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Racial variation in breast cancer treatment among Department of Defense beneficiaries

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Abstract

BACKGROUND—Although the overall age-adjusted incidence rates for female breast cancer are higher among whites than blacks, mortality rates are higher among blacks. Many attribute this discrepancy to disparities in healthcare access and to blacks presenting with later stage disease. Within the Department of Defense (DoD) Military Health System all beneficiaries have equal access to healthcare. The aim of this study was to determine if breast cancer treatment varied between white and black female breast cancer patients in the DoD system.

METHODS—The study data were drawn from the DoD cancer registry and medical claims databases. Study subjects included 2,308 white and 391 black female beneficiaries diagnosed with breast cancer between 1998 and 2000. Multivariate logistic regression analyses that controlled for demographic factors, tumor characteristics, and comorbidities were used to assess racial differences in the receipt of surgery, chemotherapy and hormonal therapy.

RESULTS—There was no significant difference in surgery type, particularly when mastectomy was compared to breast conserving surgery plus radiation (blacks vs. whites: OR=1.1; 95% CI=0.8–1.5). Among those with local stage tumors, blacks were as likely as whites to receive chemotherapy (OR=1.2; 95% CI=0.9–1.8) and hormonal therapy (OR=1.0; 95% CI=0.7–1.4). Among those with regional stage tumors, blacks were significantly less likely than whites to receive chemotherapy (OR=0.4; 95% CI=0.2–0.7) and hormonal therapy (OR=0.5; 95% CI=0.3–0.8).

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Disclaimers:

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CONCLUSION—Even within an equal access healthcare system, stage-related racial variations in breast cancer treatment are evident. Studies that identify driving factors behind these within-stage racial disparities are warranted.

Introduction

With 207,090 new diagnoses and 39,840 deaths estimated for 2010, breast cancer is the most commonly occurring cancer among U.S. women and the second most common cause of cancer death.¹ While the overall age-adjusted incidence rates for female breast cancer are higher among whites than blacks, mortality rates are higher among blacks.¹

Analyses of national data have indicated that the racial disparity in breast cancer mortality started to emerge in the 1970s and continues to grow.^{2,3} The reason for the disparity is likely multi-factorial but black women tend to present with later-stage disease compared to white women.⁴ However, racial disparities in mortality have been observed among women with similar staged tumors. These within-stage disparities have been shown to be independent of other tumor characteristics and more pronounced among later stage tumors and among women younger than 65 years of age.^{5,6} Therefore, factors other than tumor characteristics may be influential.

Variations in healthcare access and cancer treatment may partially account for racial disparities in breast cancer mortality. Although not all,^{7–9} some studies have found racial differences with respect to breast cancer treatment.^{10–15} Although many of these previous studies have been conducted among Medicare recipients^{11,13,15} or have adjusted for insurance status,^{10,12} residual racial differences in healthcare access may have existed. The Department of Defense (DoD) Military Healthcare System (MHS) provides universal healthcare to all racial groups and offers a unique opportunity to investigate racial disparities. Although a previous study¹⁴ within the MHS indicated that black women were more likely to receive chemotherapy and less likely to receive hormone therapy compared to white women, treatment was not the main focus of the study and multivariate comparisons were not conducted. Therefore, it was unclear if racial variations in breast cancer treatment exist after controlling for possible confounders such as age at diagnosis, tumor stage and hormone receptor status. Using the combined DoD cancer registry and medical claims data, the aim of this study was to determine if there were variations in breast cancer treatment between white and black women after adjustment for other variables.

Methods

This study was based on the linked data from the DoD Central Cancer Registry (CCR) and the MHS data repository (MDR). The CCR was initiated in 1998 and contains information for all cancer patients diagnosed or treated at military treatment facilities (MTFs) among DoD beneficiaries, including active-duty military personnel, retired military personnel and their dependents. Duplicate records pertaining to the same cancer patient were consolidated and quality assurance was conducted following the guidelines established by the North America Association of Central Cancer Registries (NAACCR). The CCR includes information on demographic variables (e.g., age, and race), diagnostic factors (e.g., date of

diagnosis), tumor characteristics (e.g., histology and stage), and cancer treatment (e.g. surgery, radiation, chemotherapy, and hormonal therapy). The coding of cancer was originally based on the second edition of the International Classification of Diseases for Oncology (ICD-O-2)¹⁶ but was later recoded using the third edition ICD-O-3.¹⁷ The MDR includes administrative and medical care information from October 1997 for all DoD beneficiaries, including care received at MTFs (direct care) or at non-MTFs that is paid for by the DoD (indirect care). The MDR database includes information on clinical diagnoses of all medical conditions, which are coded using the International Classification of Diseases – Ninth Revision (ICD-9), and diagnostic and treatment procedures, which are coded using ICD-9 or Current Procedural Terminology codes.

