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Emerging Trends in Surgical and Adjuvant Radiation Therapies among Women Diagnosed with Ductal Carcinoma in Situ

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Abstract

BACKGROUND—The use of surgery and radiation therapy in treating ductal carcinoma in situ (DCIS) is directed by treatment guidelines and evidence from research. We sought to investigate recent patterns in DCIS treatment by demographic factors.

METHODS—Data for women diagnosed with DCIS between 1998 and 2011 (n = 416,232) in the National Cancer Data Base were assessed for trends in treatment patterns by age group, calendar year, ancestral/ethnic group and geographic region. The likelihood of receiving specific treatment modalities was analyzed using multivariable logistic regression.

RESULTS—DCIS cases were most frequently treated with breast conserving surgery (BCS) and adjuvant radiation (45.6%). After an initial rise, the use of adjuvant radiation following BCS plateaued at around 70% after 2007, with increasing utilization of mastectomy beyond 2005. Additionally, there was an increasing trend in post-mastectomy reconstruction over time, and

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women of African ancestry (odds ratio, 0.69; 95% confidence interval,0.66–0.72) and Hispanic women were less likely to undergo reconstruction (odds ratio, 0.83; 95% confidence interval, 0.78–0.89) compared to women of European ancestry. A similar trend was observed in contralateral risk reducing mastectomy utilization, with women of European ancestry having a more rapid rise in the utilization of contralateral risk reducing mastectomy among all ancestral/ethnic groups.

CONCLUSION—Recent trends demonstrate a plateau in radiation therapy administration following BCS, with increasing utilization of mastectomy, reconstruction and contralateral risk reducing mastectomy. There are substantial differences in treatment utilization according to ancestry/ethnicity and geographical region. Further studies examining patient-physician decision making surrounding DCIS treatment are warranted.

Keywords

Breast cancer; ductal carcinoma in situ; mastectomy; reconstruction; radiation

INTRODUCTION

Ductal carcinoma in situ (DCIS) is a pre-invasive breast lesion, with one woman diagnosed with DCIS for every four women diagnosed with invasive breast cancer.[1] Prior to routine mammography, DCIS lesions accounted for less than 5% of breast cancer cases.[2] However, widespread screening mammography caused a rise in the detection of DCIS lesions.[3] The incidence of DCIS in the US increased from 1.87 per 100,000 women in 1973–1975 to 32.5 in 2004.[4]

Various treatment options to lower the risk of recurrence and prevent invasive breast cancer are available for patients with DCIS. The DCIS 5-year mortality rate is <2%.[5] Surgical excision with or without adjuvant therapy is the primary approach for DCIS treatment. Surgical options include breast conserving surgery (BCS) with or without radiotherapy, or mastectomy.[2, 6] Adjuvant tamoxifen may also be utilized, especially among women with estrogen receptor (ER) positive disease.[7]

Variations in the utilization of treatment modalities for DCIS treatment likely result in under-treatment in some cases or overly aggressive surgical therapy for others.[8, 9] Avoidance of adjuvant radiation therapy following BCS may increase the utilization of mastectomy despite the lack of overall survival benefit.[10, 11] Geographic and temporal variations have been observed in the treatment of DCIS, with the Midwest and south-central states having higher rates of mastectomies compared to Northeastern states.[8] Breast reconstruction following mastectomy is associated with geographical/regional location, institutional practice pattern, age and race/ethnicity.[8, 10]

The utilization of contralateral mastectomy (i.e. surgical removal of the uninvolved breast), particularly among high-risk women, is controversial. Factors associated with contralateral mastectomy include younger age, family history, genetic predisposition, tumor size and higher grade.[12, 13]

Given the historical variation in treatment of DCIS, we sought to examine recent trends using the National Cancer Data Base (NCDB) including the association of demographic factors with local DCIS treatment.

MATERIALS AND METHODS

Study Population

The NCDB is a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. Over 1500 cancer care institutions contribute data to the NCDB, including 70% of all newly diagnosed cancers in the United States. Further details about the NCDB have been reported elsewhere.[14, 15] We obtained data from the NCDB for women ≥20 years diagnosed with DCIS between 1998 and 2011. The study was approved by the University of Wisconsin-Madison institutional review board. Women diagnosed with DCIS were identified using International Classification of Diseases for Oncology third edition (behavior code 2 and morphology codes 8050, 8201, 8210, 8230, 8401, 8500, 8501, 8503, 8504, 8507, 8522, 8523, 8540 and 8543), and were coded as stage 0 according to the American Joint Committee on Cancer seventh edition guidelines.[16, 17] A total of 434,695 cases met these criteria. Patients with no treatment data (n= 4,248), who had an unspecified mastectomy type with no information on receipt of reconstruction or contralateral mastectomy (n=1,562), extended radical mastectomy (n=87) or did not receive any treatment (n=12,566) were excluded.

