? Results of the Danish Breast Cancer Cooperative Group (DBCG). Br J Cancer. Sep 19 2005;93(6):627-632.

Factors Influencing a Patient's Choice of Surgical Treatment for Early Stage Breast

Cancer

by

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ABSTRACT OF MANUSCRIPT 3 OF 3

Factors Influencing a Patient's Choice of Surgical Treatment for Early Stage Breast

Cancer

Dissertation Director:

Kitaw Demissie, MD, PhD

ABSTRACT

Introduction: For most women with early stage invasive cancer, either breast

conserving surgery (BCS) followed by radiation or mastectomy is an appropriate surgical

treatment, but the factors influencing patient choice of surgery are undetermined. The

objective of this study is to examine influence of surgeon's recommendation, opinion of

others, and competing priorities on patient choice of surgery.

Methods: Women 18 to 85 years of age newly diagnosed with invasive breast cancer

during 2005-2010 were identified from seven counties in eastern New Jersey. Out of the

626 recruited for this retrospective cohort study, we interviewed 367 women (59%

response rate). A semi-structured interview was used to collect predictors such as

influence of surgeon's recommendation, opinion of others, and competing priorities from

the patients. The dependent variable was the definitive surgery patient received and was

abstracted from hospital records. Binomial regression models were used to estimate the

independent association of predictors on receiving mastectomy (compared to BCS) after

adjusting for clinical factors. We also stratified the model by race to explore how

predictors differ between whites and African-Americans (AA).

Results: Patients who reported that their surgeon's recommendation was a major influence in their choice of surgery were less likely to receive mastectomy compared to BCS (RR: 0.70; 95% CI: 0.54, 0.93). Whites were less likely to receive mastectomy when their surgeon's recommendation was an influence (RR: 0.60; 95% CI: 0.43, 0.85), they had dependents to care for daily (RR: 0.64; 95% CI: 0.42, 0.97), or if they had health issues that interfered with their daily activities (RR: 0.61; 95% CI: 0.38, 0.98). AAs were more like to receive mastectomy when they reported they had health issues that interfered with their daily activities (RR: 1.65; 95% CI: 1.01, 2.69).

Conclusions: Patient choice of surgery is an important part of treatment process for early stage invasive cancer. These results suggest that patients are influenced by their surgeon's recommendations and competing priories when making surgery choices.

Factors Influencing a Patient's Choice of Surgical Treatment for Early Stage Breast

Cancer

Introduction

For a majority of women with early stage invasive breast cancer, the type of surgery is often the first treatment decision they confront after being diagnosed. Decades of randomized trials have shown survival benefits for BCS followed by radiation to be similar to that of mastectomy.[1] Since NIH's 1990 consensus statement[2] stating that BCS plus radiation is an appropriate and preferable mode of treatment, the trend in BCS use has increased.[3,4]

However, variations in the use of BCS followed by radiation have been reported by age[5-7], socioeconomic status[8] and particularly, by race. Historically, studies have shown AAs to be less likely to receive BCS. Nattinger *et al.*, in a study using Medicare beneficiaries, found AAs were 20% less likely to receive BCS.[9] Similarly, a study using the National Cancer Database found fewer low-income AAs receive BCS compared to white women with high income.[10] On the other hand, current studies show comparable rates between AAs and whites.[11,12]

In spite of evidence-based recommendation that either surgery is appropriate, the factors that contribute to choosing the surgery are unknown. Previously reported factors influencing surgical treatment decision include fear of recurrence[13,14], travel-distance to radiation facility[15], type of treatment facility[16] and physician characteristics[16-19]. Therefore, the decision between BCS and mastectomy is a composite of both physician and patient factors.

The main limitation of prior studies on choice of surgery have been the use of cancer registry data which does not record the initial surgery (BCS) that a patient may receive but records the final mastectomy instead.[19,20] Our population-based study takes advantage of the hospital records available to better capture the definitive surgery. We also utilized a semi-structured interview to evaluate factors influencing choice of surgery, e.g. competing priorities, factors not considered in other studies. The goal of this study is to examine factors influencing choice between mastectomy and BCS and whether these factors differ between AA and white women. We explored factors, such as discussions about treatment plan with the surgeon, competing priorities (caring for a dependents, transportation issues, and job demands), opinions of surgeon and others, and physical/emotional health of the patient, to observe if they predicted choice of surgical treatment.

Materials and Methods

<u>Study Population</u>

Subjects who participated in the Women's Circle of Health Study (WCHS) and who

consented to participate in our study, Breast Cancer Treatment Disparity Study (BCTDS),

were recruited. The general methodology of subject recruitment for the WCHS study has

been reported elsewhere.[21] In brief, the study is a 1:1 matched retrospective cohort study

(AA to White). Patients residing in northern and central New Jersey who were diagnosed

with stage I, II, and $T_3N_1M_0$ breast cancer during 2005-2010 were identified through

rapid case ascertainment by the New Jersey State Department of Health and Senior

Services (NJDHSS). Subjects were excluded if they were neither AA nor white, non-

residents of NJ, diagnosed with inflammatory breast cancer, diagnosed with breast cancer

with histologic features other than adenocarcinoma, or were diagnosed with any other

cancer besides non-melanoma skin cancer.

<u>Semi-Structured Phone Interview</u>

A telephone interview lasting about 45 minutes was conducted with consenting

patients by study staff. It was composed of a brief structured interview followed by a

longer semi-structured interview. The semi-structured component of the phone

interview questioned women on factors that influenced their choice between mastectomy

and BCS. Patients were asked the following about discussions with their surgeons:

recommendations on type of breast surgery, risks and benefits associated with each type

of surgery including radiation treatment, offering of reconstruction, and if the patient was

given a choice between mastectomy and breast-conserving surgery (BCS). The interview

sought information on factors that may influence patient treatment decision: the doctor's

opinion, someone else's (family/friends) opinion, availability of transport to treatment facility, job demands (if employed), caring for a dependent every day, and influence of other health issues the patient may have had at time of breast cancer diagnosis. Other variables such as availability of disability leave, medical insurance at the time of breast cancer diagnosis and during subsequent year, compliance with recommended treatments along with the patient's perception of receiving the best treatment were also recorded.

<u>Medical Record Review</u>

Medical records were obtained from each patient's primary physician, surgical oncologist, medical oncologist and radiation oncologist. Trained personnel abstracted socio-demographic and health related characteristics (age at diagnosis, comorbidities, mode of symptom recognition), and tumor characteristics (hormone receptor status, Her-2-neu status, tumor grade, size, lymph node status). The operating reports, pathology reports and discharge summary were also obtained for hospitalizations either for surgery or chemotherapy. Detailed information were abstracted regarding prior history of breast disease, comorbidity, tests performed during diagnostic and metastatic work-up, dates and types of surgeries related to treatment, and any adjuvant treatments administered. Patient data such as race, income, education, and menopause status were collected through patient interviews conducted by WHCS.

The study was approved by Institutional Review Boards (IRB) at both the University of Medicine and Dentistry of New Jersey (UMDNJ) and New Jersey Department of Health and Senior Services (for NJSCR).