Women were eligible for inclusion in this study if they had surgical treatment for histologically confirmed local or regional stage, first primary, malignant breast cancer diagnosed between 1998 and 2000. Local stage disease included invasive tumors that were confined to the breast while regional disease included invasive tumors that had spread beyond the breast either directly or via regional lymph nodes.¹⁸ Distant stage tumors were not included due to limited sample size (white: 59; black: 17).

Demographic variables and tumor characteristic data were obtained from CCR. Hormone receptor status was considered positive if either estrogen receptor (ER) or progesterone receptor (PR) status was recorded as positive, negative if both ER and PR were negative, and unknown if neither measure was recorded. Data on her2/neu expression were not available; therefore, triple negative status could not be determined. Data on surgery, radiation therapy, and chemotherapy were obtained by combining CCR and MDR data and were considered “yes” if either database recorded their occurrence. Data on hormonal therapy were obtained only from CCR because MDR prescription data were not available until 2002. Treatment within the first 6 months^{11,13,19} after diagnosis was determined and compared. Comorbidities were considered to be present if a diagnosis was recorded in the MDR data in the 12 months prior to breast cancer diagnosis. The level of comorbidity present was categorized according to the Charlson Comorbidity Index;²⁰ cancer diagnoses were excluded from the calculation.

Chi-square tests were used to compare basic demographic variables, tumor characteristics and cancer treatments between black and white women. Logistic regression was used to assess the difference in treatments between white and black women with adjustment for potential confounders. The treatments compared included: 1) mastectomy versus breast conserving surgery (BCS); 2) mastectomy versus BCS plus radiation (because radiation is conventionally combined with BCS); 3) chemotherapy and 4) hormonal therapy among those with hormone receptor-positive tumors (because hormonal therapy is conventionally provided only for these tumors). Potential confounders considered included age at diagnosis, tumor stage at diagnosis, comorbidity index, and tumor hormone receptor status. Treatments other than that under assessment were also considered potential confounders and adjusted for because of their possible relatedness to both race and the treatment being assessed. Marital status, active duty status, service branch affiliation, and year of diagnosis were also included because of their potentially complex effects on study results. Tumor characteristics other than stage (e.g., size and grade) did not appear to be confounders (point estimate for

race was not changed more than 10% when variable was included) and thereby were not included in the final logistic regression models. Effect modification of the racial difference in treatment by age, active duty status, tumor stage and hormone receptor status was assessed by including two-way interaction terms in the regression models. If the interaction term was statistically significant then stratified regression models were constructed and reported. All statistical analyses were performed using SAS (version 9.1; SAS Institute Inc, Cary, NC) and the two-sided significance level was set at $p < 0.05$.

Results

Between 1998 and 2000 there were 2,781 eligible women diagnosed with breast cancer; however, 68 white and 14 black women were excluded from the analyses because they did not have medical billing records available, did not have a breast cancer diagnosis in MDR or had breast cancer surgery of unknown type. In total, 2,308 (86%) white and 391 (14%) black women were included in the study (Table 1). Black women were significantly younger and more likely to have never been married, be active duty personnel, be an Army beneficiary, have later stage tumors, and have hormone receptor-negative tumors. When stratified by age, hormone receptor-positive tumors remained more common among white women than black women (<50: 60% vs. 51%, $p < 0.01$; >50: 69% vs. 66%, $p = 0.07$, data not shown). There was no significant racial difference observed for comorbidity, tumor size or year of diagnosis. Univariate comparisons indicated that black women were more likely to receive mastectomies and chemotherapy but less likely to have radiation and hormonal therapy.

Type of Surgery

After covariate adjustment there was no significant difference between black women compared to white women in receipt of mastectomy versus BCS (OR: 0.8, 95% CI: 0.6–1.1; Table 2). There was also no significant difference after adjustment between black versus white women when the receipt of mastectomy without radiation was compared to BCS plus radiation (OR: 1.1, 95% CI: 0.8–1.5).

