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Article type : Manuscripts

The Effect of the 2009 USPSTF Breast Cancer Screening Recommendations on Breast Cancer in Michigan: a Longitudinal Study.

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/tbj.13034

ABSTRACT

Background: In 2009 the revised United States Preventive Services Task Force (USPSTF) guidelines recommended against routine screening mammography for women age 40 to 49 years and against teaching self-breast examinations (SBE). The aim of this study was to analyze if breast cancer method of presentation changed following the 2009 USPSTF screening recommendations in a large Michigan cohort.

Study Design: Data were collected on women with newly diagnosed stage 0-III breast cancer participating in the Michigan Breast Oncology Quality Initiative (MiBOQI) registry at 25 statewide institutions from 2006-2015. Data included method of detection, cancer stage, treatment type, and patient demographics.

Results: 30,008 women with breast cancer detected via mammogram or palpation with an average age of 60.1 years were included. 38% of invasive cancers were identified by palpation. Presentation with palpable findings decreased slightly over time, from 34.6% in 2006 to 28.9% in 2015 ($p<0.001$). Over the 9 year period there was no statistically significant change in rate of palpation-detected tumors for women age <50 years or ≥50 years ($p=0.27$, 0.30 respectively).

Conclusions: Younger women were more likely to present with palpable tumors compared to older women in a statewide registry. This rate did not increase following publication of the 2009 USPSTF breast cancer screening recommendations.

Introduction

Since 1990, mortality rates due to breast cancer have been decreasing by 2.3% per year overall and by 3.3% for women 40 to 50 years of age[1]. The decrease in mortality has been attributed to early detection via screening mammography and improvements in systemic therapy[2]. A significant benefit of mammography is the ability to detect cancer at an earlier stage, which may be a contributing factor to increased survival rates and decreased breast cancer recurrence[3,4]. A reduction in breast cancer mortality rates due to teaching breast self-exam has not been confirmed. However, Mathis and colleagues[5] reported that a significant number of breast tumors (43%) were initially detected through palpation by either the patient or clinician.

In 2009 the United States Preventive Services Task Force (USPSTF) revised their breast cancer screening recommendations[6]. The most significant change was the recommendation against routine screening mammography for women 40 to 49 years of age, which received a C grade. In addition, a

recommendation against teaching self-breast examinations (SBE) was established in response to randomized studies indicating that teaching self-breast examinations had no impact on breast cancer related mortality and was associated with an increased risk of undergoing a benign breast biopsy[7]. The recently published update to the recommendations again confirmed that routine screening mammography should not be performed in this population, but rather the decision should be made on an individual basis[8].

The aim of this study was to analyze the method of breast cancer presentation before and after the USPSTF recommendations were released in 2009 for women seen at hospitals participating in the Michigan Breast Oncology Quality Initiative (MiBOQI) from 2006 to 2015.

Methods

MiBOQI is a multi-institution, statewide breast cancer registry that is a collaborative quality initiative sponsored by Blue Cross Blue Shield of Michigan/Blue Care Network[9, 10]. The MiBOQI registry contains over 300 data elements encompassing demographics, diagnosis, staging, and treatment; it does not include data prior to diagnosis. Follow-up data are obtained four, nine, eighteen, and thirty months after initial diagnosis.

We analyzed data for women diagnosed with stage 0-III breast cancer between 2006 and 2015 from 25 medical institutions with at least 270 days follow-up (to allow capture of chemotherapy and radiotherapy). Patients with missing data in any of the following fields were excluded from analysis: 1) Age at diagnosis, 2) Breast cancer presentation, and 3) TNM Stage (Figure 1). The breast cancer presentation was classified into three groups: 1) Mammography, 2) Palpation during breast examination (either self or clinician) and, 3) Other. The "Other" presentations category included: bloody nipple discharge, inverted nipple, axillary mass, or breast pain/discomfort. Only women whose cancers were identified through either palpation or mammography were included in the analysis.

All data were de-identified prior to analysis. This study was approved by the Institutional Review Board at Grand Valley State University, Allendale, Michigan (Approval #175143-1). The statistical software packages SAS and R were used to analyze and compare method of detection with categorical variables (i.e. TNM staging and surgical management), and continuous variables (i.e. age at the time of initial diagnosis). Chi-square tests and two sample t-tests were used, respectively. A statistically significant p-value was considered to be $p < 0.05$.