STATISTICAL METHODS

Outcome variable

The medical records were abstracted to determine the initial surgical procedure the patient received. It was defined as BCS (includes lumpectomy, partial mastectomy) or mastectomy (simple, modified radical, bilateral or skin sparing mastectomy).

Predictors

The semi-structured interview captured quantitative and qualitative information. For the study, five predictors were considered as factors that may influence the choice of surgical treatment; the categories for each question were yes, no, don't know.

To understand the influence of the surgeon on treatment decision the following question was asked: a) "Was your surgeon's recommendation the major reason for your decision?"

Four questions asked to probe for competing priorities that may influence a patient's decision were: a) "Was getting to and from the radiation facility a factor when making your surgery decision?", b) "At the start of your treatment for breast cancer, was anyone dependent on you for their everyday care?", c) "If employed, did your job influence your choice of surgery or treatment?", d) "Before you were diagnosed with breast cancer, did you have any conditions or health issues that interfered with your physical or social activities in any way?"

Lastly, we asked if others (besides the physician) influenced their decision: "Did you rely on someone else's (friends, family) opinion or advice in deciding your breast cancer surgery treatment?"

Other variables of interest

The following were collected from the WCHS interview: race and education. Race was self-reported and categorized as non-Hispanic white or non-Hispanic black. Education was collected as the highest level of school completed and categorized as having received college education (at least 4-years or more) or received less than college education. We abstracted clinical and tumor characteristics from the medical records: age at diagnosis (date of biopsy-proven diagnosis minus date of birth); family history of breast cancer (yes or no for first or second degree relatives with breast cancer); AJCC (American Joint Committee on Cancer) stage (stage 1 or stage 2); multifocal or multi-centric tumors (yes or no for tumors diagnosed at biopsy that were multi-focal or multi-centric); and tumor grade (well, moderate, or poorly differentiated) from the medical records.

Analyses

The dependent variable was type of initial surgery (mastectomy versus BCS). Each of the predictors of influence was coded as yes or no (transportation issues, caring for dependents, surgeon's recommendation for surgery, influence of others (family/friends), job-related demands, and interfering health issues). We calculated demographic and tumor characteristics for participants overall and by receipt of surgery. The relationship between the dependent variable and each of the factors was assessed in a univariate analysis using a chi-square test.

The independent contribution of each factor of influence, as well as, age at diagnosis, and education, on the probability of receiving mastectomy compared to BCS was evaluated using a multivariable binomial regression model after adjusting for AJCC stage, comorbidity count, family history, multi-focal or multi-centric tumors, and tumor grade. The association of predictors and receipt of surgery was also explored by race.

Employment influence was not included in the adjusted model due to inadequate sample

distribution.

   Analyses were performed using SAS 9.2 (SAS Institute, Cary, NC).

Results

Demographic and tumor characteristics of participants

Out of 626 patients whose medical records were abstracted, 58.6% were interviewed for

the semi-structured interview.   Those who were not interviewed were more likely to be

AAs than whites (59.8% versus 40%), to have non-private insurance (34% versus 21%),

and to be lymph node positive (30.5% versus 22.3%). Table 1 shows the distribution of

subject and tumor characteristics of the participants.   The participants were mostly white,

under 65 years of age, had income ≥ $70,000, and had private primary insurance. Their

tumors were mostly moderately or poorly differentiated, ≤ 1cm tumor size, with negative

lymph nodes. A majority of these patients received BCS (68.4%) as their initial surgical

treatment, while 31.6% of the participants received mastectomy. The characteristics of

patients by receipt of surgery are found in Table 2. The distribution of race was similar

by surgery; 60% to 62% of the BCS and mastectomy patients were white and 38% to

40% were AAs. Mastectomy patients were younger (< 50 years of age), had ≥ $70,000,

had private primary insurance, more likely to have > 2 cm tumor size, have

multifocality/multicentricity and have positive lymph nodes.

Factors influencing patient decision

        Table 3 describes the overall distribution of the factors influencing a patient's

surgical decision. Women in the study reported they were influenced by the surgeon's

recommendation (60%), but also depended on other's opinion to make a decision (58%).

Overall, patients were less likely to have been influenced by issues with transportation to

a treatment facility (12%), to have dependents to care for (31%), to have health problems

(26%), or to say their jobs influenced their choice of surgery (6%).

Table 4 displays the distribution of factors that influence surgical treatment decision by type of surgery. For patients who received BCS, 65% said they were influenced by the surgeon's recommendation, compared to 48% of the mastectomy patients. About 10% to 13% of the patients said transportation to a treatment facility was a factor in treatment decision. Twenty-eight percent of the BCS patients and 38% of the mastectomy patients reported they had dependents to care for everyday. Patients who received mastectomy reported that job-demands influenced their surgical decision (7%) similar to those who received BCS (6%) but this was not statistically different. Fifty-seven percent of the BCS patients and 61% of the mastectomy patients relied on other's opinion when making their surgical treatment decision. Patients who said they had health issues that interfered with their physical/social activities were distributed similarly, 26% in both surgeries.

We found that in patients who received BCS, their surgeons were more likely to discuss radiation treatment with them compared to those who received mastectomy (61% versus 28%; data not shown). Similarly, in patients who had received mastectomy, their surgeons were more likely to discuss surgical reconstruction with them as compared to the BCS patients (93% versus 22%). Fifty percent of the participants said they had a choice of surgery, while 48% said they were not offered a choice.

Association of factors influencing patient receipt of initial surgery

Table 5 displays the relative risks (RR) adjusted for clinical factors and 95% confidence intervals (CI) for variables that influenced patients' decision in receiving mastectomy compared to BCS. Patients influenced by their surgeon's recommendation for surgical treatment (p=0.0026) were less likely to get mastectomy. On the other hand,

though not significant, patients who had issues with transportation availability to a radiation facility (p=0.6329), relied on other's opinion on treatment (p=0.4068), patients < 50 years of age (p=0.4210) as compared to 50 to 64 years old or those with less than a 4-year college education (p=0.1549) were more likely to receive mastectomy.

Whites were less likely to receive mastectomy when their surgeon's recommendation was an influence (p=0.0002). They were more likely to receive mastectomy when they relied on other's opinion as an influence in deciding surgical treatment (p=0.3768), or were < 50 years of age (p=0.4686).

AA patients with health issues that interfered with everyday activities (p=0.0463) were more likely to receive mastectomy. The following predictors were not significant: AAs were less likely to receive mastectomy when their surgeon's recommendation influenced their decision (p=0.1644) or when they had dependents to care for every day (p=0.3786). In AAs, patients < 50 years of age (p=0.1126) and those ≥ 65 years of age (p=0.8650) were more likely to receive mastectomy compared to those 50 to 64 years of age.