Chemotherapy

When assessing the effect of chemotherapy, there was a significant interaction between race and stage of disease ($p < 0.01$). As a result, stage-stratified regression models are reported. Unadjusted racial comparisons among women with localized tumors indicated that black women were more likely to receive chemotherapy than white women (OR: 2.0, 95% CI: 1.5–2.6; data not shown). However, the difference was attenuated and no longer significant (OR: 1.2, 95% CI: 0.9–1.7) after covariate adjustment (Table 3). There was suggestive evidence of a further interaction ($p = 0.07$) between race and hormonal receptor-positive status (at least one positive receptor versus none). Among women with local stage receptor-positive tumors, black women remained significantly more likely than white women to receive chemotherapy (OR: 1.8, 95% CI: 1.2–2.8); no significant racial difference was observed among women with local stage receptor-negative tumors (OR: 0.6, 95% CI: 0.3–1.3; data not shown). Among women with regional stage tumors, unadjusted models did not indicate that there was a significant racial difference (OR: 0.8, 95% CI: 0.5–1.2; data not

shown); however, after covariate adjustment, black women were significantly less likely to receive chemotherapy (OR: 0.4, 95% CI: 0.2–0.7; Table 3).

Hormonal therapy

When assessing the effect of hormonal therapy, a significant interaction between race and stage of disease ($p=0.02$) was detected among receptor-positive women; therefore stage stratified regression models are reported in Table 4. Among women with local stage receptor-positive tumors, there was no significant difference between black versus white women in receipt of hormonal therapy (unadjusted OR: 0.7, 95% CI: 0.5–1.1; adjusted OR: 1.0, 95% CI: 0.7–1.4). Among women with regional stage receptor-positive tumors, black women were less likely to receive hormonal therapy (unadjusted and adjusted ORs: 0.5, 95% CIs: 0.3–0.8).

Discussion

Black women in the DoD health care system between 1998 and 2000 were more likely to present with later stage, receptor-negative breast cancer tumors than were white women. Black women were also younger and more likely to be active duty personnel at the time of diagnosis. When these factors were taken into account, there was no significant difference in the type of surgery received, particularly when mastectomy was compared to BCS plus radiation. The racial difference in receipt of chemotherapy varied by stage and hormone receptor status. Among women with localized tumors, the racial difference was apparent only for receptor-positive tumors; black women tended to be more likely to have chemotherapy than white women. However, among women with regional tumors black women were less likely to receive chemotherapy than white women. Additionally, black women with receptor-positive, regional stage tumors were less likely to receive hormonal therapy than white women.

In 1990, the National Institutes of Health Consensus Panel recommended BCS plus radiation in lieu of mastectomy for the surgical treatment of early breast cancers. The recommendation was made because BCS plus radiation was less invasive while providing equivalent survival.²¹ However, because of the lack of difference in survival, the decision to have BCS versus mastectomy likely reflects an individual's choice due to various factors (i.e., breast preservation versus side effects from radiation therapy). Although, historically, black women were less likely to have BCS, our findings are in agreement with more recent studies that have found similar surgery choices by race.^{10,22,23}

Overall, there was no racial difference in the receipt of chemotherapy or hormonal therapy among those with local stage disease. These findings are in agreement with a previous study.¹⁰ Racial differences in receipt of chemotherapy were, however, observed among women with local-stage, hormone receptor-positive tumors. Within this subgroup, black women were more likely to have chemotherapy (OR: 1.8, 95% CI: 1.2–2.8). This racial variation in treatment may be partially due to black women having more advanced within-stage tumors; 24% of these black women had tumors of grade III/IV compared to 16% of white women ($p=0.01$; data not shown). When adjusted for tumor grade the racial difference was attenuated but remained significant (OR: 1.6, 95% CI: 1.0–2.5).

