



Prognostic factor testing among older women with ductal carcinoma in situ and early invasive breast cancer

Breast Cancer Diagnostic Workup

Data Points # 15

The American Cancer Society estimates that in the United States in 2012, 229,060 new cases of invasive breast cancer were diagnosed, and 39,920 people died of the disease. In the same year, approximately 63,300 women were diagnosed with ductal carcinoma in situ (DCIS) of the breast.¹ DCIS is noninvasive breast cancer representing a wide variety of cell abnormalities confined to the ducts of the breast.² While we do not know the percentage of DCIS cases that will progress to invasive breast cancer, many studies suggest that women diagnosed with DCIS are at high risk for invasive breast cancer (see Virnig, Shamlivan, et al., for a review).³

Typical treatment for DCIS includes surgical removal of the tumor by mastectomy or breast-conserving surgery (BCS).²⁻⁴ After tumor removal, some DCIS will recur or progress to invasive cancer. However, lack of knowledge about prognostic and predictive markers makes it difficult to assess a patient's prognosis. Known risk factors for DCIS progression and recurrence include comedo histology, younger age, larger tumor size, high pathologic or nuclear grade, and positive surgical margins.³

For invasive breast cancer, specific markers of tumor aggressiveness are used to guide assessment of patient prognosis. Well-recognized treatment pathways exist; however, scant evidence supports the applicability of this knowledge to DCIS.³ In invasive breast cancer, removed tissue is tested for estrogen receptors (ERs), progesterone receptors (PRs), and human epidermal growth factor receptor 2 (HER2). These tests provide information about the tumor's aggressiveness, based on how it responds to external stimuli. ER and HER2 testing helps identify women who might benefit from treatments intended to reduce the risk of ipsilateral breast tumor recurrence (IBTR) and of contralateral breast cancer. ER and HER2 testing could be used to identify the subgroup of DCIS patients most likely to benefit from endocrine treatment or trastuzumab.^{2,5}



Estrogen receptor (ER) testing rates have increased over time for both ductal carcinoma in situ (DCIS) and early invasive cancers. However, rates of positive ER tests have not increased.

Rates of BRCA genetic testing are very low (<2%) for both DCIS and early invasive breast cancers.

Current guidelines do not recommend routine testing for human epidermal growth factor receptor 2 (HER2) for women with DCIS. Yet, rates of this testing increased between 2004 and 2007 in both DCIS and early invasive breast cancer groups.

Rates of testing varied significantly across race groups for all tests. However, the pattern of change differed between tests.

For women with ER+ DCIS and invasive breast cancer, treatment with antiestrogens such as tamoxifen and aromatase inhibitors might prevent recurrence or progression.

Randomized trials have evaluated the benefit of tamoxifen after BCS for DCIS.³ In the National Surgical Adjuvant Breast and Bowel Project (NSAPB) B-24 trial, use of tamoxifen was associated with a modest decrease in ipsilateral and contralateral breast cancer events after BCS.⁶ However, in a study conducted by the United Kingdom Coordinating Committee on Cancer Research, tamoxifen did not significantly reduce overall breast cancer events.⁷ Neither study included ER testing.

A recent meta-analysis found ER+ DCIS to be associated with significantly lower IBTR rates, while HER2+ DCIS was significantly associated with higher IBTR rates.³ However, none of the included studies had more than 140 subjects. Current National Comprehensive Cancer Network (NCCN) guidelines recommend ER testing for patients newly diagnosed with DCIS.⁴ Further, these guidelines suggest that physicians “consider” tamoxifen for ER+ DCIS but note that use of tamoxifen is of unknown benefit for ER-DCIS.⁴ ER testing is considered standard of care for women with early invasive cancer.⁴ HER2 positivity may be linked to an increased risk of recurrence, as well as to tumor sensitivity to trastuzumab (Herceptin).^{3,5}

At present, groups such as NCCN consider HER2 testing a standard of care for women with early invasive cancer but do not recommend it for women with DCIS.⁴ Studies of PR testing are inconclusive in the context of DCIS.³ Therefore, treatment guidelines do not include PR tests, despite their being considered standard care for early invasive breast cancer.⁴

Testing for BRCA (the “breast cancer gene”) helps to identify women with a hereditary risk of breast cancer. Family history of breast cancer is thought to be associated with increased risk of both DCIS and invasive breast cancer recurrence.^{3,7} BRCA testing for patients with DCIS offers the main benefit of identifying patients who have high rates of IBTR after BCS, contralateral breast cancer, and ovarian cancer.³ For patients with BRCA-associated DCIS or invasive cancer, treatment recommendations frequently include bilateral mastectomy with or without bilateral oophorectomy.⁷

Lymph node testing is used to detect whether the cancer has progressed beyond the breast tissue. In the past decade, sentinel lymph node biopsy (SLNB) has replaced routine axillary lymph node dissection (ALND) for most patients with invasive breast cancer.³ ALND has not been recommended for patients with confirmed DCIS, because the preinvasive cells do not metastasize and thus are not associated with risk of lymph node involvement.⁴ In 1991, Silverstein, et al., reported that less than 1 percent of patients with DCIS had lymph node metastases detected by ALND.⁹ Today, most DCIS diagnoses are made by image-guided core needle biopsy. About 15 percent of patients with DCIS originally diagnosed by core needle biopsy will have a final diagnosis of invasive breast cancer after excision or mastectomy.³ If invasive breast cancer is identified in the excision or mastectomy specimen, axillary staging is recommended to determine stage and guide treatment decisions. Therefore, some scientists recommend SLNB for all or selected patients with DCIS detected by core needle biopsy.¹⁰⁻¹² A systematic review of studies evaluating SLNB for pure DCIS found the incidence of lymph node positivity and lymph node micrometastases to be 0.9 percent and 1.5 percent, respectively.³ In women with invasive disease, lymph nodes are sampled to ascertain the extent to which the cancer has spread. This is an essential component to determining cancer stage.

This report examines variation in testing of ER, PR, HER2, BRCA, and lymph nodes in women ages 65 and older who were enrolled in the Medicare program and diagnosed with DCIS between 2004 and 2007. We analyzed how testing varied by patient age, tumor size, and tumor grade—all factors known to increase women’s risk of developing invasive disease. We also examine how testing varies by race and geographic location, as well as over time. We compare the rates of testing for patients with DCIS and those with invasive disease to provide context and to better understand how testing rates differ between both groups.