Discussion

Our study results indicate that a surgeon's recommendation plays a significant role as a factor that influences the patient's choice of definitive surgical treatment. Based on their surgeon's recommendation, the women in this study were more likely to receive BCS compared to mastectomy. On the other hand, patients who had less than a college education (less than 4 years), who considered travel to a radiation facility for treatments a factor, or relied on the opinion of other besides their surgeon were indicators for a patient to receive a mastectomy as their definitive surgical treatment.

Having a choice of surgery is an important part of the decision making process for a patient.[22] The women in our study saying they had a choice of surgery and not having a choice of surgery were equally distributed; this was also seen when stratified by surgery (51% of BCS patients said they had a choice, as well as, 50% of the mastectomy patients). In a study conducted in UK, patients who felt they had a choice in surgery were more likely to have low psychological distress from making their decision; although, their treatment satisfaction was mainly based on their perception of making an informed decision and not in that they were given a real choice.[23,24]

In our study, patients who were < 50 years of age at diagnosis (compared to 50 to 64 year olds) were more likely to receive mastectomy and those ≥ 65 years of age were less likely to receive mastectomy. In a single institution study in Florida, 25% of patients were eligible for breast conserving surgery yet chose to receive mastectomy and their older patients (≥ 70 years of age) were more likely to choose BCS compared to those younger (30-49 year olds) with only marginal significance.[25] Bleicher *et al.* surveyed patients who resided in the Surveillance Epidemiology and End Results program (SEER)

catchment areas of Detroit or Los Angeles to examine age as an influence of undergoing mastectomy.[26] They found that while age did not play a significant role in surgical decision-making, those with less than high school education were significantly more likely to choose mastectomy. In our study, education did not show significant influence in type of surgery received. A community-based study in North and South Carolina found that their patients who had more education (attended college) and were categorized in a higher socioeconomic status (income at diagnosis $50,000-$74,000) had a higher rate of BCS.[27]

The importance of the surgeon's influence on treatment decision has been observed in multiple studies. Our results show that patients were less likely to receive mastectomy when their surgeon's recommendation was a major influence in treatment decision regardless of race. Katz *et al.* found that even when patient said they had a choice in their surgery, a fifth of the patients in the study said their surgeons described only BCS to them and 22% reported that their surgeon made the decision for the treatment with or without patient input.[28] Contrary to our study, the population-based study of Hawley *et al.* demonstrated that patients made a choice to receive mastectomy irrespective of surgeon's recommendations.[29] That being said, another study showed no differences between mastectomy and BCS when patients were involved with their physicians in making a decision.[30]

In addition to being influenced by surgeons, patients were also influenced by family, friends, and other sources of information. In our study, mastectomy patients were more likely to be influenced by opinion of others. Benedict *et al.* found that surgical treatment choice varied by source of information.[27] In their study, patients who chose

mastectomy valued the opinion of relatives, friends, and the media. On the other hand, their BCS patients relied on local breast cancer groups, nurses and the internet. Media (including celebrity role models)[31,32] and the internet can be a basis for influencing choice in treatments. With the plethora of information available on the internet, which can include misleading information, it is important that a patient discusses with their physicians their options to make an informed choice.[27]

We did not find significant differences in surgery receipt when traveling to a radiation facility was an obstacle. Availability of transportation to a radiation facility has been shown in studies conducted with rural populations.[15,33,34] Whites were more likely to be recipients of BCS when they had dependents to care for everyday or had health issues that impeded their daily activities. One possible explanation given by Adkisson *et al.* states that patients with major medical comorbidities tend to choose BCS as it is less invasive surgery, does not require general anesthesia, and can be performed in less time.[25] On the other hand, AAs who said that they had health issues before being diagnosed with breast cancer were more likely to receive mastectomy. The reason is unclear for this result, perhaps the type of comorbidities in AAs may have influenced the receipt of mastectomy compared to BCS.

Our findings should be interpreted with recognition of some limitations. First, the study is subject to patient recall due to interviews being conducted from 6 months to more than one year after surgical treatment. Second, even though the distribution of surgical treatments was similar between races, the sample size was smaller when considering factors that influenced AAs in choice of surgery received. Lastly, this study has geographic constraints since patients were all treated in New Jersey. Other studies

have shown geographic variations in surgical treatments and therefore, the study may not be generalizable.[35]

   In spite of these limitations, this study shows that factors that influence choice of surgery is multi-faceted. We did not include factors of fear of recurrence or impact of body image due to surgery as they were not part of our study focus. Other studies have already shown these are leading indicators.[13,36,37] Nevertheless, the role of the surgeon's recommendation is an important element influencing the decision of type of surgery for early stage invasive breast cancer. We have also found that patients have competing priorities and other sources of information (family/friends/internet) that influence their surgical treatment choice. Clinicians should be aware that these factors may affect how a patient makes treatment decisions and should be open to discuss treatment options so that a patient can make an informed decision.

Tables and Figures

Table 1. Subject and tumor characteristics for participants	
Characteristics, %	N=367
Race	
White	61.3
African-American	38.7
Age at Diagnosis	
< 50	35.1
50-64	48.2
≥ 65	16.6
Annual Income	
<$35,000	15.8
$35,000-$69,999	23.7
≥ $70,000	51.5
Unknown	9
Education	
< College Education	50.4
≥ College Education	48.8
Unknown	0.8
Health Insurance	
Private Insurance	76.6
Non-private	21.5
Unknown	1.9
Tumor Grade	
Well differentiated	19.1
Moderately differentiated	39.8
Poorly differentiated	35.1
Unknown	6
Tumor Size	
≤ 1 cm	39.8
1.1 to 2 cm	33.5
> 2 cm	26.7
Node Status	
Negative	76.8
Positive	22.3
Unknown	0.8
Triple Negative	
Yes	13.9
No	85.6
Unknown	0.5
Type of Surgery	
BCS	68.4
Radiation Received	88.3
Mastectomy	31.6

BCS: Breast Conserving Surgery

Table 2. Demographic and tumor characteristics of participants by type of surgery		
Characteristics, %	BCS (n=251)	Mastectomy (n=116)
Race		
White	61.8	60.3
AA	38.2	39.7
Age at Diagnosis		
< 50	28.7	49.1
50-64	51.8	40.5
≥ 65	19.5	10.3
Annual Income		
<$35,000	16.7	13.8
$35,000-$69,999	24.7	21.6
≥ $70,000	49.8	55.2
Unknown	8.8	9.5
Education		
< College Education	48.6	54.3
≥ College Education	50.6	44.8
Unknown	0.8	0.9
Health Insurance		
Private Insurance	75.7	78.4
Non-private	21.9	20.7
Unknown	2.4	0.9
Family history of breast cancer		
Yes	40.2	44
No	59.8	56
Comorbidity Count		
0	21.1	35.3
≥ 1	78.9	64.7
Multifocal or multicentric tumor		
Yes	2.4	19
No	97.6	81
Tumor Grade		
Well differentiated	22.3	12.1
Moderately differentiated	38.2	43.1
Poorly differentiated	33.5	38.8
Unknown	6	6
AJCC Stage		
Stage 1	67.7	44
Stage 2	30.7	55.2
Tumor Size		
≤ 1 cm	43	32.8
1.1 to 2 cm	36.3	27.6
> 2 cm	20.7	39.7
Node Status		
Negative	81.3	67.2
Positive	17.9	31.9
Unknown	0.8	0.9
Triple Negative		
Yes	13.5	14.7
No	86.1	84.5
Unknown	0.4	0.9