Results

Disease presentation

30,008 women met study criteria. Patient demographic and staging data are summarized in Table 1. The average age at of diagnosis was 60.1 years [standard deviation (SD) 12.9]. DCIS without invasive breast cancer was diagnosed in 6,036 patients. In the 23,972 patients in the invasive cohort, 14,929 (62.3%) had mammographically-detected tumors, and 9,041 (37.7%) presented with a palpable tumor. Of the patients with palpable tumors, 87.0% were detected though self-examination, 8.4% were detected by clinician-examination, and 4.6% had other presenting clinical symptoms (Figure 1).

Presentation with palpable findings decreased slightly over time in the entire cohort, from 34.6% in 2006 to 28.9% in 2015 ($p<0.001$, Figure 2). For women under age 50 the rate of cancer detection by palpation decreased from 67% in 2006 to 54% in 2015, which was not a statistically significant decrease ($p=0.27$; Figure 3). For women age 50 and over, the rate remained essentially stable, and was 29% in 2006 and 30% in 2015 ($p=0.30$, Figure 3). Across the 25 participating MiBOQI sites, there was a statistically significant ($p<0.001$) variation in rates of palpation-detected tumors (Figure 4), which varied from 24% to 45%.

Associations between disease presentation and clinicopathologic characteristics

Compared to patients with invasive cancer who had mammographically-detected tumors, patients with a palpable tumor at presentation were more likely to be younger, black race, and insured by commercial (non-Medicare) plans or Medicaid. They are also more likely to have higher stage disease, higher tumor grade, ductal histology, lack ER and PR expression, and have HER2 overexpression or amplification (Table 2). On multivariate analysis, all of these factors remained statistically significant, with the exception of race and HER2 overexpression.

When specifically examining patients under age 50, compared to those with mammographically-detected tumors, patients with a palpable tumor at presentation were more likely to be black race, insured by Medicaid, have higher clinical stage disease, and have tumors with higher grade, ER and PR negativity, and HER2 overexpression $p<0.001$ (Table 3). On multivariate analysis, only higher clinical stage remained statistically significant.

Comparison of patients age 50 and older with a palpable tumor versus a mammographically-detected tumor at presentation yielded similar results. Patients with palpable tumors were more likely to be black race, insured by Medicaid, have higher clinical stage disease, and have tumors with higher grade, ER and PR negativity, and HER2 overexpression $p<0.001$ (Table 3). On multivariate analysis, only insurance payor, stage, surgery type, and PR negativity remained statistically significant.

On univariate analysis, comparing patients under age 50 with older women, there were associations between method of detection of the tumor and insurance payor, clinical stage, type of

surgery, and PR overexpression (Table 3). The association between other factors, including race, tumor grade, and histology, and method of detection of the tumor did not differ between the age groups.

Discussion

In this contemporary cohort of 30,008 breast cancer patients, approximately one-third of patients presented with a palpable tumor, and this rate decreased slightly over time from 2006 to 2015. Women with palpable cancers were younger and presented with more advanced tumor stages and more aggressive tumor profiles than those with mammography-detected cancers. Our results are concordant with prior reports in the literature.[5]

The impact the 2009 USPSTF screening recommendations have had on cancer presentation is unknown. A review of screening mammography utilization by Sharpe and colleagues in the Medicare population noted a decrease of 4.3% in 2010 in this older population after seeing annual growth of 0.5% prior to the 2009 recommendations[11]. In contrast, using claims data a smaller decrease in screening mammography use of 1.2% was identified in a cohort of insured women under the age of 50[12] . In our MiBOQI cohort of women under 50, no compensatory increase in palpable tumors was noted after the 2009 recommendations, but rather the rate remained relatively stable. The reason for this finding is uncertain, but likely multifactorial. One potential explanation is that screening mammography rates may have remained relatively unchanged despite the 2009 guidelines. In particular, the enactment of the Affordable Care Act may have enabled more women of all ages to undergo screening mammography, thereby offsetting changes related to less aggressive screening recommendations. However, as noted below, we are unable to assess this possibility in our cohort because of limitations of the MiBOQI Registry. If screening rates did in fact decline, then the inability to diagnosis more of the indolent tumors was not seen, as demonstrated by a compensatory increase in palpable method of detection, within the time frame of the study.