Among women with regional stage tumors, black women were less likely to receive chemotherapy or hormonal therapy. These findings are similar to previous findings^{10,12,14} but our study suggests that accessibility to medical care may not account for the racial differences. No significant difference by tumor grade, tumor size or number of positive lymph-nodes was observed between the two racial groups ($p>0.05$; data not shown); as such, tumor presentation does not appear to explain the observed differences in the aggressiveness of the treatment. While it is not known what the reasons are for the observed differences, they may be multi-factorial. Previous research has shown that white women tend to talk to their physicians more about the rationale for chemotherapy and tamoxifen use, and are therefore more likely to have these treatments.²⁴ It is unclear, however, whether physicians' treatment recommendations vary by the patient's race. There is also evidence that racial differences exist in the perceived benefits of receiving adjuvant therapy. For example, Schleinitz et al.²⁵ observed that black women were less likely than white women to associate chemotherapy with improved quality of life. In addition, a patient's choice of treatment is likely influenced by a combination of factors that can vary by race including knowledge of treatment options, cost burden, cultural and spiritual beliefs, and social support.^{26–29}

The main strength of this study was the use of data from a healthcare system based on equal access regardless of race. Our finding of racial differences in treatment suggests that factors other than medical care access warrant further research. Additionally, the ability to adjust for demographic variables, tumor characteristics and comorbidities was made possible through the combined use of cancer registry and medical administrative databases. Limitations of the study included those inherent in using medical administrative databases; possible limitations include incomplete data, coding inaccuracies and errors. Again, however, these limitations were minimized by combining the administrative data with the cancer registry data. A theoretical concern that completeness of case records might vary by calendar year was addressed by examination of the data after elimination of the first year's data. When the cases diagnosed in 1998 were excluded from the analyses the study inferences did not change. There is still a possibility that data are incomplete for some patients if they have other health insurance and seek care elsewhere. If such incompleteness is differential by race, the results might be affected. For example, if whites have greater access to other healthcare and are more likely to be diagnosed and treated elsewhere, the estimated racial differences in treatment for regional stage disease may be underestimated.

In summary, among women with equal healthcare access, variations between white and black women were observed for the receipt of chemotherapy and hormonal therapy. Studies that identify the driving factors behind these racial disparities are needed. In the meantime, targeted education for black women, especially women with regional disease, concerning the benefits of chemotherapy and hormonal therapy may decrease the observed racial differences.

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Table 1

Comparison of basic characteristics by race among female DoD beneficiaries diagnosed with breast cancer, 1998–2000.

	White		Black		p-value*
	N	%	N	%	
Age					
	<50	633	27%	218	56%
	50	1675	73%	173	44%
Marital Status	Married	1834	79%	301	77%
	Separated/Divorced/Widowed	363	16%	56	14%
	Single, Never married	41	2%	18	5%
	Unknown	70	3%	16	4%
Comorbidity Index**	0	1705	74%	305	78%
	1	361	16%	44	11%
	2	242	10%	42	11%
Duty Status	Non-Active Duty	2216	96%	328	84%
	Active Duty	92	4%	63	16%
Service Branch Affiliation	Army	579	25%	146	37%
	Air Force	683	30%	90	23%
	Marines	75	3%	16	4%
	Navy	382	17%	36	9%
	Other/Unknown	589	26%	103	26%
Year of diagnosis	1998	787	34%	133	34%
	1999	833	36%	151	39%
	2000	688	30%	107	27%
Tumor Stage	Local	1637	71%	223	57%
	Regional	671	29%	168	43%
Tumor Size, cm	<1	515	22%	68	17%
	1–<2	864	37%	135	35%
	2–<3	440	19%	84	21%
	3–<4	180	8%	41	10%
	4	223	10%	44	11%
	Unknown	86	4%	19	5%

	White		Black		p-value*
	N	%	N	%	
Positive Lymph Nodes	0	1427	62%	193	49%
	1	236	10%	60	15%
	2-3	186	8%	48	12%
	4-9	133	6%	43	11%
	10-74	93	4%	14	4%
	Unknown	233	10%	33	8%
Tumor Grade	Grade I	503	22%	51	13%
	Grade II	836	36%	134	34%
	Grade III-IV	646	28%	150	38%
	Unknown	323	14%	56	14%
Hormone Receptor Status	ER+ and/or PR+	1535	67%	222	57%
	ER- and PR-	345	15%	80	20%
	Unknown	428	19%	89	23%
					<0.01
Surgery/Radiation	Mastectomy only	1045	45%	182	47%
	Mastectomy plus radiation	176	8%	37	9%
	BCS only	300	13%	68	17%
	BCS plus radiation	787	34%	104	27%
					<0.01
Chemotherapy	No	1161	50%	139	36%
	Yes	1147	50%	252	64%
Hormonal Therapy	No	1319	57%	268	69%
	Yes	847	37%	103	26%
	Unknown	142	6%	20	5%
					<0.01

DoD indicates Department of Defense; ER, estrogen receptor; PR, progesterone receptor. *Chi-Square test.