BCS: Breast Conserving Surgery

Table 3. Distribution of factors influencing patient decision	
Factors, %	N=367
Influence of surgeon's recommendation	
Yes	59.9
No	34.9
Unknown	5.2
Issues with transportation availability	
Yes	12
No	86.6
Unknown	1.4
Caring for dependents	
Yes	31.3
No	68.7
Job demands	
Yes	6
No	67.8
Not Employed/Unknown	26.2
Reliance on other's opinion	
Yes	58
No	42
Health issues before diagnosis	
Yes	25.6
No	74.4

Table 4. Distribution of factors influencing patient decision by type of surgery received			
Factors, %	BCS (n=251)	Mastectomy (n=116)	*p-value*
Influence of surgeon's recommendation			*0.0011*
Yes	65.3	48.3	
No	28.7	48.3	
Unknown	6	3.4	
Issues with transportation availability			*0.6757*
Yes	12.7	10.3	
No	85.7	88.8	
Unknown	1.6	0.9	
Caring for dependents			*0.064*
Yes	28.3	37.9	
No	71.7	62.1	
Job demands			*0.2716*
Yes	5.6	6.9	
No	70.5	62.1	
Not Employed/Unknown	23.9	31	
Reliance on other's opinion			*0.403*
Yes	56.6	61.2	
No	43.4	38.8	
Health issues before diagnosis			*0.9408*
Yes	25.5	25.9	
No	74.5	74.1	

BCS: Breast Conserving Surgery

Table 5. Relative risk of factors influencing a patient's decision for receiving mastectomy compared to BCS

	Adjusted RR (95% CI)*		
	Overall	White	African-American
Surgeon recommendation is major reason for decision	0.70 (0.55, 0.88)	0.70 (0.55, 0.88)	0.67 (0.38, 1.17)
Traveling to radiation facility was a factor	1.12 (0.71, 1.77)	1.12 (0.71, 1.77)	1.22 (0.80, 1.87)
Had dependents to care for everyday	0.92 (0.67, 1.26)	0.92 (0.67, 1.26)	0.78 (0.45, 1.35)
Health issues interfered with physical or social activities	0.90 (0.66, 1.23)	0.90 (0.66, 1.23)	1.68 (1.01, 2.77)
Relied on other's opinion in deciding treatment	1.13 (0.84, 1.52)	1.13 (0.84, 1.52)	1.22 (0.80, 1.87)
Ages LT 50 compared ages 50-64	1.18 (0.79, 1.74)	1.18 (0.79, 1.74)	1.65 (0.89, 3.06)
Ages GT 65 compared ages 50-64	0.69 (0.39, 1.23)	0.69 (0.39, 1.23)	1.09 (0.40, 2.99)
No college education	1.19 (0.94, 1.51)	1.19 (0.94, 1.51)	1.06 (0.61, 1.84)

*Adjusted for all variables in table and AJCC stage, tumor grade, family history, multifocal/centric tumor, comorbidities

BCS: Breast Conserving Surgery

References

1.   Fisher B, Anderson S, Bryant J, *et al.* Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med. Oct 17 2002;347(16):1233-1241.

2.   Conference NC. Treatment of early-stage breast cancer. JAMA. 1991;265:391-395.

3.   Lazovich D, Solomon CC, Thomas DB, Moe RE, White E. Breast conservation therapy in the United States following the 1990 National Institutes of Health Consensus Development Conference on the treatment of patients with early stage invasive breast carcinoma. Cancer. Aug 15 1999;86(4):628-637.

4.   McCloskey SA, Botnick LE, Rose CM, *et al.* Long-term outcomes after breast conservation therapy for early stage breast cancer in a community setting. Breast J. Mar-Apr 2006;12(2):138-144.

5.   Shavers VL, Harlan LC, Stevens JL. Racial/ethnic variation in clinical presentation, treatment, and survival among breast cancer patients under age 35. Cancer. Jan 1 2003;97(1):134-147.

6.   Enger SM, Thwin SS, Buist DS, *et al.* Breast cancer treatment of older women in integrated health care settings. J Clin Oncol. Sep 20 2006;24(27):4377-4383.

7.   Joslyn SA. Radiation therapy and patient age in the survival from early-stage breast cancer. Int J Radiat Oncol Biol Phys. Jul 1 1999;44(4):821-826.

8.   Michalski TA, Nattinger AB. The influence of black race and socioeconomic status on the use of breast-conserving surgery for Medicare beneficiaries. Cancer. Jan 15 1997;79(2):314-319.

9.   Nattinger AB, Gottlieb MS, Veum J, Yahnke D, Goodwin JS. Geographic variation in the use of breast-conserving treatment for breast cancer. N Engl J Med. Apr 23 1992;326(17):1102-1107.

10.   Osteen RT, Karnell LH. The National Cancer Data Base report on breast cancer. Cancer. Apr 1 1994;73(7):1994-2000.

11.   Enewold L, Zhou J, McGlynn KA, *et al.* Racial variation in breast cancer treatment among Department of Defense beneficiaries. Cancer. Feb 1 2012;118(3):812-820.

12.   Banerjee M, George J, Yee C, Hryniuk W, Schwartz K. Disentangling the effects of race on breast cancer treatment. Cancer. Nov 15 2007;110(10):2169-2177.

13.   Nold RJ, Beamer RL, Helmer SD, McBoyle MF. Factors influencing a woman's choice to undergo breast-conserving surgery versus modified radical mastectomy. Am J Surg. Dec 2000;180(6):413-418.

14.   Stafford D, Szczys R, Becker R, Anderson J, Bushfield S. How breast cancer treatment decisions are made by women in North Dakota. Am J Surg. Dec 1998;176(6):515-519.

15.   Celaya MO, Rees JR, Gibson JJ, Riddle BL, Greenberg ER. Travel distance and season of diagnosis affect treatment choices for women with early-stage breast cancer in a predominantly rural population (United States). Cancer Causes Control. Aug 2006;17(6):851-856.

16.   Gilligan MA, Neuner J, Sparapani R, Laud PW, Nattinger AB. Surgeon characteristics and variations in treatment for early-stage breast cancer. Arch Surg. Jan 2007;142(1):17-22.

17.   Keating NL, Weeks JC, Landrum MB, Borbas C, Guadagnoli E. Discussion of treatment options for early-stage breast cancer: effect of provider specialty on type of surgery and satisfaction. Med Care. Jul 2001;39(7):681-691.

18.   Fancher TT, Palesty JA, Thomas R, *et al.* A woman's influence to choose mastectomy as treatment for breast cancer. J Surg Res. May 1 2009;153(1):128-131.

19.   Hershman DL, Buono D, Jacobson JS, *et al.* Surgeon characteristics and use of breast conservation surgery in women with early stage breast cancer. Ann Surg. May 2009;249(5):828-833.