Our study only included women with a breast cancer diagnosis and did not include the general screening population, so no comparisons can be made regarding screening efficacy. Data collected represents only a snapshot of each patient's presentation without information on previous screening practices. Conflicting recommendations have been made regarding the age at which to initiate screening mammography. Work by Hayse et al, suggest that screen detected tumors have more indolent biology than cancers with a palpable presentation[13]. In our cohort, palpable tumors were more likely to be ER negative or HER2 positive amongst women of all age groups. However, information regarding whether these tumors represent interval cancers between mammograms or if they were mammographically occult was not captured in the Registry. In a study by Bellio et al, 20% of patients in a mammographic screening program presented with interval breast cancers, and these tumors had worse prognostic features and

clinical outcomes than screen detected tumors [14]. These findings further strengthen the argument that women and clinicians should not rely on mammography alone for breast cancer detection. A considerable strength of this analysis is the large size of the cohort, which is derived from practices that are heterogeneous, and reflect community- and academic-based practices, urban, suburban, and rural areas, and communities with low and high socioeconomic status. In this statewide registry, we demonstrate that that there is considerable variability across hospital systems in method of breast cancer presentation. This variability could be due to differences in practice patterns across the state, or could reflect differences in patient mix at different institutions.

During this time period regardless of health care policy changes, 22.3% of the cancers in this cohort were in women under the age of 50, and these women presented with palpable tumors at a much greater frequency than those over the age of 50. A higher stage of presentation, more aggressive biology, and more extensive surgical management then follows in younger women. Clinicians should consider these data when determining the impact screening recommendations will have on their patient population.

Conclusion

This cohort demonstrates no increase in the diagnosis of breast cancer because of presentation with palpable findings following the USPSTF 2009 recommendations based on comparison of rates for 3 years before and 6 years after their publication. These multi-institutional data derived from a large Registry cohort provide a robust view of the clinical presentation of breast cancer in a modern cohort. Women with breast cancer detected by mammography presented with earlier stage disease in all age groups and often underwent less aggressive local therapy. Women under the age of 50, who accounted for almost one-quarter of the Registry cohort, were more likely to present with a palpable mass, although this rate did not increase following the 2009 recommendations. These findings underscore the importance of recognizing and thoroughly evaluating of breast masses and breast symptoms in this population.

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Figure 1 : Exclusion Criteria Diagram