METHODS

We identified women diagnosed with DCIS and early invasive breast cancer (i.e., stage 1) in the SEER-Medicare data linkage from 2004 to 2007. The Surveillance, Epidemiology, and End Results program (SEER) is a network of cancer registries collecting information on persons with cancer from Medicare eligibility until death.¹³ We limited the sample to women aged 65 and older enrolled in fee for service Medicare Parts A and B (entitlement indicator of “3” and HMO indicator of “0” or “A”) for at least two months prior to diagnosis and four months post-diagnosis (see **Table 1** for population statistics). We excluded women with another cancer diagnosed before the breast cancer diagnosis and women without microscopically confirmed disease. We also excluded women diagnosed in Louisiana in 2005 because of the disruption in data collection following hurricane Katrina.

Definitions

DCIS: We defined DCIS using data on histology, stage, and behavior information collected by the SEER registries. Specifically, we included International Classification of Diseases for Oncology, Third Edition (ICD-O-3) histologies 8500, 8521, 8501, 8230, 8522, and 8523 with an ICD-O-3 behavior code of 2 and ICD-O-3 histology 8500 with an ICD-O-3 behavior code of 5.

Comedo subtype: Comedo subtype was defined using ICD-O-3 behavior code of 2 and ICD-O-3 histology 8501. We included women with comedo histology in the definition of DCIS. Results are presented separately for the comedo subtype where appropriate.

Early invasive breast cancer: We defined early invasive breast cancer using SEER summary local stage and ICD-O-3 behavior code of 3. SEER stage takes into account all information available through the first course of treatment.

Race/ethnicity: We defined race using the SEER Race Recode Y variable. We used the SEER origin variable to indicate Hispanic ethnicity among whites, resulting in the following race/ethnicity categories: white, white Hispanic, black, Asian or Pacific Islander.

Urban/rural: We defined urban/rural status using the 2003 Rural/Urban Continuum Codes from the Department of Agriculture’s Economic Research Service.¹⁴ The codes categorize people based on their county of residence. “Big Metro” refers to counties in metro areas with at least 1 million in population. “Metro” refers to other counties in metro areas. “Urban” refers to counties not in metro areas with at least 20,000 population. “Less Urban” refers to counties with 2,500-19,999 people. “Rural” refers to counties with fewer than 2,500 residents.

Tumor size: We defined tumor size using the SEER collaborative staging tumor extension field. We report rates for microscopic, <1 cm, <2 cm, 2-5 cm, and >5 cm. Other categories are included in the cohort but not reported (e.g., unknown and diffuse).

Grade: We defined grade using the data fields provided by SEER: well differentiated, moderately/intermediately differentiated, poorly differentiated, and undifferentiated/anaplastic. Unknowns are included but not reported.

Surgery type: We determined whether women had BCS or mastectomy using the SEER Surgery of the Primary Site (sxprif1) values (BCS: 20-24 and mastectomy: 40-80).

ER/PR: For this report, we used ER and PR testing information from Medicare claims data; however, claims data do not allow separating of ER only, PR only, and combined ER/PR testing. We considered cases with a pathology claim within four months of diagnosis with a Health Care Procedure Coding System (HCPCS) code 88360, 88361, or 88342 (either technical or professional component or both) to have been tested for ER/PR positivity. Since SEER registries also collect information about ER and PR testing, we conducted a sensitivity analysis comparing the SEER testing rates to those detected using our claims-based algorithm. We classified women as “not tested” if they were reported by SEER as being not tested. The results of this analysis showed that our claims-based measure was, although slightly lower, close to SEER rates of testing (e.g., ER testing rates of 78 percent in SEER and 76 percent in the claims among DCIS patients; see **Figure 1** and **Appendix A**). Both datasets led to similar conclusions about testing patterns.

Lymph node testing: SEER registries collect information regarding lymph node sampling and positivity. We excluded from this measure the women for whom node testing status was unknown (n=307).

By definition, this cohort contains no women with positive lymph nodes. The SEER database re-classifies women originally diagnosed with DCIS or early invasive cancer who have positive lymph nodes as having regional disease. Therefore, this is a measure of the proportion of node negative women who had nodes tested.

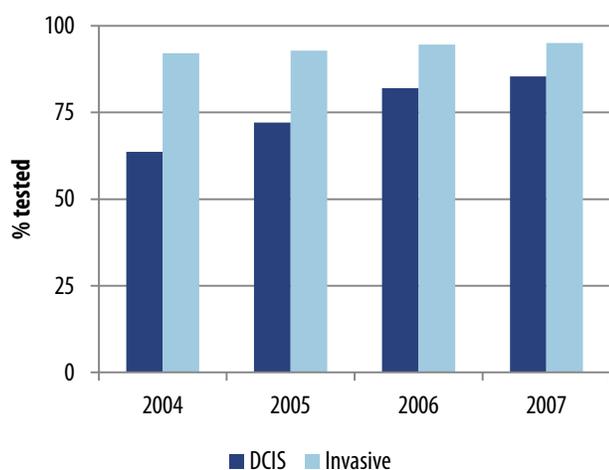
RESULTS

Between 2004 and 2007, 31,217 women in the SEER program who were also Medicare enrolled were diagnosed with either DCIS or early invasive breast cancer. Most of these women (81.5%) were diagnosed with early invasive breast cancer. Eleven percent of women with DCIS had comedo subtype.

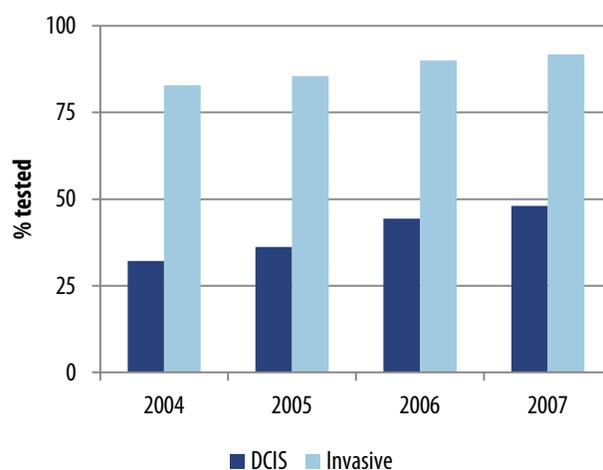
Women with DCIS were younger than women diagnosed with early invasive breast cancer. In addition, a higher percentage of women with DCIS was black. Women with DCIS also had a higher incidence of unknown tumor size and grade (**Table 1**).