20.   Hawley ST, Lantz PM, Janz NK, *et al.* Factors associated with patient involvement in surgical treatment decision making for breast cancer. Patient Educ Couns. Mar 2007;65(3):387-395.

21.   Ambrosone CB, Ciupak GL, Bandera EV, *et al.* Conducting Molecular Epidemiological Research in the Age of HIPAA: A Multi-Institutional Case-Control Study of Breast Cancer in African-American and European-American Women. J Oncol. 2009;2009:871250.

22.   (NCCN) NCCN. Clinical Practice Guidelines in Oncology. Breast Cancer. http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf V. 2. , 2010.

23.   Fallowfield L. Offering choice of surgical treatment to women with breast cancer. Patient Educ Couns. Mar 1997;30(3):209-214.

24.   Fallowfield LJ HA, Maguire P, Baum M, A'Hern RP. . A question of choice: results of a prospective 3-year follow-up study of women with breast cancer. The Breast. 1994;3:202–208.

25.   Adkisson CD, Bagaria SP, Parker AS, *et al.* Which Eligible Breast Conservation Patients Choose Mastectomy in the Setting of Newly Diagnosed Breast Cancer? Ann Surg Oncol. Oct 6 2011.

26.   Bleicher RJ, Abrahamse P, Hawley ST, Katz SJ, Morrow M. The influence of age on the breast surgery decision-making process. Ann Surg Oncol. Mar 2008;15(3):854-862.

27.   Benedict S, Cole DJ, Baron L, Baron P. Factors influencing choice between mastectomy and lumpectomy for women in the Carolinas. J Surg Oncol. Jan 2001;76(1):6-12.

28.   Katz SJ, Lantz PM, Janz NK, *et al.* Patient involvement in surgery treatment decisions for breast cancer. J Clin Oncol. Aug 20 2005;23(24):5526-5533.

29.   Hawley ST, Griggs JJ, Hamilton AS, *et al.* Decision involvement and receipt of mastectomy among racially and ethnically diverse breast cancer patients. J Natl Cancer Inst. Oct 7 2009;101(19):1337-1347.

30.   Mandelblatt J, Kreling B, Figeuriedo M, Feng S. What is the impact of shared decision making on treatment and outcomes for older women with breast cancer? J Clin Oncol. Oct 20 2006;24(30):4908-4913.

31.   Nattinger AB, Hoffmann RG, Howell-Pelz A, Goodwin JS. Effect of Nancy Reagan's mastectomy on choice of surgery for breast cancer by US women. JAMA. Mar 11 1998;279(10):762-766.

32.   Du X, Freeman DH, Jr., Syblik DA. What drove changes in the use of breast conserving surgery since the early 1980s? The role of the clinical trial, celebrity action and an NIH consensus statement. Breast Cancer Res Treat. Jul 2000;62(1):71-79.

33.   Athas WF, Adams-Cameron M, Hunt WC, Amir-Fazli A, Key CR. Travel distance to radiation therapy and receipt of radiotherapy following breast-conserving surgery. J Natl Cancer Inst. Feb 2 2000;92(3):269-271.

34.   Schroen AT, Brenin DR, Kelly MD, Knaus WA, Slingluff CL, Jr. Impact of patient distance to radiation therapy on mastectomy use in early-stage breast cancer patients. J Clin Oncol. Oct 1 2005;23(28):7074-7080.

35.   Ayanian JZ, Guadagnoli E. Variations in breast cancer treatment by patient and provider characteristics. Breast Cancer Res Treat. 1996;40(1):65-74.

36.   Stanton AL, Estes MA, Estes NC, Cameron CL, Danoff-Burg S, Irving LM. Treatment decision making and adjustment to breast cancer: a longitudinal study. J Consult Clin Psychol. Apr 1998;66(2):313-322.

37.   Wolberg WH, Tanner MA, Romsaas EP, Trump DL, Malec JF. Factors influencing options in primary breast cancer treatment. J Clin Oncol. Jan 1987;5(1):68-74.

CONCLUSION

Breast cancer accounts for 1 in 3 cancers diagnosed among women in the United States.[1]

From 2004 to 2008 incidence rates were stable among all racial groups, yet in AAs the

average death rates from 2003 to 2007 was still the highest compared to whites.[1]

Treatment disparity has been suggested as a possible reason for racial disparity. The

disparity in treatment can include either not getting standard treatments or delay in

receipt of appropriate treatments.

      The results of the dissertation show there were differences between AAs and

whites in receiving standard NCCN guideline treatments. Also, AAs were more likely to

delay receiving biopsy proven diagnosis and surgical treatment compared to whites.

Once surgical treatment had initiated AAs did not have significant delays in receiving

adjuvant chemotherapy or radiation. Finally, AAs were more likely consider interfering

health issues as an influential factor in their surgical treatment decision to receive

mastectomy.

      Receiving adjuvant therapies have been shown to decrease mortality and

morbidity from early-stage breast cancer.[2] In Aim 1, AAs were more likely to not

receive optimal treatment after accounting for clinical factors (using "standard plus

additional" treatment definition). Though insurance and low SES was not significantly

associated with treatment receipt in this study, other studies have considered these factors

as important predictors. Ward *et al.* considered socioeconomic factors such as poverty,

inadequate education, and lack of health insurance to be far more important than

biological differences.[3] Income, education, and health insurance coverage can influence

access to appropriate early detection, treatment, and palliative care.[3] Studies have shown

that African-American women are more likely to have limited access to health care and get less appropriate or less aggressive therapeutic management.[4-6] Studies have found that adjusting for SES can eliminate survival differences[7,8] while others have found the differences to remain.[9,10]

Besides receipt of appropriate treatments, delay of treatment receipt is a possible reason for racial disparity. A literature review by Unger-Saldaña *et al.* reported that prolonged delay in diagnosis and treatment impacted the patient's survival, their clinical stage at diagnosis, lymph node involvement, tumor size, and their quality of life.[11] In Aim 2, the results show AAs took longer time to receive a diagnostic biopsy as well as their first surgical treatment, but they received adjuvant treatments in comparatively similar time as whites. In our study, even though mode of discovery was not a significant predictor, a higher proportion of AAs self-discovered an abnormal symptom compared to having their invasive cancer discovered by a physician or through routine screening mammogram. Although rates of mammography screening have improved among women of all racial/ethnic group there are still barriers to timely performance between abnormal mammography that differ and the first diagnostic test by race/ethnicity.[12]

An overall significant predictor of delay to receipt of biopsy in this study was low SES. Uninsured women and women who rely on public assistance to finance their medical care appear to have greater barriers to accessing that care for non-emergent problems.[13,14] As a result, some investigators have found that poor women with breast cancer have a longer symptomatic period before seeking medical attention.[10,14,15] Factors that are interrelated to diagnostic delays could be poor patient–provider

communication[16-18]; logistical barriers to access of care[16,19,20]; and negative

mammography experiences[19] may hinder receipt of diagnostic procedures.[21]

The last aim of the dissertation explored the choices in receipt of surgical

treatment. Since BCS with radiation and mastectomy result in equivalent survival for

women with early-stage breast cancer, the decision to have BCS versus mastectomy is

likely influenced by physician and patient preferences.[22]   Aim 3 of the dissertation has

shown that in this study population AAs and whites have similar distributions in receipt

of BCS and mastectomy. The dissertation results showed that predictors such as a

surgeon's recommendation and competing priorities play a complex role in influencing

the patient's decision for type of surgery received.