**Charlson Comorbidity Index excluding cancer diagnoses from the calculation.

Table 2

Adjusted odds of surgery among female DoD beneficiaries diagnosed with breast cancer, 1998–2000.

	Mastectomy vs. BCS (n=2699)		Mastectomy without radiation vs. BCS with radiation (n=2118)	
	OR [*]	95% CI	OR [*]	95% CI
Race		reference		reference
White				
Black	0.8	0.6 1.1	1.1	0.8 1.5
Age, years		reference		reference
<50				
50	0.7	0.6 0.9*	0.9	0.7 1.2
Marital Status		reference		reference
Married				
Separated/Divorced/Widowed	0.9	0.6 1.3	1.3	0.9 1.7
Single, never married	0.6	0.3 1.2	1.0	0.5 2.0
Unknown	0.6	0.4 1.1	0.9	0.5 1.5
Comorbidity Index ^{**}		reference		reference
0				
1	1.1	0.9 1.5	1.0	0.8 1.3
2	1.3	1.0 1.8*	1.1	0.8 1.5
Duty Status		reference		reference
Non-Active Duty				
Active Duty	0.9	0.6 1.4	0.7	0.4 1.1
Service Branch Affiliation		reference		reference
Army				
Air Force	0.9	0.7 1.2	0.9	0.7 1.2
Marines	1.1	0.6 2.0	1.3	0.7 2.2
Navy	1.0	0.7 1.3	0.9	0.7 1.2
Other/Unknown	1.2	0.9 1.6	1.1	0.8 1.5
Year of diagnosis		reference		reference
1998				
1999	1.1	0.8 1.3	1.0	0.8 1.2
2000	0.8	0.6 1.0	0.9	0.7 1.1
Tumor Stage		reference		reference
Local				
Regional	2.3	1.9 3.0*	2.6	2.1 3.3*
Hormone Receptor Status		reference		reference
ER+ and/or PR+				
ER- and PR-	0.9	0.6 1.1	0.9	0.7 1.2
Unknown	1.0	0.8 1.2	0.8	0.6 1.0
Radiation		reference		--
No				

		Mastectomy vs. BCS (n=2699)		Mastectomy without radiation vs. BCS with radiation (n=2118)	
		OR*	95% CI	OR*	95% CI
Chemotherapy	Yes	0.1	0.1	0.1*	--
	No		reference		reference
Hormonal therapy	Yes	1.4	1.1	1.7*	1.1
	No		reference		1.8*
	Yes	1.7	1.3	2.1*	reference
	Unknown	0.7	0.4	1.0	0.7
				0.9	0.6

DoD indicates Department of Defense; BCS, breast conserving surgery; OR, odds ratio; 95% CI, confidence interval; ER, estrogen receptor; PR, progesterone receptor.

Logistic regression analysis controlling for the effects of all listed variables.

* p<0.05

** Charlson Comorbidity Index excluding cancer diagnoses from the calculation.

Adjusted odds of chemotherapy by demographic and clinical characteristics among female DoD beneficiaries diagnosed with breast cancer, 1998–2000.

