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Rebecca J. Nash April 22, 2016

State variation in contralateral prophylactic mastectomy among U.S. women diagnosed with unilateral early stage breast cancer, 2004-2012.

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An abstract of
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Abstract

State variation in contralateral prophylactic mastectomy among U.S. women diagnosed with unilateral early stage breast cancer, 2004-2012.

By Rebecca J. Nash

Importance: The use of contralateral prophylactic mastectomy (CPM) among patients with unilateral breast cancer is increasing in the United States. However, the extent of state variation in this trend is unclear.

Objective: To determine state variation in the temporal trend and in the proportion of patients with unilateral breast cancer undergoing CPM.

Design and Settings: A retrospective cohort study of 1.06 million women ≥ 20 years of age diagnosed with early stage unilateral breast cancer from 2004 through 2012 and treated with surgery in 46 states and the District of Columbia (representing 91.3% of the US population), as compiled by the North American Association of Central Cancer Registries.

Main Outcomes and Measures: The proportion of CPM among unilateral early stage breast cancer patients treated with surgery examined by age, year of diagnosis, state, and region.

Results: Of the 1.06 million women who underwent surgery for early stage unilateral breast cancer over the nine-year study period (2004-2012), about 93,000 (8.8%) underwent CPM. The proportion of CPM for patients diagnosed in 2004 vs. in 2012 increased from 3.5% to 10.4% for women ages ≥45 years and from 10.6% to 33.5% for ages 20-44 years nationally. This pattern is evident in all states although the magnitude of the increase varied substantially across states. In women 20-44 years old for example, the proportion of CPM increased by 63% (from 30% during 2004-2006 to 49% during 2010-2012) in South Dakota compared to 420% (from 5% to 27%) in West Virginia. Four contiguous states (NE, CO, IA, SD) showed the highest proportion of CPM (43.6% to 49.2%) in women aged 20-44 during 2010-2012. By region, the South showed the highest CPM proportion and the Northeast the lowest, with adjusted odds ratio of 1.5 (95% confidence interval: 1.46, 1.52) undergoing CPM among patients in the South vs. the Northeast. There was evidence that the rate of CPM increase is slowing in every region. Differences in percentage of non-Hispanic white residents accounted for about 12% of the state variation in CPM proportion for patients 20-to-44 years old but not for patients 45 years and older.

Conclusions and Relevance: Despite lack of convincing evidence of a survival benefit, the use of CPM continued to increase in the US with the pattern substantially varying by state. Notably, in four contiguous Western and Midwest states, nearly half of young women underwent CPM in recent years. Differences in racial/ethnic distributions accounted for a small proportion of the CPM state variations for younger women but not for older women.

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INTRODUCTION:

Breast cancer is the second leading cause of cancer death, and the most commonly diagnosed invasive malignancy among women in the U.S. (1). Treatment for breast cancer varies by hormone status, stage, and histology, and may include a combination of surgery, chemotherapy and radiation. Breast-conserving surgery (BCS) for early stage disease has long been established as an effective treatment that provides an equivalent survival as mastectomy with fewer surgical complications and frequently no need for reconstruction (2-5). However, many women with unilateral early-stage breast cancer are electing to undergo a more aggressive bilateral mastectomy, in which the healthy contralateral breast is removed.

Patients diagnosed with breast cancer are at an increased risk of developing a second primary breast cancer in the contralateral breast compared to the risk of developing a first primary breast cancer in the general population (6-8). This increased risk, along with fear and anxiety surrounding their breast cancer diagnosis, may prompt many women to elect a contralateral prophylactic mastectomy (CPM) (9-12). Although the evidence that CPM is effective in reducing mortality is lacking (13, 14) and contralateral breast cancer incidence is declining nationwide (15, 16), an increasing proportion of patients elect to undergo this procedure (17-19). It is possible that CPM has a role among women who are less likely to benefit from adjuvant therapy such as those diagnosed with estrogen receptor negative (ER-) breast cancer. However, studies limited to ER- breast cancers have also found conflicting results regarding survival (20-23).