Figure 1: Trends in ER/PR, HER2, BRCA, and lymph node testing among ductal carcinoma in situ and early invasive breast cancer diagnoses in SEER, 2004-2007

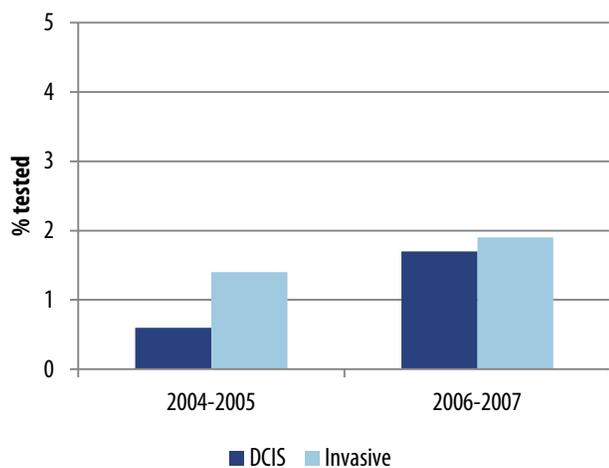
ER/PR testing



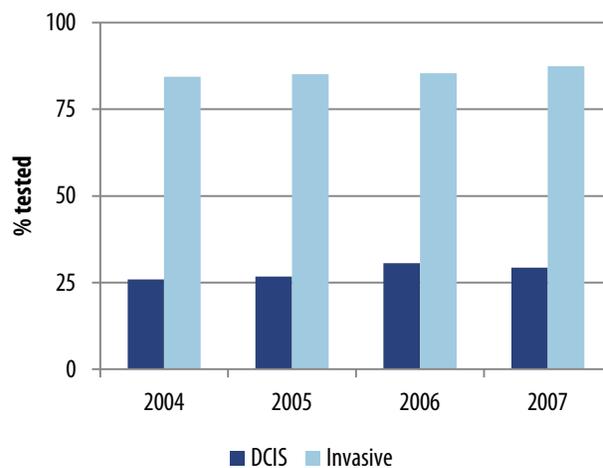
HER2 testing



BRCA testing



Lymph node evaluation



Of those with known size and grade, women with DCIS were more likely to have smaller tumors and higher grade tumors. Women with DCIS were more likely to be treated with BCS.

Estrogen and Progesterone Receptor Testing

Rates of ER/PR testing for women with DCIS varied strongly over the study period from 63.6 percent in 2004 to 85.4 percent in 2007 (**Figure 1, Appendices B, C, and D**). Therefore we could not easily interpret overall estimates.

We discuss results for 2007 only in the body of the report. See **Appendices B, C, and D** for data on years 2004-2006.

ER/PR testing rates did not vary importantly by age (**Table 2**). Among women with DCIS, black women were less likely to have ER/PR testing than other racial groups (82.1% versus >85% for all other races). Rates of testing varied greatly by SEER registry, from 71.4 percent in Utah to 97 percent in San Jose. Women in big metropolitan areas were the most likely to receive ER/PR testing.

Table 2: ER/PR and HER2 testing among ductal carcinoma in situ and early invasive breast cancer diagnoses in SEER, 2007

	DCIS			Invasive				DCIS			Invasive		
	n	ER/PR %	HER2 %	n	ER/PR %	HER2 %		n	ER/PR %	HER2 %	n	ER/PR %	HER2 %
Total	1,395	85.4	48.0	6,348	95.0	91.7							
Age (years)													
65-69	408	85.5	45.3	1,693	92.9	90.3	San Jose	33	97.0	42.4	184	94.6	90.2
70-74	391	85.9	48.1	1,529	96.1	92.5	Seattle	95	80.0	29.5	381	95.3	94.0
75-79	298	85.9	48.7	1,347	95.8	92.7	Utah	35	71.4	34.3	156	96.8	89.7
80-84	209	84.2	50.7	1,013	95.5	92.0	Urbanicity						
85+	89	84.3	51.7	766	95.2	90.7	Big metro	776	87.2	48.5	3,574	95.4	92.6
Race							Metro	430	85.8	46.2	1,863	94.9	91.9
White	1,114	85.5	46.9	5,282	95.3	92.1	Urban	78	73.1	50.0	384	92.7	87.0
White Hispanic	70	87.1	55.7	270	95.9	92.2	Less urban	90	78.9	38.5	431	94.0	87.5
Black	106	82.1	51.9	372	92.5	88.4	Rural	21	85.7	*	95	93.7	90.5
Asian/Pacific Islander	80	87.5	51.3	277	91.3	87.0	Tumor Size						
SEER Registry							Microscopic	35	80.0	37.1	106	93.4	78.3
Atlanta	54	92.6	44.4	205	98.5	92.2	<1 cm	415	81.2	42.7	1,727	95.8	92.6
Connecticut	116	77.6	46.6	441	96.6	93.2	<2 cm	277	89.5	50.2	2,695	95.2	92.6
Detroit	89	94.4	50.6	407	99.3	95.6	2-5 cm	194	93.3	56.2	1,538	94.1	90.6
Greater California	273	85.7	48.0	1,358	93.7	92.0	>5 cm	48	95.8	56.3	152	96.1	92.1
Hawaii	27	77.8	51.9	101	90.1	89.1	Grade						
Iowa	84	85.7	54.8	419	97.6	90.0	Well differentiated	149	82.6	46.3	1,876	96.0	92.3
Kentucky	101	86.1	49.5	477	95.6	89.3	Moderately differentiated	451	86.5	45.5	2,712	94.8	92.0
Los Angeles	109	81.7	52.3	469	94.0	93.4	Poorly differentiated	426	90.1	52.6	1,334	93.8	90.6
Louisiana	89	79.8	59.6	376	92.3	89.4	Undifferentiated	162	85.2	49.4	46	97.8	93.5
New Jersey	202	91.1	48.0	970	95.1	91.6	Surgery						
New Mexico	22	90.9	54.5	138	92.8	86.2	BCS	1,055	84.8	45.6	4,443	95.7	92.7
San Francisco	63	88.9	50.8	252	91.3	91.3	Mastectomy	340	87.4	55.6	1,896	93.4	89.4

* Number suppressed to protect patient confidentiality.