Table 3

	Local stage disease (n=1860)			Regional stage disease (n=839)		
	OR*	95% CI	OR*	95% CI	OR*	95% CI
Race		reference		reference		reference
	White					
	Black	1.2	0.9 1.7	0.4	0.2 0.7*	
Age, years	<50		reference		reference	
	50	0.3	0.2 0.4*	0.2	0.1 0.3*	
Marital Status	Married		reference		reference	
	Separated/Divorced/Widowed	0.4	0.2 0.6*	0.3	0.2 0.6*	
	Single, never married	0.7	0.3 1.6	0.8	0.2 3.3	
	Unknown	0.7	0.4 1.2	0.4	0.1 1.4	
Comorbidity Index**	0		reference		reference	
	1	0.9	0.6 1.2	0.6	0.3 1.0	
	2	0.8	0.6 1.2	0.8	0.4 1.6	
Duty Status	Non-Active Duty		reference		reference	
	Active Duty	1.7	1.0 3.0*	0.8	0.2 3.0	
Service Branch Affiliation	Army		reference		reference	
	Air Force	0.9	0.7 1.2	0.9	0.5 1.6	
	Marines	0.5	0.2 1.0	3.9	0.5 30.5	
	Navy	0.9	0.7 1.3	1.2	0.6 2.7	
	Other/Unknown	1.0	0.7 1.5	1.3	0.7 2.6	
Year of diagnosis	1998		reference		reference	
	1999	1.6	1.2 2.1*	1.2	0.7 1.9	
	2000	1.9	1.5 2.5*	1.4	0.8 2.4	
Hormone Receptor Status	ER+ and/or PR+		reference		reference	
	ER- and PR-	3.3	2.4 4.5*	2.1	1.0 4.5*	
	Unknown	1.1	0.8 1.5	0.9	0.5 1.6	
Surgery/Radiation	Mastectomy Only		reference		reference	
	Mastectomy +rad	1.4	0.8 2.5	0.9	0.5 1.6	

	Local stage disease (n=1860)		Regional stage disease (n=839)				
	OR*	95% CI	OR*	95% CI			
Hormonal therapy	BCS only	0.7	0.5	1.0	0.8	0.4	1.6
	BCS +rad	0.6	0.5	0.8*	1.0	0.5	1.7
	No		reference			reference	
	Yes	0.4	0.3	0.6*	0.3	0.2	0.4*
	Unknown	0.5	0.3	0.7*	0.6	0.3	1.6

DoD indicates Department of Defense; OR, odds ratio; 95% CI, confidence interval; ER, estrogen receptor; PR, progesterone receptor.
Logistic regression analysis controlling for the effects of all listed variables.

* p<0.05

** Charlson Comorbidity Index excluding cancer diagnoses from the calculation.

Adjusted odds of hormonal therapy by demographic and clinical characteristics among female DoD beneficiaries diagnosed with ER and/or PR positive breast cancer, 1998–2000.

Table 4

		Local stage disease (n=1208)		Regional stage disease (n=549)			
		OR	95% CI	OR	95% CI		
Race	White		reference		reference		
	Black	1.0	0.6	1.4	0.5	0.3	0.8*
Age	<50		reference		reference		
	50	1.3	1.0	1.8*	1.5	1.0	2.4*
Marital Status	Married		reference		reference		
	Separated/Divorced/Widowed	0.6	0.4	0.9*	0.8	0.4	1.4
	Single, never married	0.7	0.3	1.8	1.1	0.4	3.0
	Unknown	1.0	0.5	1.9	0.7	0.1	2.9
Comorbidity Index**	0		reference		reference		
	1	1.4	1.0	1.9*	0.7	0.4	1.2
	2	0.8	0.6	1.2	0.8	0.4	1.5
Duty Status	Non-Active Duty		reference				
	Active Duty	1.0	0.5	1.9	1.7	0.7	4.2
Service Branch Affiliation	Army		reference		reference		
	Air Force	1.2	0.9	1.6	0.9	0.6	1.4
	Marines	0.8	0.4	1.5	0.5	0.2	1.5
	Navy	1.1	0.8	1.6	0.9	0.5	1.7
	Other/Unknown	1.6	1.1	2.4*	1.1	0.6	2.0
Year of diagnosis	1998		reference		reference		
	1999	1.2	0.9	1.6	1.3	0.9	2.0
	2000	1.0	0.7	1.3	1.0	0.6	1.6
Surgery/Radiation	Mastectomy Only		reference		reference		
	Mastectomy +rad	0.9	0.4	1.6	1.1	0.7	1.8
	BCS only	0.7	0.5	1.0	0.4	0.2	0.8*
	BCS +rad	1.0	0.8	1.3	1.6	1.0	2.6*

	Local stage disease (n=1208)		Regional stage disease (n=549)	
	OR	95% CI	OR	95% CI
Chemotherapy	No	reference	reference	
	Yes	0.5 0.4 0.7*	0.4	0.3 0.6*

DoD indicates Department of Defense; OR, odds ratio; 95% CI, confidence interval; ER, estrogen receptor; PR, progesterone receptor.

Logistic regression analysis controlling for the effects of all listed variables.

* p<0.05

** Charlson Comorbidity Index excluding cancer diagnoses from the calculation.