In the meantime the U.S. data indicate a continual rise in the proportion of unilateral breast cancer patients who elect to undergo CPM. A study based on the data

from the Surveillance Epidemiology and End Results (SEER) program, found that CPM use among women with invasive early-stage unilateral breast cancer increased 150% between the years 1998 and 2003. The study also noted considerable variation of CPM use across SEER registries, however, no specific geographic trend was identified (24).

More recent studies utilizing the National Cancer Data Base (NCDB) have also found that the proportion of patients undergoing CPM is on the rise. In 1998, only 1.9% of women with unilateral early-stage breast cancer underwent CPM, but by 2011, this proportion reached 11.2%, nearly a six-fold increase over a 14-year period (25). The proportion of patients electing CPM is reported to be even greater and also vary regionally among younger patients (18).

A major limitation of previous studies is that they are not suitable for analyses related to regional variation across the entire U.S. population. SEER is a population-based network of cancer registries that cover only 28% of the U.S. population, and operate in selected parts of the country. Further, SEER coverage of racial minorities varies from 26% of African Americans to 67% of Hawaiian/Pacific Islanders (26). While NCDB provides national coverage, it is a hospital-based registry and therefore captures only cases from hospitals that are accredited by the American College of Surgeons Commission on Cancer. Cancer patients who are never treated at an approved hospital are not reported to the NCDB, resulting in the inclusion of less than three-quarters of breast cancer patients in the U.S. Currently, all states have hospitals that report to NCDB, but coverage varies greatly across the country. For example, the overall case coverage in Arizona is only 27% (27, 28). For this reason, a better understanding of the geographic

variation in CPM use requires both national and population-based data such as those available through state cancer registries.

This study aims to assess the variation of CPM rate by state among women with unilateral breast cancer over a nine-year period from 2004 through 2012. We utilized data from the North American Association of Central Cancer Registries (NAACCR), an organization that maintains registry standards and compiles cancer surveillance data from all registry members (29). Each state in the U.S. is required by law to maintain a cancer registry and all central cancer registries in the U.S. are members of NAACCR (30). This represents the most comprehensive, nationwide cancer incidence data of the U.S.

METHODS:

Data Source and Variables: Demographic and clinical information was extracted for newly diagnosed cases of unilateral breast cancer among women aged 20 years and older (n=1,296,609), between 2004 and 2012 and reported to NAACCR cancer registries. We only selected patients undergoing surgery at the time of treatment for the first primary breast cancer. We only included cases classified as having local or regional disease because most distant stage breast cancers are treated systemically and bilateral mastectomy in patients with metastatic tumors would not be considered prophylactic (31).

Surgical interventions were categorized as breast-conserving surgery (BCS), unilateral mastectomy (UM), or CPM. Cases with unknown (n=12,183, 0.9%) or not clear (n=14,628, 1.1%) surgical procedures were excluded from analyses. AJCC stage was not available for all registries and to maximize the number of states included in

analysis, we used summary stage since this is the most widely reported variable. Stage was categorized as localized, regional by direct extension only, regional by lymph node involvement only, and regional by both direct extension and lymph node involvement. Tumor size was grouped into three categories, less than 2 cm, 2-4.9 cm, and 5 cm or greater. Cases with unknown stage (n=8,883, 0.7%) those with unknown tumor size (n=19,819, 1.5%) and those with a likely erroneously recorded tumor size of greater than 20 cm (n=1,067, 0.1%) were excluded. There was also a potential for misclassification of histology and therefore we excluded all cases with histology that could not be identified as ductal or lobular (n=85,143, 6.6%). Tumor grade was categorized as well differentiated, moderately differentiated, poorly differentiated or undifferentiated. Cases with unknown grade (n=89,893, 6.9%) were excluded.

Race was categorized as non-Hispanic White, non-Hispanic Black, Hispanic, and Other. Race was coded from a combination of two variables, one indicating race and the other indicating Hispanic origin. Cases were considered Hispanic if any Hispanic origin was known. If Hispanic was unknown but the race variable was known, cases were considered non-Hispanic. If both race/ethnicity variables were unknown, the case was excluded (n=3,995, 0.3%). After all exclusions the final sample size was 1,061,007 representing 82% of the extracted cases.