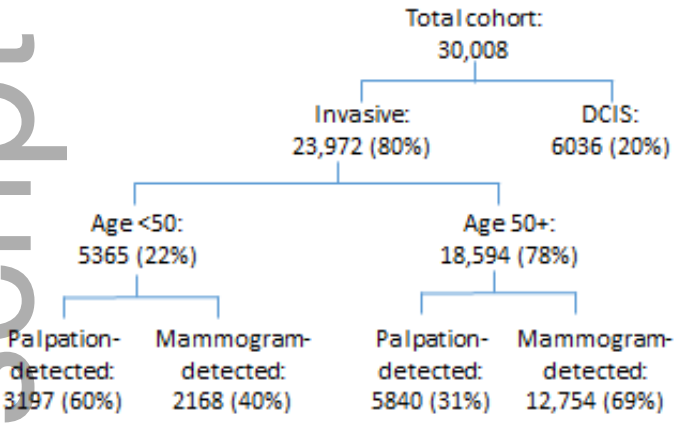

Figure 2. Percent of Patients with Tumors Diagnosed by Palpation, by Year

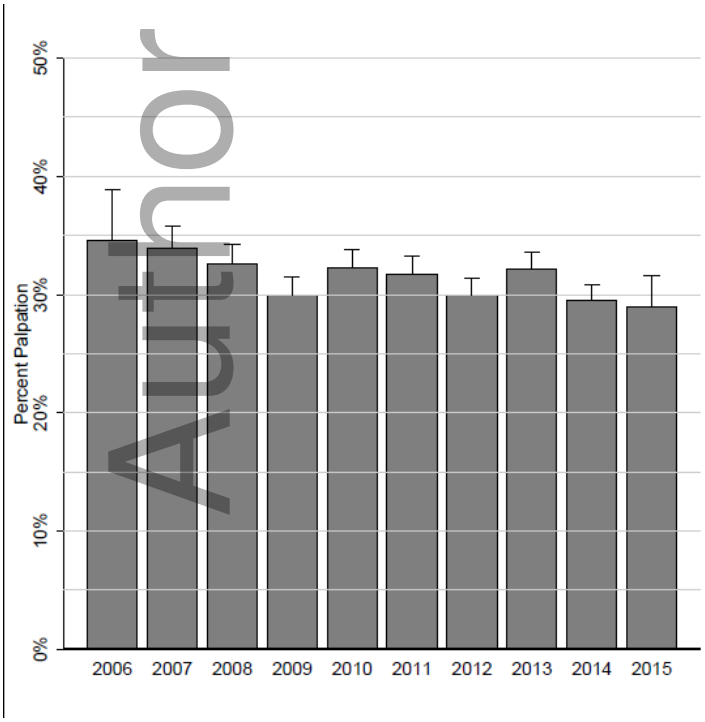

Figure 3. Percent of Patients with Tumors Diagnosed by Palpation Age <50, ≥ 50 by Year

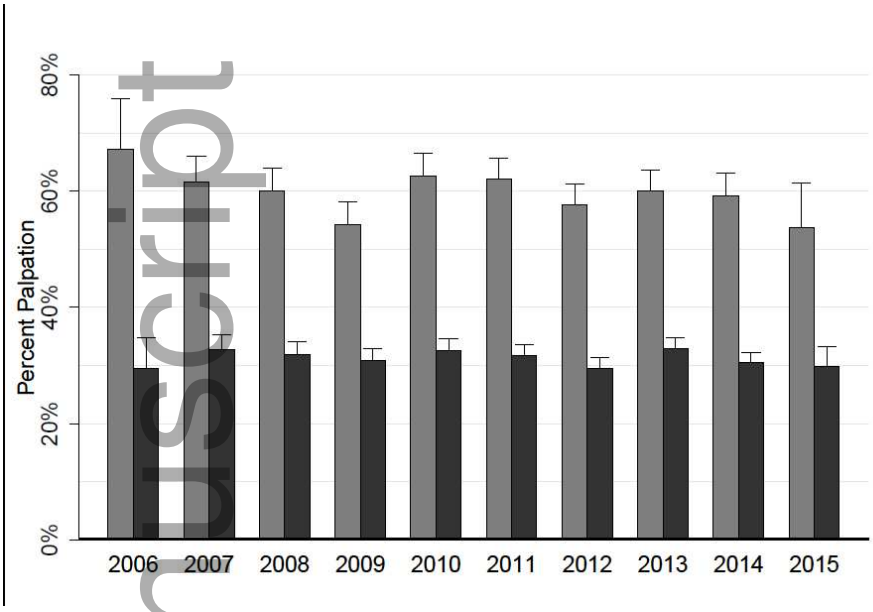

Figure 4. Percent of Patients with Tumors Diagnosed by Palpation, by Michigan Breast Oncology Quality Initiative Participating Site

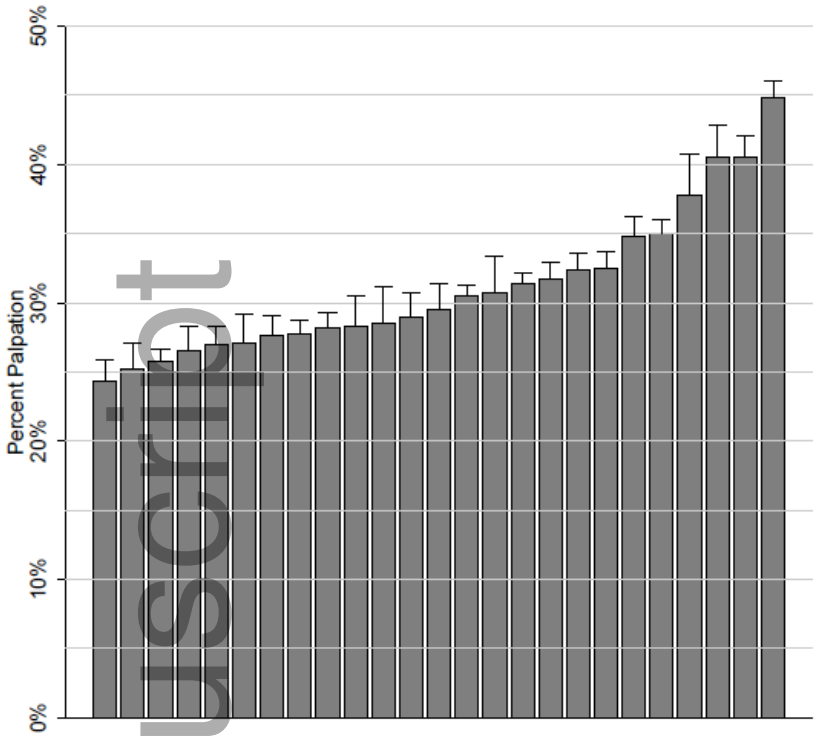

Table 1. Demographic and clinicopathologic characteristics of the entire cohort. N/a: not applicable.