** ER = estrogen receptor, PR = progesterone receptor, HER2 = human epidermal growth factor receptor-2.

Rates of ER/PR testing were higher for larger tumor size (≥ 2 cm) and for higher versus lower tumor grades (90.1% vs. 82.6%). Undifferentiated tumors presented an exception to this pattern, with a rate of 85.2 percent. Rates of ER/PR testing were slightly lower for women treated with BCS as compared to mastectomy (84.8% vs. 87.4%; **Table 2**).

Women with DCIS had lower rates of ER/PR testing in 2007 than women with invasive disease (85.4% vs. 95.0%; **Table 2**). In contrast to DCIS patterns, Hispanic whites had the highest rates of testing for ER/PR status among women with early invasive tumors. Likewise, the association between tumor size and ER/PR testing differed between DCIS and invasive cancer. In women with invasive cancer, rates of ER/PR testing were relatively stable across tumor size. Registries with comparatively high rates of ER/PR testing for women with invasive cancer did not necessarily have comparatively high rates of ER/PR testing for DCIS; for example, Utah had the lowest rate of ER/PR testing for DCIS patients but among the highest (96.8%) for women with invasive disease. Women with invasive disease who had mastectomies were slightly less likely to receive ER/PR testing than those receiving BCS (93.4% vs. 95.7%; **Table 2**).

Although rates of ER/PR testing increased dramatically over the study period, rates of ER positivity held stable for both groups, according to SEER registry data. Women with DCIS had ER positivity rates of 82 percent in 2004 and 81 percent in 2007. Women with invasive disease had ER positivity rates of 85 percent in 2004 and 86 percent in 2007 (**Figure 2**). The percentage of women with ER+ tumors was similar for the DCIS and invasive cancer groups.

HER2 Testing

As with ER/PR testing, HER2 testing increased dramatically among women with DCIS between 2004 and 2007 (32.2% to 48.0%; **Figure 1**). Therefore, we could not easily interpret overall estimates and thus discuss results for 2007 only in the body of the report. See **Appendices B, C, and D** for data on 2004-2006. Rates of HER2 testing increased by age (45.3% for ages 65-69 vs. 51.7% for ages 85+; **Table 2**). White women had the lowest rates of HER2 testing (46.9%), and White Hispanics the highest (55.7%).

Figure 2: Percentage of ER+ and ER testing among ductal carcinoma in situ and early invasive breast cancer diagnoses in SEER, 2004-2007

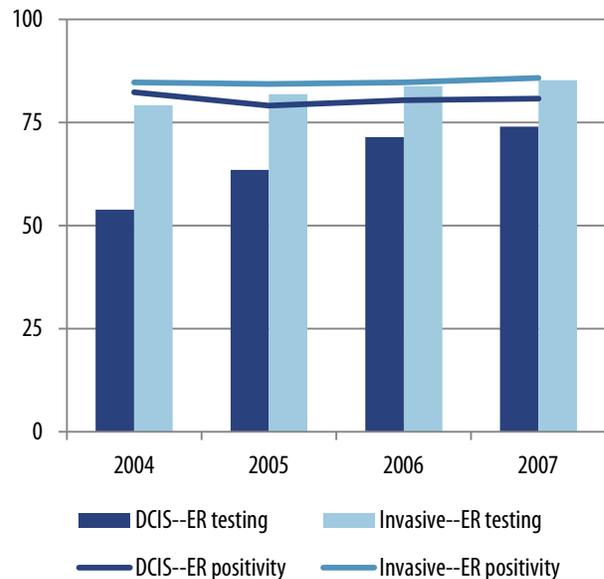


Table 3: BRCA testing among ductal carcinoma in situ and early invasive breast cancer diagnoses in SEER, 2004-2007

Diagnosis Year	DCIS		Invasive	
	n	BRCA %	n	BRCA %
2004-2005	2,949	0.6	12,715	1.4
2006-2007	2,832	1.7	12,734	1.9
Age (years)				
65-74	3,329	1.4	12,551	2.2
75-84	2,090	0.9	10,007	1.2
85+	362	0.0	2,891	0.6
Urbanicity				
Big metro	3,403	1.3	14,428	1.9
Not big metro	2,378	0.8	11,020	1.3
Tumor Size				
<2 cm	3,038	1.1	18,120	1.7
2+ cm	1,048	1.2	6,812	1.5
Grade				
Low-intermediate	2,451	1.1	18,059	1.7
High	2,474	1.2	5,757	1.6
Surgery				
BCS	4,412	1.0	17,939	1.7
Mastectomy	1,362	1.6	7,481	1.5

Rates of HER2 testing varied from a low of 29.5 percent in Seattle to 59.6 percent in Louisiana. Tumors larger than 1 cm and high-grade tumors were associated with higher rates of HER2 testing except for women with undifferentiated tumors. Women treated with mastectomy were more likely to have HER2 testing than women receiving BCS (55.6% vs. 45.6%). Women with DCIS had lower rates of HER2 testing than women with invasive disease in 2007 (48.0% vs. 91.7%). In general, we found less variability in HER2 testing rates among women with invasive disease, with one exception. Like those with DCIS, rates of HER2 testing were noticeably lower among those with microscopic tumors (78.3% vs. >90% for all other sizes).

BRCA Testing

We found a low rate (0.6%) of BRCA testing among women with DCIS. From 2004 to 2007, rates increased slightly but remained low (0.6% to 1.7%; **Figure 1**). Due to small numbers, we cannot report annual rates for subgroups. Women undergoing mastectomy were more likely than women with BCS to have BRCA testing (1.6% vs. 1.0%; **Table 3**). Rates of BRCA testing among women with invasive cancer were only slightly higher (1.4%) than for women with DCIS. Among the Medicare older population, BRCA testing is not yet a major component of breast cancer workup.