Region was determined by the U.S. census division as follows: Northeast (CT, ME, MA, NH, NJ, NY, PA, RI), Midwest (IN, IA, MI, MO, NE, ND, OH, SD, WI), South (AL, AR, DE, D.C., FL, GA, KY, LA, MS, NC, OK, DC, TN, TX, VA, WV), and West (AK, AZ, CA, CO, HI, ID, MT, NV, NM, OR, UT, WA, WY). Data from Illinois,

Kansas, Maryland, Minnesota, and Vermont were unavailable. The proportion of NH Whites in each state was determined by data from the 2010 U.S. census.

Statistical Analysis: The proportion of cases undergoing CPM was reported as a percent for each state by 3-year period and by age category (<45 years versus 45 years and older). Temporal trends in the proportion of cases undergoing CPM between 3-year periods were performed for each state using a 2-sided Cochran-Armitage Trend test. To illustrate variation by state, U.S. maps were created in ArcMap 10.3.1. To show changes in the temporal trend over time for each of the four U.S. regions, a joinpoint model, with a maximum of 1 joinpoint allowed, was used. In this method, annual percent change (APC) is calculated by fitting a least-squares regression line to the natural logarithm of the proportion, using year of diagnosis as the regressor variable (32). In the presence of a significant joinpoint, two values for annual percent change (APC) were calculated, one preceding and one following the identified joinpoint. Multivariable analysis was conducted using logistic regression, where the outcome variable was CPM vs. not CPM. A second logistic regression model was fit restricting only to patients who underwent mastectomy. Results were reported as adjusted odds ratios (aORs) and 95% confidence intervals (CIs). Since the main variable of interest was region, a two-way interaction between region and each of the patient variables was tested by stratification. Statistical analyses were performed using SAS 9.4 (Cary, NC) and joinpoint analysis was performed using Joinpoint Regression Program version 4.2.0.2.

RESULTS:

Among 1,061,007 identified patients who were diagnosed with unilateral early-stage breast cancer and underwent surgery between 2004 and 2012, 58.9% (n=625,405) had BCS, 32.3% (n=342,681) had UM, and 8.8% (n=92,921) had CPM. As shown in Table 1, the proportion of cases undergoing CPM decreased with increasing age. CPM was more common among patients with regional by lymph node involvement disease (11.9%) compared to other stage disease, lobular (12.3%) compared to ductal histology, poorly differentiated (10.3%) compared to other tumor grades, and tumors greater than 5 centimeters (14.5%) compared to smaller tumor size. Non-Hispanic whites (9.4%) and women with private insurance (13.2%) were more likely to undergo CPM than the corresponding comparison groups. We also observed an increasing temporal trend with CPM-treated patients constituting 5.1% of cases diagnosed in 2004-2006, 6.9% of cases diagnosed 2007-2009, and 12.0% of cases diagnosed in 2010-2012. Over the study period, CPM increased from 10.6% in 2004 to 33.5% in 2012 among 20- to 44-year-old patients and from 3.5% to 10.4% among patients 45 years and older (Figure 1).

The proportion of cases undergoing CPM by year of diagnosis for each available NAACCR registry is presented in Table 2. In general, the highest and the lowest proportions of CPM-treated cases during each of the three time periods were observed in the South and in the Northeast, respectively. Even within each region, there was substantial variation across the states. For example, in the Northeast region, Rhode Island consistently had the lowest proportion of CPM in each of the three periods (2.5%, 4.9%, 6.5%) while Maine had the highest proportions (6.8%, 9.9%, 13.3%). There was also state variation within each time period with up to a five-fold difference between the states

with the highest and lowest estimates. For example, during 2010-2012, Colorado had 20.4% of patients electing CPM while the corresponding proportion in D.C. was only 4.7%.