Characteristic	**Invasive Cancer N=23.972**		**DCIS N=6,036**
Age at diagnosis, years			
<50	5365 (22%)		1375 (23%)
≥50	18596 (78%)		4661 (77%)
Missing	11		6
Race			
Black	3113 (13%)		872 (14%)
White	19414 (81%)		4770 (79%)
Other	1445 (6%)		400 (7%)
Insurance Payor			
Commercial	10511 (55%)		2933 (61%)
Government	116 (1%)		18 (0%)

Medicaid	1154 (6%)		203 (4%)
Medicare	7282 (38%)		1635 (34%)
Other	39 (0%)		17 (0%)
Uninsured	78 (0%)		9 (0%)
Missing	4792		1227
Clinical Stage			
Stage 0	n/a		6042 (100%)
Stage I	13722 (57%)		n/a
Stage II	7840 (33%)		n/a
Stage III	2410 (10%)		n/a
Histologic Grade			
Grade 1	6069 (26%)		n/a
Grade 2	10106 (44%)		n/a
Grade 3	7004 (30%)		n/a
Other	25 (0%)		n/a
Missing	768		n/a
Surgery			
BCS	15268 (64%)		4409 (73%)
Mastectomy	8285 (35%)		1573 (26%)
Other	419 (2%)		60 (1%)
Estrogen Receptor Positive			
No	4243 (18%)		n/a
Yes	19628 (82%)		n/a
Missing	101		n/a
Progesterone Receptor Positive			
No	6452 (27%)		n/a
Yes	17364 (73%)		n/a
Missing	156		n/a
HER2 Positive			
No	20728 (87%)		n/a
Yes	3206 (13%)		n/a
Missing	38		n/a
Triple Negative			

No	22118 (93%)		n/a
Yes	1675 (7%)		n/a
Missing	179		n/a

Table 2. Multivariate analysis of associations between demographic and clinicopathologic characteristics and method of breast cancer detection.

Characteristic	Palpation N=9,041	Mammogram N=14,929	Univariate p-value	Multivariate p-value
Age at diagnosis, years				
<50	3197 (35%)	2168 (15%)	<0.001	<0.001
≥50	5840 (65%)	12754 (85%)		
Missing	4	7		
Race				
Black	1408 (16%)	1705 (11%)	<0.001	0.2980
White	7032 (78%)	12380 (83%)		
Other	601 (7%)	844 (6%)		
Insurance Payor				
Commercial	4232 (58%)	6279 (53%)	<0.001	<0.001
Government	40 (1%)	76 (1%)		
Medicaid	682 (9%)	472 (4%)		
Medicare	2228 (31%)	5052 (42%)		
Other	12 (0%)	27 (0%)		
Uninsured	52 (1%)	26 (0%)		
Missing	1795	2997.00		
Clinical Stage				

Stage I	2782 (31%)	10940 (73%)	<0.001	<0.001
Stage II	4556 (50%)	3282 (22%)		
Stage III	1703 (19%)	707 (5%)		
Tumor Grade				
Grade 1	1325 (15%)	4744 (33%)	<0.001	<0.001
Grade 2	3518 (40%)	6588 (46%)		
Grade 3	3915 (45%)	3088 (21%)		
Other	9 (0%)	15 (0%)		
Missing	274	494		
Histology				
Invasive Ductal	7711 (85%)	12432 (83%)	<0.001	0.0272
Invasive Ductal and Lobular	173 (2%)	331 (2%)		
Invasive Lobular	882 (10%)	1569 (11%)		
Other	275 (3%)	597 (4%)		
Missing				
Estrogen Receptor Positive				
No	2338 (26%)	1903 (13%)	<0.001	<0.001
Yes	6664 (74%)	12964 (87%)		
Missing	39	62		
Progesterone Receptor Positive				

No	3183 (35%)	3267 (22%)	<0.001	0.0064
Yes	5810 (65%)	11554 (78%)		
Missing	48	108		
HER2 Positive				
No	7469 (83%)	13258 (89%)	<0.001	0.3739
Yes	1549 (17%)	1656 (11%)		
Missing	9	3		
Triple Negative	48	108		
No	8217 (91%)	13899 (94%)	<0.001	n/a
Yes	765 (9%)	910 (6%)		
Missing	23	15		
Surgery				
BCS	4449 (49%)	10817 (72%)	<0.001	<0.001
Mastectomy	4340 (48%)	3945 (26%)		
Other	252 (3%)	167 (1%)		

Table 3. Univariate analysis of associations between demographic and clinicopathologic characteristics and patient age at time of breast cancer diagnosis.