Variables of Interest

Treatments were categorized as BCS, BCS with radiation, and mastectomy (i.e. total mastectomy). Women undergoing mastectomy were sub-classified based on whether they received contralateral mastectomy and/or breast reconstruction. Ancestry/ethnicity was classified as Non-Hispanic European, Non-Hispanic African, Hispanic, and other. Region of residence was categorized as Northeast, Midwest, West and South. Facility type was classified into community cancer program, comprehensive community cancer program, academic/research program (including NCI-designated comprehensive cancer centers) and other. Treatment facilities were divided into patient volume tertiles based on the number of women treated for DCIS.

Statistical Analysis

We estimated the odds ratios (OR) and 95% confidence intervals (CI) of receiving adjuvant radiation therapy following BCS and the utilization of BCS (with or without radiation therapy) compared to mastectomy using multivariable logistic regression models. Additionally, we evaluated breast reconstruction following mastectomy and contralateral breast removal following therapeutic mastectomy. In all models, covariates included age of diagnosis, ancestry/ethnicity, year of diagnosis and geographic region. We also adjusted for comorbidity, health insurance, tumor size and grade, treatment facility and institutional volume. Two sided *P*-values <0.05 were considered to be statistically significant. Interaction between ancestry/ethnicity and year of diagnosis were examined. Age-adjusted rates of surgeries following therapeutic mastectomy (i.e. breast reconstruction and contralateral risk-

reducing mastectomy) by ancestral/ethnic groups were calculated using the 2000 U.S. standard million population.[18] Analyses were performed using SAS®, version 9.3.

RESULTS

We identified 416,232 women diagnosed with DCIS between 1998 and 2011 (Table 1). Women in the 45–54 and 55–64 age groups accounted for most cases (over 26% each). Women of non-Hispanic European ancestry comprised most cases (80.4%). Over 95% had health insurance. 46% were treated with adjuvant radiation therapy and 29% received adjuvant endocrine therapy.

BCS and Mastectomy

Women ≥45 years were more likely to undergo BCS (Table 2). Compared to 1998–1999, women diagnosed since 1999 were more likely to undergo BCS, peaking during 2006–2007 (OR, 1.23; 95% CI, 1.16–1.31) and subsequently declining. Ancestry/ethnicity was associated with BCS treatment, as women of African and Hispanic ancestry were more likely to undergo BCS. Surgery patterns changed over time according to ancestry/ethnicity with BCS rates for women of African ancestry being lowest in 1998, while women of European ancestry had the lowest rates in 2011 (data not shown). Women outside the Northeast had lower odds of undergoing BCS.

BCS with Adjuvant Radiation Therapy

Age was associated with the likelihood of undergoing adjuvant radiation therapy following BCS (Table 3). There was an increase in the proportion of women undergoing adjuvant radiation therapy following BCS from 58.5% in 1998–1999 to 70% during 2006–2011. Women of European ancestry were more likely to undergo adjuvant radiation therapy following BCS than other ancestral/ethnic groups. Women in the Midwest were more likely to receive adjuvant radiation therapy following BCS.

Breast Reconstruction following Mastectomy

Younger age at diagnosis was associated with undergoing breast reconstruction (Table 4). Women diagnosed in 2010–2011 were more likely to undergo reconstruction following mastectomy compared to women in 1998–1999 (OR, 3.57; 95% CI, 3.27–3.91). Breast reconstruction rates have been increasing among the three racial/ancestral groups with women of European ancestry having the highest rates (Figure 1A). Women in the Northeast were more likely to undergo breast reconstruction following mastectomy.

Contralateral Risk Reducing Mastectomy

Rates of contralateral risk reducing mastectomy decreased with increasing age at diagnosis (Table 4). Women diagnosed in 2010 were more likely to undergo contralateral mastectomy than women diagnosed in 1998–1999 (OR, 4.56; 95% CI, 4.09–5.08). The annual proportion of women undergoing contralateral mastectomy increased in all 3 racial/ancestral groups (Figure 1B). Women outside the Northeast were more likely to undergo contralateral mastectomy.