When cases were categorized according to age, the respective CPM proportions were highest and lowest in the Midwest and West among 20- to 44-year-old patients, and in the South and Northeast among cases 45 years of age and older (Table 3). Figure 2 presents the state variation of the overall proportion of patients electing CPM during the nine-year study period (A, B) and the percent increase between the first (2004-2006) and last (2010-2012) three-year period (C, D) by age category. For all states, the proportion of CPM in younger women (20-44 years) is greater than the proportion among older women (>45 years). Among women 20-44 years old, four contiguous states located in the West and Midwest (Colorado, Nebraska, South Dakota, Iowa) had the highest overall CPM proportions, which ranged from 33.2% in Iowa to 39.6% in South Dakota. These states also were among the highest overall CPM proportions for older women with an observed range from 9.9% in Iowa to 13.4% in Colorado. When the percent change rather than the overall proportion is considered, the difference between the two age categories is less evident and the majority of states show a 100-200% increase in CPM prevalence over the study period. Among younger women, the percent increase between the two time periods ranged from 62% in South Dakota to 420% in West Virginia. The corresponding range among older women was from 12% in D.C. to 327% in Utah.

Figure 3 presents the results of the joinpoint analyses. In each of the four U.S. regions we observed a significant joinpoint indicating that the increase in the proportion of CPM appears to be less pronounced in more recent years. The timing of the change

differed by region: 2008 in the Northeast and in the South, 2009 in the Midwest, and 2010 in the West. The upward trend, although less steep, remained statistically significant in the Northeast, South, and Midwest following the joinpoint. By contrast, the post-2010 APC in the West was no longer statistically significant.

In the multivariable logistic regression analyses, no significant differences in adjusted ORs were observed when the model was stratified by region, the main variable of interest, and therefore no interaction terms were included in the model (Table 4). The most important predictors of CPM were age and year of diagnosis. Compared to the reference age category of 50-59 years, younger women were more likely to undergo CPM with the most pronounced association for those 20-29 years of age (aOR=4.9; 95% CI: 4.44, 5.03). By contrast, the corresponding aORs (95% CIs) for women 60-69 and 70+ years of age were 0.6 (0.59, 0.61) and 0.2 (0.23, 0.25), respectively. The likelihood of CPM also increased with later years of diagnosis, compared to 2004-2006 (aOR=1.9 during 2007-2009 and aOR=2.9 during 2010-2012). Other patient characteristics that were significantly associated with electing CPM included regional by lymph node involvement disease (aOR= 1.3, 95% CI: 1.27-1.32) compared to localized disease, lobular (OR= 1.8, 95% CI: 1.73-1.81) compared to ductal histology, undifferentiated (aOR= 1.2, 95% CI: 1.11-1.33) or poorly differentiated (aOR= 1.2, 95% CI: 1.18-1.23) compared to well differentiated grade, and tumor size 5 cm or greater (aOR= 1.6, 95% CI: 1.53-1.61) compared to less than 2 cm. Non-Hispanic white women (reference category) underwent CPM significantly more often than women of other races. The aOR for non-Hispanic Blacks was the lowest (aOR=0.4, 95% CI: 0.41-0.43). Women with private insurance also elected CPM significantly more often than women with other types

of insurance; and uninsured women had the lowest odds of having this procedure (aOR=0.5, 95% CI: 0.46, 0.52). CPM use also significantly differed by region; the procedure was especially more common in the South compared to the Northeast (aOR=1.5, 95% CI: 1.46-1.52).

A second multivariable logistic regression model compared CPM to unilateral mastectomy because those women who elect BCS may be different than women who elect a more aggressive surgery. We observed attenuation of the dose-response relationship between age of diagnosis and CPM, although the general trend was maintained. The observed associations for year of diagnosis, histology, race, insurance status and, region were also similar in the two models. Unlike the base analysis comparing CPM to any other surgery, CPM receipt in the second model was inversely associated with stage and tumor size.

Figure 4 presents the results of the linear regression analysis of the association between the overall state-specific proportion of CPM and the proportion of the state residents who are NH White. The regression coefficient was statistically significant among women aged 20-44 years (β=0.15, p<0.01) but not among women 45 years of age and older (β=0.03, p=0.17).