Patient preference for type of surgery was recognized as an important factor by

the NIH Consensus Development Conference.[23,24] In a study by Bruera *et al.*, women

demonstrated a strong desire to be involved in making decisions regarding their breast

carcinoma treatment; 89% of women preferred to play either an active or a shared

decision-making role.[25] True patient preference may be difficult to elicit due to the

complex nature of the physician-patient interaction.[23] Women with breast carcinoma rely

on their physicians for information and guidance about their illness and its treatment and

may or may not engage actively in the decision process, depending on their age,

education, illness severity or anxiety level.[23,26]

Opportunities to reduce cancer disparities exist across an entire cancer spectrum.[3]

Access to care is an important aspect of getting treatment for any breast cancer patient.

Those without insurance or with low SES are part of the medically underserved

population along with women who are older and/or minority.[27] This dissertation shows

that these women are at particular high risk of not obtaining access to standard treatments or to delay receiving the treatments required.

It is evident that racial disparities can't be explained by one factor alone. Instead multiple factors based on patient, physician, and health care system interplay. Because early detection is vital to reducing mortality from breast cancer, interventions need to be put in place to reach the medically vulnerable. Interventions such as patient reminders for screening, improved physician-patient communication, and decision aids for increasing informed decision-making are a few avenues already in place. Yet barriers still exist for those who are financially unstable, the elderly and minorities. Further research is needed to identify new ways that will be cost-efficient and improve patient outcomes.

REFERENCES

1.   DeSantis C, Siegel R, Bandi P, Jemal A. Breast cancer statistics, 2011. CA Cancer J Clin. Nov-Dec 2011;61(6):409-418.
2.   Edwards BK, Brown ML, Wingo PA, *et al.* Annual report to the nation on the status of cancer, 1975-2002, featuring population-based trends in cancer treatment. J Natl Cancer Inst. Oct 5 2005;97(19):1407-1427.
3.   Ward E, Jemal A, Cokkinides V, *et al.* Cancer disparities by race/ethnicity and socioeconomic status. CA Cancer J Clin. Mar-Apr 2004;54(2):78-93.
4.   Howard J, Hankey BF, Greenberg RS, *et al.* A collaborative study of differences in the survival rates of black patients and white patients with cancer. Cancer. May 1 1992;69(9):2349-2360.
5.   Natarajan N, Nemoto T, Mettlin C, Murphy GP. Race-related differences in breast cancer patients. Results of the 1982 national survey of breast cancer by the American College of Surgeons. Cancer. Oct 1 1985;56(7):1704-1709.
6.   McWhorter WP, Mayer WJ. Black/white differences in type of initial breast cancer treatment and implications for survival. Am J Public Health. Dec 1987;77(12):1515-1517.
7.   Bassett MT, Krieger N. Social class and black-white differences in breast cancer survival. Am J Public Health. Dec 1986;76(12):1400-1403.
8.   Dayal HH, Power RN, Chiu C. Race and socio-economic status in survival from breast cancer. J Chronic Dis. 1982;35(8):675-683.
9.   Bain RP, Greenberg RS, Whitaker JP. Racial differences in survival of women with breast cancer. J Chronic Dis. 1986;39(8):631-642.
10.   Vernon SW, Tilley BC, Neale AV, Steinfeldt L. Ethnicity, survival, and delay in seeking treatment for symptoms of breast cancer. Cancer. Apr 1 1985;55(7):1563-1571.
11.   Unger-Saldana K, Infante-Castaneda C. Delay of medical care for symptomatic breast cancer: a literature review. Salud Publica Mex. 2009;51 Suppl 2:s270-285.
12.   Chang SW, Kerlikowske K, Napoles-Springer A, Posner SF, Sickles EA, Perez-Stable EJ. Racial differences in timeliness of follow-up after abnormal screening mammography. Cancer. Oct 1 1996;78(7):1395-1402.
13.   Access of Medicaid recipients to outpatient care. N Engl J Med. May 19 1994;330(20):1426-1430.
14.   Moormeier J. Breast cancer in black women. Ann Intern Med. May 15 1996;124(10):897-905.
15.   Coates RJ, Bransfield DD, Wesley M, *et al.* Differences between black and white women with breast cancer in time from symptom recognition to medical consultation. Black/White Cancer Survival Study Group. J Natl Cancer Inst. Jun 17 1992;84(12):938-950.
16.   Arnsberger P, Fox P, Ryder P, Nussey B, Zhang X, Otero-Sabogal R. Timely follow-up among multicultural women with abnormal mammograms. Am J Health Behav. Jan-Feb 2006;30(1):51-61.
17.   Poon EG, Haas JS, Louise Puopolo A, *et al.* Communication factors in the follow-up of abnormal mammograms. J Gen Intern Med. Apr 2004;19(4):316-323.

18.   Karliner LS, Patricia Kaplan C, Juarbe T, Pasick R, Perez-Stable EJ. Poor patient comprehension of abnormal mammography results. J Gen Intern Med. May 2005;20(5):432-437.

19.   Jones BA, Dailey A, Calvocoressi L, *et al.* Inadequate follow-up of abnormal screening mammograms: findings from the race differences in screening mammography process study (United States). Cancer Causes Control. Sep 2005;16(7):809-821.

20.   Kaplan CP, Eisenberg M, Erickson PI, Crane LA, Duffey S. Barriers to breast abnormality follow-up: minority, low-income patients' and their providers' view. Ethn Dis. Autumn 2005;15(4):720-726.

21.   Allen JD, Shelton RC, Harden E, Goldman RE. Follow-up of abnormal screening mammograms among low-income ethnically diverse women: findings from a qualitative study. Patient Educ Couns. Aug 2008;72(2):283-292.

22.   Shavers VL, Brown ML. Racial and ethnic disparities in the receipt of cancer treatment. J Natl Cancer Inst. Mar 6 2002;94(5):334-357.

23.   Lazovich D, Solomon CC, Thomas DB, Moe RE, White E. Breast conservation therapy in the United States following the 1990 National Institutes of Health Consensus Development Conference on the treatment of patients with early stage invasive breast carcinoma. Cancer. Aug 15 1999;86(4):628-637.

24.   Conference NC. Treatment of early-stage breast cancer. JAMA. 1991;265:391-395.

25.   Bruera E, Willey JS, Palmer JL, Rosales M. Treatment decisions for breast carcinoma: patient preferences and physician perceptions. Cancer. Apr 1 2002;94(7):2076-2080.