DISCUSSION

In analyzing the patterns of care for DCIS among women using a large nationwide clinical database, we observed an increase in BCS among women diagnosed with DCIS between 1998 and 2005. This was followed by a decline in BCS through 2011, with a corresponding rise in mastectomy utilization. This is consistent with previous observations of increasing mastectomy rates among women with early stage breast cancer.[19, 20] Unlike previous studies which included small invasive node negative cancers and in situ cancer, we observed these findings specifically among DCIS patients.

Using the NCDB, we observed an increase in adjuvant radiation therapy utilization following BCS until 2007. BCS and adjuvant radiation treatment is beneficial in preventing localized ipsilateral breast cancer recurrence compared to BCS alone, with similar survival benefit to mastectomy.[11, 21] Although most women were treated with BCS and adjuvant radiation therapy (46%), the proportion of women undergoing adjuvant radiation therapy following BCS has plateaued at 70% after 2007. The increasing trend in the proportion of women undergoing adjuvant radiation therapy following DCIS diagnosis has been previously shown.[8, 22] However, our findings suggest adjuvant radiation therapy utilization may be at a saturation level. Not all women diagnosed with DCIS undergoing BCS are ideal candidates for adjuvant radiation therapy and women may have concerns regarding adverse effects of radiation. Social factors such as cultural beliefs, marital status and social support may be related to choice of undergoing radiation therapy following BCS.[23, 24] In terms of population density/metro area, previous research has demonstrated differences in receipt of radiotherapy among breast cancer patients.[25] Specifically, a greater proportion of women dwelling in urban areas receive adjuvant radiation treatment compared to women with rural residence locations. Additionally, women living at an increased distance from a hospital with a radiotherapy facility were less likely to undergo BCS.[26]

Since 2005, the proportion of women undergoing mastectomy following DCIS has increased, despite BCS with adjuvant radiation therapy generally being an appropriate and less extensive treatment option. Apart from concerns about the effects of radiation therapy, some women may be dissatisfied with their cosmetic outcome following BCS.[27] Breast reconstruction following mastectomy may be favored for cosmetic and psychological reasons.[28, 29] Legislative mandates such as the Women's Health and Cancer Rights Act (WHCRA) requiring coverage for breast reconstruction following mastectomy by most insurance plans may have influenced the increase. A recent study observed 2-to-4-fold increases in reconstruction following the enactment of the legislation.[30]

Throughout the study period, women of European ancestry consistently had higher proportions undergoing breast reconstruction following mastectomy. However, women of African ancestry and Hispanic women showed an increasing trend in post-mastectomy reconstruction, almost parallel to that observed among women of European ancestry. Lack of insurance coverage, lack of knowledge about post-mastectomy reconstruction, cultural issues and socioeconomic status have been previously associated with observed differences in post-mastectomy reconstruction by ancestry/ethnicity.[31, 32]

We observed an increasing trend in the utilization of contralateral risk reducing mastectomy among women undergoing mastectomy and a more rapid rise among women of European ancestry compared to other racial/ancestral groups. This trend has been observed previously among woman <45 years of age diagnosed with early stage breast cancer.[33] Previous research has also shown similar prevalence of *BRCA1/2* mutations among breast cancer patients of European, African, and Hispanic ancestry.[34] Mammography screening rates appear to be higher among women of European ancestry.[35, 36] Ancestral/ethnic differences in screening may be lead to differences in diagnosis and treatment. Furthermore, previous research has shown that women of European ancestry are less likely to delegate treatment decisions to their physicians.[37] This may be related to higher educational attainment.[38] Women with higher levels of educational attainment have increased participation in surgical decision making and are more likely to undergo mastectomy.[39, 40]

Breast cancer diagnosed in younger women is associated with a higher risk of recurrence following breast conserving surgery.[41] Undergoing lifelong surveillance may be disruptive and anxiety provoking for some. Hence, younger women may prefer to undergo mastectomy including the removal of the uninvolved breast. The decision to undergo mastectomy may be influenced by multifocal or widespread disease, positive margins, age, physician's preference, access to radiation facilities, fear of recurrence and insurance coverage.[19, 20, 42] For many women, bilateral mastectomy may be considered aggressive treatment given the generally low absolute risk of a future invasive carcinoma. There is no overall survival benefit for contralateral risk reducing mastectomy in early stage breast cancer among ER-negative patients.[43] Survival benefits seen in some studies may be due to selection bias.[44] Among *BRCA1/2* mutation carriers, contralateral mastectomy may confer a survival advantage.[45] Despite comparable overall survival to BCS with adjuvant radiation therapy, mastectomy in some instances may be a preferred treatment option among women diagnosed with DCIS without any deleterious BRCA mutations (such as in multifocal disease).[6, 11]The role of contralateral mastectomy for DCIS treatment in general, is debatable.