DISCUSSION:

Our study of breast cancer patients who chose CPM versus other surgical interventions demonstrates a significant geographic variation in the proportion of women electing this aggressive procedure. We observed up to a five-fold difference in the CPM proportions across individual states in a given three-year time period. The difference

became less pronounced if states were grouped according to the four major census regions. In general, we found that the overall proportion of breast cancer patients electing CPM is highest in the South and lowest in the Northeast for all time periods investigated. When we divided the study population according to age (<45 versus 45+ years), we found that the regions with the highest and lowest CPM proportions were different for the two groups. Notably, in four contiguous Western and Midwest states (NE, CO, IA, SD), nearly half of young women underwent CPM in recent years.

We also observed that the proportion of women with unilateral breast cancer electing CPM increased over the study period, which is consistent with other studies addressing this issue. However unlike previous studies, we also investigated the regional variation of the temporal trend. We showed that with the exception of D.C., all states displayed a statistically significant increasing trend in the proportion of cases undergoing CPM between 2004-2006 and 2007-2009. When comparing 2007-2009 to 2010-2012, nine more states, which were generally located in the West and Midwest (N.H., R.I., N.E., N.D., S.D., A.K., H.I., N.V., and W.Y.) did not show significant increasing trend, suggesting that the surge in CPM use observed in recent years in the U.S. may be slowing down. This observation was further supported by the results of the joinpoint regression analysis, which showed significant inflexion points in recent years across all regions.

Several studies, including ours, have found that NH White women are more likely than other races to undergo CPM (4, 33, 34). The states with the highest proportions of CPM during the 2010-2012 period, Colorado, South Dakota and Tennessee, are also states with high proportions of whites compared to other races (70.0%, 84.7%, 75.6% NH White, respectively). We examined the correlation between the proportion of breast

cancer patients electing CPM and the proportion of NH Whites in the state determined by the 2010 census and found that the proportion of NH Whites in the state explains 12.5% of the state variation for younger women but does not contribute to the state variation in older women, suggesting there are other state-level variables that may be important in the observed CPM proportions. CPM proportions were rather low in states with very high proportions of NH White such as West Virginia and New Hampshire. West Virginia and New Hampshire have very similar overall CPM proportions, however these states are quite different. Most of West Virginia, a largely rural state located in Appalachia is designated as medically underserved (35). In contrast, New Hampshire residents have high incomes and high overall life satisfaction (36). A study conducted by the United Health Foundation put New Hampshire as the 5th and West Virginia as the 47th healthiest state. Although the overall CPM proportions are very similar in these two states, the reasons women choose this procedure over other surgical procedures is likely to be different, strongly suggesting that there are other factors influencing the decision to undergo CPM. Additionally, treatment practices may vary by state as we found four contiguous states, located in the West and Midwest (CO, NE, SD, IA), had the highest overall proportions of CPM. One study found that use of neoadjuvant chemotherapy for patients with early stage breast cancer was lowest in the Midwest, suggesting that providers in this region of the country may be more likely to advocate for more aggressive surgical intervention (37). Future studies should investigate other state-level or provider-level characteristics that could be contributing to the variation of CPM proportion.

To our knowledge, this study represents the first examination of CPM receipt using nationwide, population-based data. Previous studies investigating regional variation in CPM have not analyzed data at the state-level and have not used a study sample that is representative of the entire U.S. population. CPM rates in SEER data have been shown to vary by SEER registry but considering how widespread and noncontiguous SEER registries are, no specific trend was observed (19). Sariego (2008) studied cases reported to NCDB to investigate regional variation in breast cancer treatment and found that the proportion of breast cancer patients electing BCS was highest in the Northeast and lowest in the South, which is the reverse of our findings for CPM (38). In another NCDB study Pesce et al. (2014) described regional variation in CPM use among only younger breast cancer patients and found CPM rates to be highest in the Midwest and lowest in the Northeast, which is partially consistent with our findings among younger patients (18). Consistent with our findings, an earlier NCDB study found that overall, women in the South were more likely to have CPM than women in other regions of the country (17).