	Patients 49 & Under			Patients 50 & Over			p-value
Characteristic	**Palpation N=3,197**	**Mammogram N=2,168**	**P value**	**Palpation N=5,840**	**Mammogram N=12,754**	**P value**	**Between Age Groups**
Race							0.546
Black	537 (17%)	259 (12%)	<0.001	870 (15%)	1444 (11%)	<0.001	
White	2398 (75%)	1735 (80%)		4631 (79%)	10640 (83%)		
Other	262 (8%)	174 (8%)		339 (6%)	670 (5%)		
Insurance Payor							
Commercial	2055 (82%)	1474 (87%)	<0.001	2175 (46%)	4802 (47%)	<0.001	0.027
Government	18 (1%)	16 (1%)		22 (0%)	60 (1%)		
Medicaid	334 (13%)	152 (9%)		348 (7%)	319 (3%)		
Medicare	68 (3%)	48 (3%)		2158 (46%)	5004 (49%)		
Other	7 (0%)	7 (0%)		5 (0%)	20 (0%)		
Uninsured	27 (1%)	5 (0%)		25 (1%)	21 (0%)		
Missing	688	466		1107	2528		
Clinical Stage							
Stage I	963 (30%)	1417 (65%)	<0.001	1816 (31%)	9518 (75%)	<0.001	<0.001
Stage II	1631 (51%)	594 (27%)		2924 (50%)	2686 (21%)		
Stage III	603 (19%)	157 (7%)		1100 (19%)	550 (4%)		
Tumor Grade							
Grade 1	390	619 (30%)	<0.001	934	4124 (33%)		0.766

	(13%)			(17%)			
Grade 2	1137 (37%)	935 (45%)		2379 (42%)	5648 (46%)		
Grade 3	1574 (51%)	535 (26%)		2340 (41%)	2553 (21%)		
Other	3 (0%)	3 (0%)		6 (0%)	12 (0%)		
Missing	93	76		181	417		
Invasive Ductal	2854 (89%)	1861 (86%)	<0.001	4854 (83%)	10566 (83%)	<0.001	0.162
Invasive Ductal and Lobular	41 (1%)	44 (2%)		132 (2%)	287 (2%)		
Invasive Lobular	222 (7%)	180 (8%)		660 (11%)	1388 (11%)		
Other Histology	80 (3%)	83 (4%)		194 (3%)	513 (4%)		
ER Positive							
No	922 (29%)	280 (13%)	<0.001	1414 (24%)	1622	<0.001	0.257
Yes	2260 (71%)	1873 (87%)		4402 (76%)	11085 (87%)		
Missing	15	15		24	47		
PR positive							
No	1124 (35%)	380 (18%)	<0.001	2058 (35%)	2886 (23%)	<0.001	0.005
Yes	2057 (65%)	1763 (82%)		3750 (65%)	9785 (77%)		
Missing	16	25		32	83		
HER2 Positive							
No	2532 (79%)	1850 (85%)	<0.001	4934 (85%)	11403 (89%)	<0.001	0.349
Yes	656 (21%)	315 (15%)		892 (15%)	1339 (11%)		
Missing	9	3		14	12		

Triple Negative							
No	2802 (88%)	1941 (91%)	0.002	5411 (93%)	11953 (94%)	0.002	0.9250
Yes	375 (12%)	200 (9%)		390 (65%)	708 (6%)		
Missing	20	27		39	93		
Surgery							
BCS	1347 (42%)	1170 (54%)	<0.001	3099 (53%)	9642 (76%)	<0.001	<0.0010
Mastectomy	1796 (56%)	979 (45%)		2543 (44%)	2966 (23%)		0.925
Other	54 (2%)	19 (1%)		198 (3%)	146 (1%)		0.349