Table 4: Lymph node testing among ductal carcinoma in situ and early invasive breast cancer diagnoses in SEER, 2007

	DCIS		Invasive			DCIS		Invasive	
	n	Lymph Node %	n	Lymph Node %		n	Lymph Node %	n	Lymph Node %
Total	1,384	29.3	6,297	87.4					
Age (years)									
65-69	405	28.4	1,678	95.4	San Francisco	63	17.5	250	84.4
70-74	385	31.7	1,523	95.6	San Jose	33	36.4	183	87.4
75-79	296	34.1	1,338	90.1	Seattle	95	37.9	380	90.5
80-84	209	23.4	1,000	80.5	Utah	35	*	156	87.8
85+	89	21.3	758	57.3	Urbanicity				
Race					Big metro	770	28.2	3,545	87.4
White	1,104	30.3	5,236	87.2	Metro	425	30.1	1,847	87.1
White Hispanic	69	33.3	268	88.8	Urban	78	17.9	382	88.0
Black	106	19.8	370	88.1	Less urban	90	40.0	430	87.9
Asian/Pacific Islander	80	25.0	277	91.7	Rural	*	*	92	85.9
SEER Registry					Tumor Size				
Atlanta	54	24.1	202	92.1	Microscopic	35	*	106	73.6
Connecticut	115	19.1	431	77.3	<1 cm	412	22.8	1716	88.2
Detroit	87	26.4	404	88	<2 cm	276	30.8	2675	89.8
Greater California	269	32	1,352	90.8	2-5 cm	191	41.4	1522	85.0
Hawaii	27	*	101	91.1	>5 cm	48	68.8	152	82.9
Iowa	84	41.7	416	86.5	Grade				
Kentucky	100	41	468	86.1	Well differentiated	146	20.5	1,865	87.8
Los Angeles	108	32.4	468	88.2	Moderately differentiated	448	23.2	2,694	87.8
Louisiana	88	34.1	373	91.7	Poorly differentiated	423	36.2	1,323	88.9
New Jersey	201	21.4	961	84.7	Undifferentiated	161	43.5	45	77.8
New Mexico	22	*	138	81.2	Surgery				
					BCS	1,046	18.3	4,407	84.6
					Mastectomy	338	63.6	1,882	93.8

* Number suppressed to protect patient confidentiality.

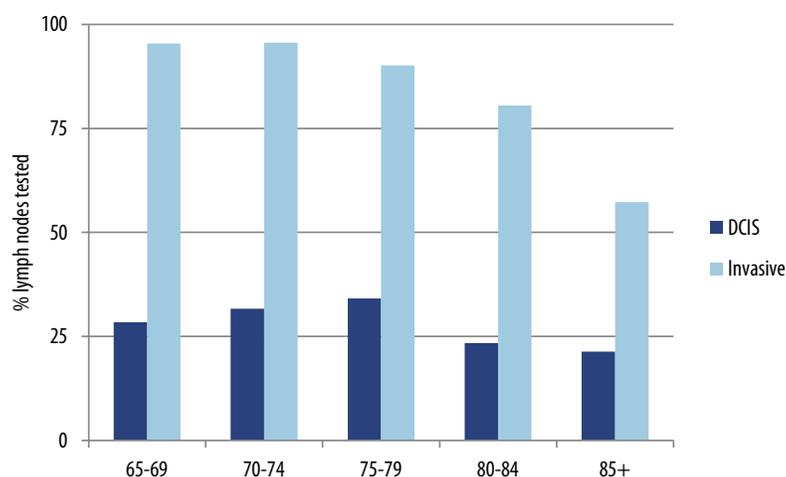
Lymph Node Testing

Rates of lymph node testing were typically low among women with DCIS, although they increased slightly from 26.0 percent in 2004 to 29.3 percent in 2007. For consistency with our reporting of other tests, we discuss here patterns for 2007 only (see **Appendices E, F, and G** for other years). Lymph node testing rates were lowest among older women (<25% for women over 80; **Table 4** and **Figure 3**). Among racial groups, rates were highest (33.3%) for Hispanic white women and lowest for black women (19.8%).

Rates were highest among women with large tumors (68.8%) and those who received a mastectomy (63.6% vs. 18.3% in women with BCS). Rates were lowest in San Francisco (17.5%) and highest in Iowa (41.7%). Women with comedo subtype DCIS were more likely to have nodes tested than those without (34.6% versus 27.3%).

Women with invasive disease have higher rates of lymph node testing overall than women with DCIS, and the rate increased over time from 84.4 percent to 87.4 percent. In 2007, women with mastectomy were more likely to have nodes tested (93.8% vs. 84.6% with BCS). The rates of lymph node testing for women with invasive disease and women with DCIS differed greatly across geographic areas. Rates in nonurban areas were the highest for women with DCIS, but among the lowest for women with invasive disease. Similarly, Hawaii had one of the highest rates of lymph node testing for women with invasive disease (91.1%) but one of the lowest for women with DCIS (<20%, number suppressed to protect patient confidentiality; **Table 4**).

Figure 3: Percent lymph node testing among ductal carcinoma in situ and early invasive breast cancer diagnoses, by age at diagnosis in SEER, 2007



As with DCIS, the rate of lymph node testing decreased with age for women with invasive breast cancer. Of women ages 65-69, 95.4 percent had lymph nodes evaluated compared with 57.3 percent of women age 85 and older. Unlike with DCIS, however, tumor size and grade were not associated with differing patterns of lymph node testing in women with invasive disease.

DISCUSSION

This report provides population-based information about the types of diagnostic data obtained for older women with DCIS or early invasive breast cancer. We found large increases in the use of ER/PR and HER2 testing between 2004 and 2007. These increases point to wider access to the benefits of current therapies.

Medicare data are not well suited to differentiating between ER and PR testing; however, testing rates are also available from SEER-based sources. In both cases, reported testing points to large changes in clinical practice.

Two key messages emerged from analysis of ER positivity: first, rates of positivity were almost identical for the DCIS and invasive breast cancer groups. Second, positivity rates were stable over time for both DCIS and invasive disease, despite dramatic increases in testing. This finding suggests that physicians have no information suggesting ER positivity on which to base testing and are thus testing randomly. Treatment targeted to ER+ tumors is very effective for women with invasive cancers and ER testing is considered vital for treatment decisions in that context.¹⁶

HER2 is overexpressed in about one-third of patients with DCIS. While current guidelines do not recommend routine testing of HER2 for DCIS, we found that HER2 testing significantly increased from 2004 to 2007. While trastuzumab is integral to treatment for HER2+ invasive breast cancer, it is not used in the treatment of DCIS. In one study using preoperative single-dose monotherapy for patients with HER2+ DCIS, trastuzumab resulted in no significant histologic or antiproliferative changes.¹⁷ The NSABP is studying the potential efficacy and role of postoperative trastuzumab for DCIS in a Phase III randomized trial for patients treated with BCS.¹⁸

We found more variability by race and geography in HER2 testing rates among women with DCIS than we did among women with early invasive disease. Some of this variability may result from selective testing of DCIS patients assumed to be at higher risk of positivity. We cannot assess whether rates of HER2 positivity are similar between DCIS and early invasive breast cancer because neither SEER nor Medicare data contain HER2 testing results.