A notable limitation of our study is the lack of data for five states; three of which are concentrated in the Midwest (IL, KS, MN). Two of the states missing data, Maryland and Illinois, have over 80% case coverage in NCDB and may explain discrepancies between our findings and previous studies (27). Additionally, data for 2010-2012 were unavailable for one state and data for 2011-2012 were unavailable for one state.

Our study also did not consider BRCA1/2 mutation status or family history, which are important factors in making breast cancer treatment decisions. The Society for Surgical Oncology indicates CPM as an appropriate risk reducing measure in breast cancer patients who are at high risk for contralateral breast cancer, such as those with a

BRCA1/2 mutation or family history of disease (39). Earlier studies have confirmed that patients with a BRCA1/2 mutation and those with a family history of breast cancer are more likely to elect CPM (4, 9, 33, 40). Some studies have also suggested that just being tested for BRCA1/2, but not necessarily having a positive result, increased the likelihood of undergoing CPM (9, 34).

In summary, the results of this study demonstrate substantial geographic variation in the use of CPM among women with unilateral breast cancer. The overall CPM use continues to increase although more recent data indicate that the rate of increase is beginning to slow down. Future research will provide additional insight into the reasons for temporal changes and regional variation of CPM receipt.

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TABLES AND FIGURES:

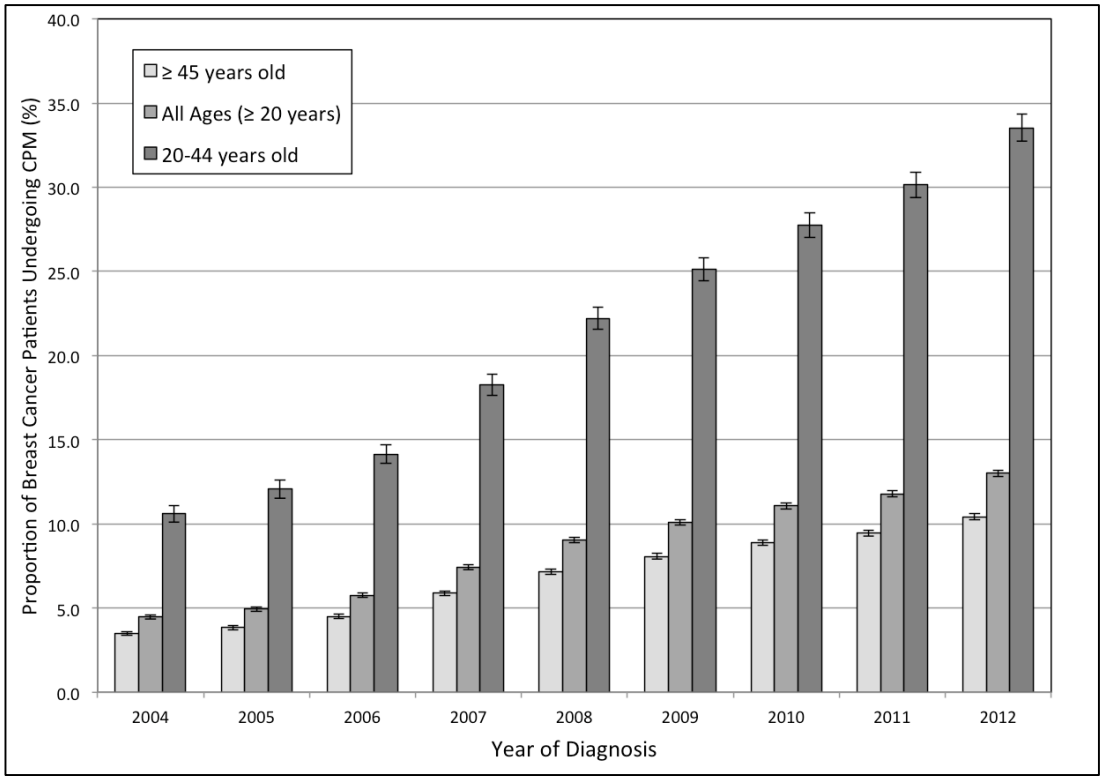
Table 1. Patient Characteristics by surgery type among women diagnosed with unilateral, early stage breast cancer, 2004-2012