26.   Degner LF, Kristjanson LJ, Bowman D, *et al.* Information needs and decisional preferences in women with breast cancer. JAMA. May 14 1997;277(18):1485-1492.

27.   Richardson LC. Treatment of breast cancer in medically underserved women: a review. Breast J. Jan-Feb 2004;10(1):2-5.

APPENDICES

APPENDIX I: Supplemental Tables for Manuscript 2

Table 1. Predictors of Time to Diagnosis in Geometric Mean Days Stratified by Race

Predictors	White	African-Americans
Age at Diagnosis		
< 50	40.8 (28.7, 58)	56.2 (38.6, 82.1)
50-64	40.2 (27.7, 58.2)	52.7 (36, 77.1)
≥ 65	40.2 (24.5, 65.9)	36.7 (20, 67.4)
	p=0.9965	*p=0.4086*
Annual Income		
< $70,000	44.2 (32, 61)	50.9 (35.4, 73.2)
≥ $70,000	36.9 (27.2, 50.1)	44.8 (29.5, 68.1)
	p=0.3331	*p=0.4955*
Health Insurance		
Private Insurance	37.6 (27.5, 51.5)	41.3 (27.7, 61.6)
Non-private	43.3 (27.7, 67.9)	55.2 (36.5, 83.4)
	p=0.6328	*p=0.1797*
Mode of Detection		
Patient finding	45 (32.5, 62.2)	52.8 (34.8, 80.3)
Doctor Finding/Screening	36.3 (26.7, 49.2)	43.1 (30.3, 61.4)
	p=0.2474	*p=0.2511*
Family History of Breast Cancer		
Yes	39.9 (29.9, 53.3)	51 (34.2, 76.1)
No	40.8 (30.1, 55.4)	44.7 (31.1, 64.2)
	p=0.8857	*p=0.4133*
Comorbidity Count		
0	39 (27, 56.4)	48.2 (29.2, 79.5)
≥ 1	41.8 (32.5, 53.8)	47.3 (34.6, 64.6)
	p=0.7105	*p=0.9393*
Tumor Size		
≤ 1 cm	43.8 (32.1, 59.7)	57.4 (37.7, 87.4)
> 1 cm	37.3 (27.5, 50.5)	39.7 (27.6, 57)
	p=0.3512	*p=0.0493*
Tumor Grade		
Well differentiated	40.6 (28.2, 58.4)	44.6 (26.5, 75)
Moderately or Poorly differentiated	40.2 (31.2, 51.8)	51.1 (38, 68.8)
	p=0.9569	*p=0.5782*
Node Status		
Negative	37 (28.5, 48.1)	49.3 (35.4, 68.8)
Positive	44 (30.5, 63.6)	46.2 (29.9, 71.4)
	p=0.3694	*p=0.7096*
Caring Demand		
Yes	29.5 (19.6, 44.5)	64.6 (34.4, 121.1)
No	42.8 (29, 63.2)	55.6 (30, 103)
	p=0.0579	*p=0.5280*
Transportation Issues		
Yes	30.9 (17.3, 55)	66.7 (31.6, 140.9)
No	40.9 (30, 55.9)	53.8 (30.8, 94)
	p=0.3593	*p=0.5045*
Job related demands		
Yes	45.2 (25.7, 79.6)	72.7 (24.9, 212.8)
No	27.9 (20.4, 38.3)	49.4 (35.6, 68.5)
	p=0.1054	*p=0.4813*

^Adjusted for all variables in table

Table 2. Predictors of Time to Surgery in Geometric Mean Days Stratified by Race

Predictors	White	African-Americans
Age at Diagnosis		
< 50	31.1 (26.2, 36.9)	38.1 (29.9, 48.5)
50-64	27.5 (22.9, 33)	47.3 (37.3, 60)
≥ 65	32.6 (25.7, 41.2)	38.9 (25.4, 59.7)
	p=0.2341	*p=0.1642*
Annual Income		
< $70,000	32.5 (27.8, 37.9)	38.4 (30.3, 48.6)
≥ $70,000	28.3 (24.5, 32.7)	44.3 (33.6, 58.4)
	p=0.1179	*p=0.2311*
Health Insurance		
Private Insurance	30.5 (26.2, 35.4)	37 (28.6, 48)
Non-private	30.2 (24.3, 37.5)	46 (35, 60.3)
	p=0.9441	*p=0.1156*
Family History of Breast Cancer		
Yes	30.5 (26.6, 35)	40.7 (31.2, 53.1)
No	30.1 (26.1, 34.9)	41.8 (33, 53)
	p=0.8767	*p=0.7894*
Comorbidity Count		
0	30.1 (25.2, 35.9)	41.5 (30.2, 57)
≥ 1	30.6 (27.2, 34.3)	41 (33.2, 50.6)
	p=0.8509	*p=0.9260*
Tumor Size		
≤ 1 cm	31.3 (27, 36.2)	40.9 (31.3, 53.3)
> 1 cm	29.4 (25.5, 33.9)	41.6 (32.4, 53.5)
	p=0.4351	*p=0.8757*
Tumor Grade		
Well differentiated	31.2 (26.3, 36.9)	48.1 (34.2, 67.7)
Moderately or Poorly differentiated	29.5 (26.2, 33.3)	35.4 (29, 43)
	p=0.5088	*p=0.0556*
Node Status		
Negative	32.1 (28.4, 36.4)	39.7 (32, 49.2)
Positive	28.6 (24.2, 33.8)	42.9 (31.9, 57.7)
	p=0.1711	*p=0.5253*
Type of Hospital		
Community Based	27.9 (23.8, 32.6)	42 (32.7, 53.9)
Teaching Facility	33 (29, 37.5)	40.5 (31.4, 52.2)
	p=0.0282	*p=0.7295*
Type of Surgery		
BCS	24.9 (21.8, 28.5)	35.2 (27.6, 44.8)
Mastectomy	36.9 (31.6, 43)	48.4 (37.1, 63.1)
	p=0<.0001	*p=0.0047*
Caring Demand		
Yes	27.6 (20, 38.1)	39.7 (20.6, 76.4)
No	24.7 (18.3, 33.3)	35.9 (18.8, 68.7)
	p=0.4652	*p=0.6826*
Transportation Issues		
Yes	29.9 (19.2, 46.7)	42.9 (19.7, 93.2)
No	22.8 (17.9, 28.9)	33.2 (18.4, 59.9)
	p=0.2481	*p=0.4405*
Job related demands		
Yes	24.4 (15.8, 37.7)	49.5 (15.9, 153.7)
No	27.9 (21.9, 35.6)	28.8 (20.6, 40.2)
	p=0.5541	*p=0.3516*