We found that rates of BRCA testing were quite low, likely as a result of the cohort selected for our study. Medicare coverage rules for BRCA testing require that older women have at least two primary breast tumors, personal history of ovarian cancer, two (one if male) close blood relatives with epithelial ovarian or breast cancers, or be a member of an ethnicity associated with higher BRCA mutation frequency. Importantly, neither SEER nor Medicare data include information on family history of breast or ovarian cancer, or information on the use of genetic counseling. The data do suggest that BRCA testing is not widely used in the Medicare population age 65 and older.

Rates of lymph node testing between DCIS and early invasive disease differ, which may be due to multiple factors. First, lymph node testing is considered a standard of care for women with invasive disease but is not uniformly recommended for women with DCIS. Second, the estimated rates of testing for both groups will be biased downward, because our cohort did not include women in whom positive lymph nodes were detected. Our findings are consistent with current recommendations regarding lymph node evaluation.

Within the DCIS population, we found that lymph node evaluation was significantly more frequent among mastectomy patients (63.6%) than among those undergoing BCS (18.3%). This is not surprising since SLNB can still be performed after BCS if occult invasive breast cancer is identified in the excised specimen. On the other hand, SLNB cannot be performed if occult invasive cancer is identified in the mastectomy specimen. However, lymph nodes may have been inadvertently retrieved from some of the women with DCIS who underwent mastectomy; thus, it is possible that for some women, the evaluation of lymph nodes was not intentional.

CONCLUSION

As the incidence of DCIS has increased, so has the interest in factors predicting recurrence or subsequent invasive disease. For all examined tests, we found lower rates of testing for women with DCIS than for women with early invasive disease. In addition to significant geographic and racial variation in testing, we found large increases in the use of diagnostic tests over a relatively short period of time.

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Appendix A: Agreement between SEER and Medicare claims data analyses of testing, 2004-2008

	n	SEER ER Tested	Claims ER Tested	Total Agreement
		%	%	%
DCIS	5,788	78.1	75.6	80.8
Invasive	25,439	97.9	93.6	92.3

Appendix B: ER/PR testing and HER2 testing among ductal carcinoma in situ and early invasive breast cancer diagnoses in SEER, 2004

	DCIS			Invasive		
	n	ER/PR %	HER2 %	n	ER/PR %	HER2 %
Total	1,496	63.6	32.2	6,638	92.1	82.8
Age (years)						
65-69	473	67.4	35.9	1,642	79.8	90.1
70-74	392	62.8	30.1	1,597	81.5	93.0
75-79	329	64.7	31.6	1,541	78.7	92.7
80-84	207	56.5	27.5	1,138	78.3	93.4
85+	95	60.0	34.7	720	74.7	91.4
Race						
White	1,230	62.1	31.3	5,721	79.6	92.6
White Hispanic	73	63.0	37.0	216	76.4	92.1
Black	108	74.1	35.2	385	77.9	89.9
Asian/Pacific Islander	65	70.8	36.9	228	74.1	86.0
SEER Registry						
Atlanta	66	78.8	36.4	224	86.6	70.1
Connecticut	114	54.4	28.1	526	97.0	87.8
Detroit	112	65.2	22.3	474	96.4	82.1
Greater California	296	53.0	25.7	1,292	90.6	85.1
Hawaii	24	66.7	*	79	86.1	82.3
Iowa	99	68.7	33.3	491	91.4	73.3
Kentucky	108	63.9	33.3	506	92.5	80.0
Los Angeles	104	75.0	32.7	436	94.3	86.9
Louisiana	105	58.1	35.2	472	89.6	87.1
New Jersey	203	73.9	47.8	1,018	94.1	88.9
New Mexico	35	57.1	34.3	152	88.2	66.4
San Francisco	54	51.9	27.8	244	83.6	65.2

	DCIS			Invasive		
	n	ER/PR %	HER2 %	n	ER/PR %	HER2 %
San Jose	37	56.8	32.4	145	93.1	86.9
Seattle	98	72.4	35.7	369	92.7	84.8
Utah	35	62.9	*	202	91.1	78.2
Urbanicity						
Big metro	868	66.7	32.9	3,689	92.4	83.5
Metro	421	58.9	29.5	1,943	93.2	85.2
Urban	83	62.7	39.8	405	86.7	71.9
Less urban	100	62.0	35.0	504	89.9	76.8
Rural	24	45.8	*	97	95.9	84.5
Tumor Size						
Microscopic	62	48.4	21.0	91	72.5	84.6
<1 cm	418	62.2	30.4	1,866	82.7	92.6
<2 cm	324	67.6	36.1	2,768	79.7	92.8
2-5 cm	199	69.3	33.2	1,651	76.1	91.6
>5 cm	68	76.5	42.6	132	76.5	91.7
Grade						
Well differentiated	162	59.3	28.4	1,872	80.4	92.0
Moderately differentiated	442	60.4	30.1	2,768	79.7	92.9
Poorly differentiated	412	68.2	33.7	1,426	79.3	92.7
Undifferentiated	231	64.9	30.7	74	68.9	90.5
Surgery						
BCS	1,121	63.2	32.1	4,586	92.9	83.7
Mastectomy	373	64.6	32.4	2,045	90.5	80.9

* Number suppressed to protect patient confidentiality.

ER = estrogen receptor, PR = progesterone receptor, HER2 = human epidermal growth factor receptor-2.

Appendix C: ER/PR testing and HER2 testing among ductal carcinoma in situ and early invasive breast cancer diagnoses in SEER, 2005

	DCIS			Invasive		
	n	ER/PR %	HER2 %	n	ER/PR %	HER2 %
Total	1,453	72.1	36.2	6,075	92.8	85.5
Age (years)						
65-69	450	70.2	36.4	1,507	91.4	85.1
70-74	393	77.1	37.7	1,463	93.2	86.4
75-79	340	73.2	37.9	1,386	93.4	85.1
80-84	180	68.9	36.1	1,053	92.8	85.5
85+	90	61.1	22.2	666	93.7	85.4
Race						
White	1,160	72.2	36.5	5,138	93.4	85.7
White Hispanic	70	72.9	40.0	281	89.3	83.6
Black	114	73.7	39.5	317	88.3	84.2
Asian/Pacific Islander	69	68.1	29.0	251	90.8	85.7
SEER Registry						
Atlanta	56	75.0	33.9	225	93.8	78.7
Connecticut	138	65.9	35.5	440	93.6	85.0
Detroit	142	86.6	38.7	502	95.6	89.0
Greater California	310	64.2	34.2	1,292	91.4	86.1
Hawaii	20	90.0	*	88	88.6	86.4
Iowa	76	84.2	51.3	459	93.2	78.2
Kentucky	100	64.0	28.0	499	92.2	84.2
Los Angeles	119	63.9	35.3	486	93.0	90.7
Louisiana**	n/a	n/a	n/a	n/a	n/a	n/a
New Jersey	230	83.0	43.5	932	94.0	89.8
New Mexico	24	79.2	*	146	92.5	80.1
San Francisco	65	63.1	30.8	235	84.3	75.3