Geographical variations in the utilization of surgical treatments including post-mastectomy reconstruction among women diagnosed with DCIS have been documented previously.[8] We observed persistent geographic variations in the utilization of DCIS treatment options. For instance, the Northeast had the greatest odds of undergoing breast conserving surgery and reconstruction following mastectomy, and the smallest odds of undergoing contralateral mastectomy. This may suggest a preference towards aesthetic preservation in the Northeast. Regional variations may reflect practice differences among institutions and available surgical expertise. In our study, the West and South compared to Northeast had the highest odds ratios for contralateral mastectomy and the least odds ratios for breast conserving surgery alone and with adjuvant radiation therapy. The variations observed in the utilization of contralateral mastectomy may be related to physician preferences including institutional practice patterns, and access to radiation treatment facilities.[26, 46] The presence of more surgeons with reconstruction expertise in treatment facilities is associated with increased utilization of these procedures following mastectomy.[10]

The NCDB is a rich resource for examining patterns of DCIS treatment, but it does have limitations. Cancer cases are from only Commission on Cancer accredited hospitals. Hence, the NCDB may represent selected cases. The inability to differentiate between immediate and delayed reconstruction was another limitation. The absence of data on hormone receptor status and human epidermal growth factor receptor 2 (*HER2/neu*) for most patients and lack of information on some genetic markers such as *BRCA* gene status precluded the assessment of treatment variation according DCIS molecular subtypes and genetic risk. Finally, we lacked information on patients' preferences and physician's characteristics including variations in the geographic distribution of reconstructive surgeons and radiation oncologists. However, our study findings corroborate findings from population based cancer registry data such as SEER.[19, 20] The NCDB has the added advantage of being the largest national cancer registry, with data from over 70% of new cancer cases, from health facilities ranging from academic to community based cancer facilities. With this resource, we have been able to provide updated information regarding trends in local therapies for DCIS treatment with the discovery of some new findings.

CONCLUSION

In assessing patterns of care for women diagnosed with DCIS, substantial variation exists in all four major local treatment decisions. Significant differences between treatment types were observed according to ancestry/ethnicity and geographical region. There was increasing utilization of adjuvant radiation treatment following breast conserving surgery and breast reconstruction following mastectomy since 1998. These increases coincided with the introduction of policies and clinical guidelines that favored their utilization. The study period mostly encompassed the years prior to the passage of the Patient Protection and Affordable Care Act of 2010. It will be interesting to examine trends in DCIS treatment following the implementation of this legislation. Finally, the impact of treatment variation on cancer recurrence and progression to invasive cancer warrants further investigation.

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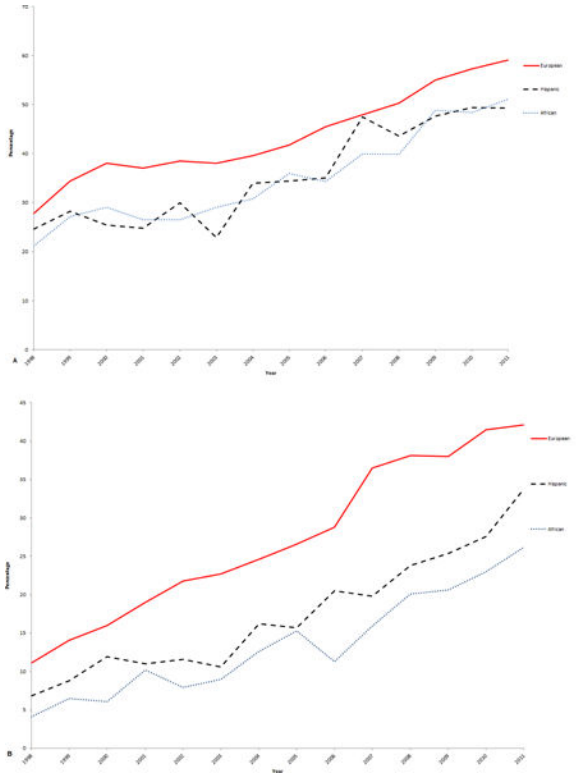

Figure 1.