^Adjusted for all variables in table

Table 3. Predictors of Time to Chemotherapy in Geometric Mean Days Stratified by Race		
Predictors	White	African-Americans
Age at Diagnosis		
< 50	39.7 (33.8, 46.5)	54.7 (44.1, 67.7)
50-64	43.5 (36.3, 52)	51.3 (41.1, 63.9)
≥ 65	52.6 (39, 70.9)	53.8 (38.3, 75.5)
	p=0.1709	*p=0.6990*
Annual Income		
< $70,000	42.6 (35.4, 51.3)	51 (41.1, 63.1)
≥ $70,000	47.4 (39.8, 56.4)	55.6 (44.1, 70)
	p=0.2488	*p=0.2501*
Health Insurance		
Private Insurance	45.3 (38.5, 53.4)	49 (38.8, 61.9)
Non-private	44.5 (35.4, 55.9)	57.8 (46.3, 72.2)
	p=0.8820	*p=0.0692*
Family History of Breast Cancer		
Yes	44.1 (37.4, 52)	51 (40.5, 64.3)
No	45.8 (38.3, 54.7)	55.5 (44.9, 68.7)
	p=0.6089	*p=0.2472*
Comorbidity Count		
0	46.3 (38, 56.3)	48.9 (38, 63.1)
≥ 1	43.6 (37.5, 50.7)	57.9 (47.1, 71.1)
	p=0.4667	*p=0.0891*
Tumor Size		
≤ 1 cm	47.8 (38.7, 58.9)	57.5 (43.7, 75.8)
> 1 cm	42.3 (36.5, 49)	49.2 (40.8, 59.3)
	p=0.1974	*p=0.1461*
Tumor Grade		
Well differentiated	43.6 (35.1, 54.2)	61.3 (43.2, 86.9)
Moderately or Poorly differentiated	46.2 (40.1, 53.3)	46.2 (39.8, 53.7)
	p=0.5603	*p=0.0996*
Node Status		
Negative	46.5 (39.1, 55.2)	53.9 (42.9, 67.9)
Positive	43.4 (36.6, 51.6)	52.5 (42.4, 64.9)
	p=0.3698	*p=0.6939*
Type of Surgery		
BCS	42.3 (35.7, 50.2)	52.3 (41.8, 65.5)
Mastectomy	47.7 (40.2, 56.6)	54.1 (43.6, 67.1)
	p=0.1009	*p=0.6107*
Caring Demand		
Yes	50.5 (36.4, 69.9)	40.6 (33.3, 49.5)
No	53.7 (38.6, 74.7)	48.2 (39, 59.5)
	p=0.5332	*p=0.0508*
Transportation Issues		
Yes	56 (35.4, 88.5)	48.1 (36.8, 62.7)
No	48.4 (37.6, 62.3)	40.7 (34.2, 48.5)
	p=0.4658	*p=0.1991*
Job related demands		
Yes	61.7 (36.2, 105.2)	40.9 (29.3, 57)
No	43.9 (36, 53.6)	47.9 (42.1, 54.4)
	p=0.1846	*p=0.3527*

^Adjusted for all variables in table

Table 4. Predictors of Time to Radiation Treatment in BCS patients: Geometric Mean Days Stratified by Race

Predictors	White	African-Americans
Age at Diagnosis		
< 50	38 (29.1, 49.6)	37.5 (26.8, 52.3)
50-64	32 (25.1, 40.7)	33.2 (24.2, 45.5)
≥ 65	32.2 (24, 43.3)	16.2 (9.9, 26.7)
	p=0.4210	*p=0.0058*
Annual Income		
< $70,000	34.5 (28, 42.6)	29 (21.6, 39.1)
≥ $70,000	33.4 (27.1, 41.1)	25.5 (18, 36.3)
	p=0.7829	*p=0.3590*
Health Insurance		
Private Insurance	35.9 (29.4, 43.8)	21.3 (15.4, 29.5)
Non-private	32.1 (23.9, 43.2)	34.8 (24.3, 49.8)
	p=0.5631	*p=0.0067*
Family History of Breast Cancer		
Yes	35 (28.7, 42.8)	23.9 (16.8, 33.8)
No	32.9 (27, 40)	31.1 (23.1, 41.8)
	p=0.5538	*p=0.0517*
Comorbidity Count		
0	36.1 (28.4, 45.8)	24.5 (16, 37.5)
≥ 1	31.9 (26.6, 38.3)	30.2 (23.6, 38.8)
	p=0.3536	*p=0.2676*
Tumor Size		
≤ 1 cm	30.5 (24.7, 37.6)	24.4 (17, 34.9)
> 1 cm	37.8 (30.9, 46.2)	30.4 (22.3, 41.3)
	p=0.0743	*p=0.1691*
Tumor Grade		
Well differentiated	34.1 (27.1, 42.8)	23.9 (15.6, 36.6)
Moderately or Poorly differentiated	33.8 (28.5, 40.1)	31.1 (24.1, 40)
	p=0.9442	*p=0.1731*
Node Status		
Negative	31.8 (26.6, 38)	29.2 (22.3, 38.1)
Positive	36.3 (28.2, 46.7)	25.4 (17.1, 37.8)
	p=0.3506	*p=0.4133*
Type of Radiation Facility		
Community Based	37.7 (31.6, 44.8)	30.8 (22.5, 42.3)
Teaching Facility	30.6 (24.3, 38.5)	24 (17.4, 33.3)
	p=0.0788	*p=0.0494*
Radiation Sequence		
After Chemotherapy	26 (20.8, 32.6)	23.7 (16.5, 34)
After Surgery	44.2 (36, 54.5)	31.3 (23, 42.6)
	p=0.0002	*p=0.0928*
Caring Demand		
Yes	43.8 (32.9, 58.2)	42.7 (23.6, 77.2)
No	39.6 (31.1, 50.4)	35 (19.8, 61.9)
	p=0.4502	*p=0.3202*
Transportation Issues		
Yes	42.9 (30.1, 61.2)	44.9 (22.6, 89.2)
No	40.4 (32.4, 50.3)	33.3 (20.1, 55.2)
	p=0.7439	*p=0.2466*
Job related demands		
Yes	47.2 (32.2, 69.1)	39.5 (14.3, 109.6)
No	36.8 (30.2, 44.8)	37.8 (29.1, 49.2)
	p=0.2188	*p=0.9296*

^Adjusted for all variables in table

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Publications

1. Briss P, Rimer B, Reilley B, Coates RC, Lee NC, Mullen P, Corso P, Hutchinson AB, Hiatt R, Kerner J, **George P**, White C, Gandhi N, Saraiya M, Breslow R, Isham G, Teutsch SM, Hinman AR, Lawrence R; Task Force on Community Preventive Services. Promoting Informed Decisions About Cancer Screening in Communities and Healthcare Systems. *American Journal of Preventive Medicine*. 2004; 26(1): 81-83.

2. Simard EP, Miller J, **George PA,** Wasley A, Alter MJ, Bell BP, Finelli L. Hepatitis B Vaccination Coverage Levels Among Healthcare Workers in the United States, 2002-2003. *Infection Control and Hospital Epidemiology*. July 2007; Vol. 28, No. 7: 783-790

3. Bialek SR, **George PA**, Xia GL *et al.* Use of Molecular Epidemiology to Confirm a Multistate Outbreak of Hepatitis A Caused by Consumption of Oysters. *Clinical Infectious Diseases*. 2007; 44(6):838-40