	DCIS			Invasive		
	n	ER/PR %	HER2 %	n	ER/PR %	HER2 %
San Jose	36	69.4	*	161	96.3	87.6
Seattle	97	69.1	30.9	427	93.0	87.4
Utah	37	67.6	*	173	94.2	77.5
Urbanicity						
Big metro	922	73.0	36.7	3,562	92.8	87.2
Metro	373	70.5	35.7	1,664	93.3	85.8
Urban	67	65.7	31.3	356	90.7	72.8
Less urban	73	71.2	39.7	395	92.9	83.5
Rural	18	83.3	*	98	90.8	72.4
Tumor Size						
Microscopic	47	70.2	42.6	88	93.2	81.8
<1 cm	403	70.7	35.5	1,735	93.0	86.1
<2 cm	292	71.9	37.7	2,506	92.6	85.8
2-5 cm	220	80.9	41.4	1,503	92.7	85.2
>5 cm	58	70.7	24.1	130	92.3	80.0
Grade						
Well differentiated	177	72.3	35.0	1,705	92.0	83.5
Moderately differentiated	454	72.9	35.2	2,538	94.2	87.4
Poorly differentiated	409	76.0	36.4	1,381	92.3	85.8
Undifferentiated	209	71.8	38.8	52	94.2	78.8
Surgery						
BCS	1,148	71.8	34.7	4,327	93.3	86.5
Mastectomy	302	72.8	42.4	1,742	91.5	83.1

* Number suppressed to protect patient confidentiality.

** Numbers not calculated for Louisiana in 2005 due to Hurricane Katrina.

ER = estrogen receptor, PR = progesterone receptor, HER2 = human epidermal growth factor receptor-2.

Appendix D: ER/PR testing and HER2 testing among ductal carcinoma in situ and early invasive breast cancer diagnoses in SEER, 2006

	DCIS			Invasive				DCIS			Invasive		
	n	ER/PR %	HER2 %	n	ER/PR %	HER2 %		n	ER/PR %	HER2 %	n	ER/PR %	HER2 %
Total	1,434	82.0	44.4	6,378	94.6	90.0	San Jose	34	82.4	35.3	131	96.2	93.1
Age (years)							Seattle	76	73.7	28.9	402	93.5	89.6
65-69	452	83.4	43.8	1,645	92.4	87.5	Utah	34	64.7	*	156	96.8	91.0
70-74	367	85.3	47.1	1,468	95.0	90.3	Urbanicity						
75-79	332	79.5	44.0	1,428	96.0	91.3	Big metro	834	83.8	43.9	3,598	94.5	89.9
80-84	195	80.0	44.1	1,098	96.0	92.3	Metro	424	80.4	46.2	1,869	95.3	91.2
85+	88	75.0	37.5	739	94.0	88.6	Urban	68	83.8	50.0	401	92.8	86.5
Race							Less urban	96	76.0	38.5	425	94.1	88.5
White	1,135	82.2	43.1	5,366	95.3	90.7	Rural	12	*	*	85	96.5	89.4
White Hispanic	61	82.0	50.8	284	90.5	84.9	Tumor Size						
Black	129	81.4	47.3	348	89.7	83.6	Microscopic	53	66.0	37.7	88	90.9	81.8
Asian/Pacific Islander	73	80.8	52.1	258	92.6	90.3	<1 cm	420	82.1	37.4	1,785	96.6	90.9
SEER Registry							<2 cm	290	84.8	50.7	2,658	94.1	90.2
Atlanta	59	84.7	35.6	210	94.3	75.7	2-5 cm	204	85.8	51.5	1,548	95.0	91.2
Connecticut	108	78.7	44.4	488	97.5	92.6	>5 cm	56	91.1	51.8	155	89.0	85.2
Detroit	127	88.2	36.2	434	96.8	91.9	Grade						
Greater California	285	77.5	43.9	1,297	93.1	90.1	Well differentiated	176	80.7	36.9	1,789	95.2	90.3
Hawaii	22	81.8	*	84	95.2	92.9	Moderately differentiated	440	80.9	41.1	2,762	94.9	91.2
Iowa	99	89.9	42.4	432	94.9	86.3	Poorly differentiated	431	85.2	49.0	1,390	94.5	89.2
Kentucky	98	71.4	37.8	498	95.6	91.6	Undifferentiated	191	85.3	53.4	51	88.2	82.4
Los Angeles	93	86.0	59.1	463	95.5	93.3	Surgery						
Louisiana	102	79.4	52.9	388	92.8	88.1	BCS	1,086	81.8	42.4	4,575	95.2	92.7
New Jersey	221	91.0	54.3	979	94.7	90.9	Mastectomy	346	82.7	50.3	1,796	93.1	89.4
New Mexico	20	90.0	*	155	92.3	83.2							
San Francisco	55	80.0	50.9	245	92.7	90.6							

* Number suppressed to protect patient confidentiality.
 ER = estrogen receptor, PR = progesterone receptor, HER2 = human epidermal growth factor receptor-2.