Age-adjusted annual proportion of patients undergoing (A) reconstruction and (B) risk reducing contralateral mastectomy among women with mastectomy for ductal carcinoma in situ according to European, African, and Hispanic ancestry, National Cancer Data Base, 1998–2011.

Table 1

Characteristics of Women Diagnosed with Ductal Carcinoma in situ in the National Cancer Data Base, 1998–2011

Characteristic	N	%
Total	416,232	
Age group, y		
<45	47,567	11.4
45–54	108,907	26.2
55–64	109,767	26.4
65–74	89,712	21.5
≥75	60,285	14.5
Year of diagnosis		
1998–1999	48,002	11.5
2000–2001	54,101	13.0
2002–2003	56,418	13.5
2004–2005	56,421	13.6
2006–2007	61,994	14.9
2008–2009	70,605	17.0
2010–2011	68,691	16.5
Ancestry/ethnicity		
Non-Hispanic, European	334,757	80.4
Non-Hispanic, African	42,648	10.2
Hispanic	16,354	3.9
Other	22,473	5.4
Geographic region		
Northeast	103,564	25.0
Midwest	102,289	24.5
South	139,354	33.5
West	71,025	17.0
Health insurance		
Private	250,004	60.1
Government	151,069	36.3
Uninsured	6,173	1.5
Unknown	8,986	2.2
Primary treatment		
Breast conserving surgery without adjuvant radiation	95,076	22.8
Breast conserving surgery with adjuvant radiation	189,847	45.6
Mastectomy	131,309	31.5
Adjuvant endocrine therapy		
Yes	120,607	29.0

Characteristic	N	%
No	270,859	65.1
Unknown	24,766	5.9
Facility type		
Community cancer program	40,832	9.8
Comprehensive community cancer program	247,915	59.5
Academic/research program	118,025	28.4
Other specified types of cancer programs	9,460	2.3

Table 2

Demographics of Breast Conserving Surgery among Women Diagnosed with Ductal Carcinoma in situ, National Cancer Data Base, 1998–2011

Variable	Mastectomy (N= 131,309) Row %	BCS (N= 284,923) Row %	OR[a] (95% CI)
Age group, y			
<45	43.5	56.5	1
45–54	32.9	67.1	1.60 (1.54–1.65)
55–64	29.2	70.8	1.92 (1.85–1.99)
65–74	28.4	71.6	2.14 (2.05–2.23)
≥75	28.6	71.4	2.11 (2.02–2.21)
Year of diagnosis			
1998–1999	33.4	66.6	1
2000–2001	31.9	68.1	1.12 (1.08–1.16)
2002–2003	29.9	70.1	1.21 (1.15–1.26)
2004–2005	29.3	70.7	1.21 (1.13–1.29)
2006–2007	30.2	69.8	1.23 (1.16–1.31)
2008–2009	32.8	67.2	1.12 (1.05–1.19)
2010–2011	33.1	66.9	1.12 (1.05–1.20)
Ancestry/ethnicity			
Non-Hispanic, European	31.4	68.6	1
Non-Hispanic, African	32.2	67.8	1.05 (1.01–1.08)
Hispanic	31.6	68.4	1.14 (1.08–1.21)
Other	32.3	67.7	1.00 (0.94–1.06)
Geographic region			
Northeast	25.9	74.1	1
Midwest	31.7	68.3	0.75 (0.73–0.77)
South	35.2	64.8	0.64 (0.62–0.66)
West	32.4	67.6	0.70 (0.68–0.73)

[a]Adjusted for comorbidity index, health insurance, facility type, DCIS patient volume, tumor size and grade

Test of interaction between year of diagnosis and ancestry/ethnicity: X^2=42.70, df=18, P< 0.01

Table 3

Demographics of Radiation Treatment Following Breast Conserving Surgery for Ductal Carcinoma in situ, National Cancer Data Base, 1998–2011