Appendix E: Lymph node testing among ductal carcinoma in situ and early invasive breast cancer diagnoses in SEER, 2004

	DCIS		Invasive			DCIS		Invasive	
	n	Lymph Node %	n	Lymph Node %		n	Lymph Node %	n	Lymph Node %
Total	1,483	26.0	6,552	84.4	San Jose	37	*	143	89.5
Age (years)					Seattle	98	35.7	366	89.0
65-69	467	29.6	1,627	94.0	Utah	35	*	202	87.6
70-74	391	26.6	1,574	91.9	Urbanicity				
75-79	324	26.2	1,524	87.1	Big metro	861	25.8	3,639	84.8
80-84	206	21.8	1,118	77.1	Metro	416	26.0	1,923	84.3
85+	95	13.7	709	51.3	Urban	83	28.9	396	86.6
Race					Less urban	99	26.3	497	80.5
White	1,220	25.0	5,643	84.2	Rural	*	*	79	81.4
White Hispanic	72	36.1	215	86.5	Tumor Size				
Black	107	28.0	381	82.2	Microscopic	60	*	91	69.2
Asian/Pacific Islander	64	31.3	227	93.4	<1 cm	415	16.6	1,850	84.5
SEER Registry					<2 cm	320	26.6	2,732	86.1
Atlanta	66	21.2	222	82.4	2-5 cm	199	40.7	1,620	83.3
Connecticut	114	20.2	517	77.8	>5 cm	68	55.9	132	81.8
Detroit	110	23.6	461	84.8	Grade				
Greater California	296	24.3	1,287	87.0	Well differentiated	162	14.2	1,853	84.1
Hawaii	*	*	*	*	Moderately differentiated	439	23.0	2,766	85.0
Iowa	98	30.6	483	85.0	Poorly differentiated	410	31.2	1,402	85.8
Kentucky	105	27.6	497	83.3	Undifferentiated	228	36.4	74	78.4
Los Angeles	103	30.1	433	87.8	Surgery				
Louisiana	105	28.6	464	83.0	BCS	1,112	15.3	4,527	81.0
New Jersey	199	27.6	997	81.1	Mastectomy	369	58.0	2,018	92.2
New Mexico	35	*	150	1.0					
San Francisco	53	*	243	82.7					

* Number suppressed to protect patient confidentiality.

ER = estrogen receptor, PR = progesterone receptor, HER2 = human epidermal growth factor receptor-2.

Appendix F: Lymph node testing among ductal carcinoma in situ and early invasive breast cancer diagnoses in SEER, 2005

	DCIS		Invasive			DCIS		Invasive	
	n	Lymph Node %	n	Lymph Node %		n	Lymph Node %	n	Lymph Node %
Total	1,445	26.8	6,015	85.2					
Age (years)					San Jose	36	33.3	160	86.0
65-69	447	30.4	1,497	95.3	Seattle	95	21.1	425	90.6
70-74	391	25.6	1,445	92.2	Utah	37	32.4	172	84.0
75-79	338	27.2	1,375	88.7	Urbanicity				
80-84	179	22.9	1,042	76.2	Big metro	919	26.4	3,533	85.3
85+	90	20.0	656	53.2	Metro	370	25.7	1,645	85.0
Race					Urban	67	28.4	355	87.0
White	1,153	26.5	5,090	85.1	Less urban	71	33.8	387	85.3
White Hispanic	70	38.6	276	87.3	Rural	*	*	73	76.8
Black	113	26.5	313	81.5	Tumor Size				
Asian/Pacific Islander	69	21.7	249	87.1	Microscopic	47	*	87	69.0
SEER Registry					<1 cm	401	18.0	1,723	86.2
Atlanta	56	25.0	224	84.8	<2 cm	292	26.4	2,485	87.4
Connecticut	138	15.9	432	77.3	2-5 cm	219	40.2	1,485	83.1
Detroit	142	23.9	499	86.6	>5 cm	58	44.8	128	73.4
Greater California	309	30.7	1,281	86.7	Grade				
Hawaii	*	*	88	85.0	Well differentiated	177	18.6	1,693	84.1
Iowa	75	38.7	459	86.0	Moderately differentiated	453	19.9	2,519	86.3
Kentucky	96	29.2	481	85.0	Poorly differentiated	407	33.2	1,364	86.7
Los Angeles	119	21.8	486	86.2	Undifferentiated	207	39.1	52	86.5
Louisiana**	n/a	n/a	n/a	n/a	Surgery				
New Jersey	230	30.0	922	84.7	BCS	1,141	16.0	4,284	82.2
New Mexico	*	*	143	84.6	Mastectomy	301	67.8	1,727	92.6
San Francisco	65	21.5	233	78.5					

* Number suppressed to protect patient confidentiality.

** Numbers not calculated for Louisiana in 2005 due to Hurricane Katrina.

ER = estrogen receptor, PR = progesterone receptor, HER2 = human epidermal growth factor receptor-2.

Appendix G: Lymph node testing among ductal carcinoma in situ and early invasive breast cancer diagnoses in SEER, 2006

	DCIS		Invasive			DCIS		Invasive	
	n	Lymph Node %	n	Lymph Node %		n	Lymph Node %	n	Lymph Node %
Total	1,420	30.6	6,314	85.4	San Jose	34	32.4	130	90.8
Age (years)					Seattle	76	26.3	402	91.0
65-69	448	31.9	1,628	94.0	Utah	34	*	155	85.8
70-74	364	33.5	1,457	92.0	Urbanicity				
75-79	328	27.7	1,414	88.8	Big metro	826	28.6	3,563	85.6
80-84	193	30.1	1,090	79.9	Metro	420	33.8	1,852	85.3
85+	87	23.0	725	53.9	Urban	66	36.4	398	86.7
Race					Less urban	96	29.2	417	84.7
White	1,124	30.5	5,312	85.4	Rural	*	*	60	71.4
White Hispanic	61	41.0	283	83.7	Tumor Size				
Black	127	25.2	343	84.8	Microscopic	53	24.5	88	79.5
Asian/Pacific Islander	72	34.7	256	88.7	<1 cm	413	22.8	1,765	84.9
SEER Registry					<2 cm	289	31.8	2,629	87.5
Atlanta	58	20.7	210	89.5	2-5 cm	203	41.4	1,535	84.3
Connecticut	106	21.7	482	78.6	>5 cm	55	61.8	155	81.9
Detroit	126	23.0	430	85.6	Grade				
Greater California	283	35.7	1,280	87.3	Well differentiated	174	21.8	1,770	83.7
Hawaii	*	*	*	*	Moderately differentiated	434	24.2	2,736	86.8
Iowa	97	33.0	430	84.0	Poorly differentiated	427	37.0	1,379	86.9
Kentucky	98	40.8	489	83.0	Undifferentiated	191	43.5	51	86.3
Los Angeles	92	42.4	462	83.8	Surgery				
Louisiana	101	42.6	386	89.9	BCS	1,074	17.9	4,524	82.8
New Jersey	218	23.9	961	84.0	Mastectomy	344	69.8	1,783	91.9
New Mexico	20	*	155	76.0					
San Francisco	55	*	243	81.5					

* Number suppressed to protect patient confidentiality.

ER = estrogen receptor, PR = progesterone receptor, HER2 = human epidermal growth factor receptor-2.