Variable	BCS Only (N=95,076) Row %	BCS with Adjuvant Radiation (N=189,847) Row %	OR[a] (95% CI)
Age group, y			
<45	31.0	69.0	1
45–54	29.1	70.9	1.07 (1.04–1.11)
55–64	28.3	71.8	1.10 (1.07–1.14)
65–74	32.7	67.3	0.95 (0.92–0.98)
≥75	52.2	47.8	0.41 (0.39–0.43)
Year of diagnosis			
1998–1999	41.4	58.6	1
2000–2001	39.1	60.9	1.07 (1.04–1.11)
2002–2003	36.2	63.8	1.12 (1.08–1.16)
2004–2005	32.4	67.6	1.19 (1.13–1.25)
2006–2007	29.2	70.8	1.38 (1.31–1.46)
2008–2009	29.1	70.9	1.40 (1.32–1.47)
2010–2011	29.9	70.1	1.32 (1.25–1.39)
Ancestry/ethnicity			
Non-Hispanic, European	32.9	67.1	1
Non-Hispanic, African	34.2	65.8	0.92 (0.90–0.95)
Hispanic	36.8	63.2	0.86 (0.83–0.90)
Other	35.6	64.4	0.89 (0.86–0.93)
Geographic region			
Northeast	36.2	63.8	1
Midwest	25.8	74.2	1.62 (1.58–1.65)
South	35.0	65.0	0.99 (0.97–1.01)
West	36.9	63.1	0.83 (0.81–0.85)

[a]Adjusted for comorbidity index, health insurance, facility type, DCIS patient volume, tumor size and grade

Test of interaction between year of diagnosis and ancestry/ethnicity: X^2=21.03, df=18, P= 0.28

Table 4

Demographics of Reconstruction and Contralateral Risk Reduction Mastectomy among Women Diagnosed with Ductal Carcinoma in situ, National Cancer Data Base, 1998–2011

Variable	Mastectomy alone (N=87,130) Row %	Mastectomy with Reconstruction (N=44,179) Row %	OR[a] (95% CI)	Unilateral Mastectomy (N=104,970) Row %	Contralateral Mastectomy (N=26,339) Row %	OR[a] (95% CI)
Age group, y						
<45	45.5	54.5	1	67.1	32.9	1
45–54	52.0	48.0	0.75 (0.72–0.79)	73.6	26.4	0.67 (0.65–0.70)
55–64	66.0	34.0	0.42 (0.41–0.44)	80.3	19.7	0.45 (0.43–0.47)
65–74	83.9	16.1	0.24 (0.23–0.25)	88.8	11.2	0.29 (0.27–0.31)
≥75	95.9	4.1	0.06 (0.05–0.06)	94.8	5.2	0.13 (0.12–0.14)
Year of diagnosis						
1998–1999	78.7	21.3	1	91.4	8.6	1
2000–2001	74.5	25.5	1.31 (1.24–1.38)	88.4	11.6	1.43 (1.33–1.54)
2002–2003	72.9	27.1	1.40 (1.31–1.49)	85.0	15.0	1.85 (1.70–2.01)
2004–2005	69.9	30.1	1.57 (1.43–1.72)	82.0	18.0	2.12 (1.93–2.41)
2006–2007	64.5	35.5	2.04 (1.86–2.23)	77.3	22.7	2.95 (2.64–3.29)
2008–2009	58.5	41.5	2.76 (2.52–3.02)	72.8	27.2	3.79 (3.40–4.23)
2010–2011	53.6	46.4	3.57 (3.27–3.91)	69.7	30.3	4.56 (4.09–5.08)
Ancestry/ethnicity						
Non-Hispanic, European	65.5	34.5	1	78.5	21.5	1
Non-Hispanic, African	72.0	28.0	0.69 (0.66–0.72)	88.5	11.5	0.43 (0.41–0.45)
Hispanic	66.3	33.7	0.83 (0.78–0.89)	83.2	16.8	0.57 (0.53–0.62)
Other	68.0	32.0	0.66 (0.63–0.70)	82.9	17.1	0.56 (0.52–0.60)
Geographic region						
Northeast	60.6	39.5	1	81.2	18.8	1
Midwest	66.0	34.0	0.88 (0.85–0.92)	80.6	19.5	1.14 (1.10–1.20)
South	68.5	31.5	0.81 (0.78–0.84)	80.0	20.0	1.29 (1.24–1.34)
West	69.0	31.0	0.72 (0.68–0.75)	77.4	22.6	1.49 (1.42–1.56)

[a]Adjusted for comorbidity index, health insurance, facility type, DCIS patient volume, tumor size and grade

Reconstruction: Test of interaction between year of diagnosis and ancestry/ethnicity: X^2=25.90, df=18, P=0.10

Contralateral risk reducing mastectomy: Test of interaction between year of diagnosis and ancestry/ethnicity: X^2=27.63, df=18, P=0.07