Patient Characteristic	Total N	Breast Conserving Surgery n (%)		Unilateral Mastectomy n (%)		Bilateral Mastectomy (CPM) n (%)	
	1,061,007	625,405	(58.9)	342,681	(32.3)	92,921	(8.8)
Age at Diagnosis							
20-29 years	5,311	1,834	(34.5)	1,856	(35.0)	1,621	(30.5)
30-39 years	49,912	19,945	(40.0)	17,197	(34.5)	12,770	(25.6)
40-49 years	193,970	101,747	(52.5)	62,159	(32.1)	30,064	(15.5)
50-59 years	267,028	161,281	(60.4)	80,069	(30.0)	25,678	(9.6)
60-69 years	264,647	169,208	(63.9)	79,380	(30.0)	16,059	(6.1)
70+ years	280,139	171,390	(61.2)	102,020	(36.4)	6,729	(2.4)
Year of Diagnosis							
2004-2006	329,773	198,581	(60.2)	114,463	(34.7)	16,729	(5.1)
2007-2009	364,575	213,129	(58.5)	119,086	(32.7)	32,360	(8.9)
2010-2012	366,659	213,695	(58.3)	109,132	(29.8)	43,832	(12.0)
Summary Stage[1]							
L	700,269	476,754	(68.1)	172,038	(24.6)	51,477	(7.4)
RE	19,546	9,181	(47.0)	9,110	(46.6)	1,255	(6.4)
RN	300,090	131,680	(43.9)	132,724	(44.2)	35,686	(11.9)
RE + RN	41,102	7,790	(19.0)	28,809	(70.1)	4,503	(11.0)
Histology							
Ductal	973,330	583,208	(59.9)	307,985	(31.6)	82,137	(8.4)
Lobular	87,677	42,197	(48.1)	34,696	(39.6)	10,784	(12.3)
Tumor Grade							
Well Differentiated	224,993	155,570	(69.1)	53,996	(24.0)	15,427	(6.9)
Moderately Differentiated	465,686	276,663	(59.4)	149,519	(32.1)	39,504	(8.5)
Poorly Differentiated	363,615	189,805	(52.2)	136,414	(37.5)	37,396	(10.3)
Undifferentiated	6,713	3,367	(50.2)	2,752	(41.0)	594	(8.9)
Tumor size, cm							
< 2 cm	626,106	439,002	(70.1)	141,638	(22.6)	45,466	(7.3)
2-4.9 cm	364,835	173,656	(47.6)	153,902	(42.2)	37,277	(10.2)
≥ 5 cm[2]	70,066	12,747	(18.2)	47,141	(67.3)	10,178	(14.5)
Race							
Non-Hispanic White	841,927	504,597	(59.9)	258,416	(30.7)	78,914	(9.4)
Non-Hispanic Black	105,644	60,500	(57.3)	39,127	(37.0)	6,017	(5.7)
Non-Hispanic Other	44,973	23,300	(51.8)	18,677	(41.5)	2,996	(6.7)
Hispanic	68,463	37,008	(54.1)	26,461	(38.7)	4,994	(7.3)
Insurance Status							

Private	345,014	202,784	(58.8)	96,770	(28.0)	45,460	(13.2)
Medicaid	47,668	24,084	(50.5)	19,530	(41.0)	4,054	(8.5)
Medicare	282,187	170,750	(60.5)	99,886	(35.4)	11,551	(4.1)
Other	96,138	55,934	(58.2)	29,929	(31.1)	10,275	(10.7)
Uninsured	18,305	9,151	(50.0)	7,805	(42.6)	1,349	(7.4)
Unknown	271,695	162,702	(59.9)	88,761	(32.7)	20,232	(7.5)

[1]Summary stage abbreviations: L=Localized, RE=Regional by direct extension only, RN=Regional by lymph node involvement, RE+RN=Regional by both direct extension and lymph node involvement
[2]Excluded cases with tumor size greater than 20 cm due to implausibility

Figure 1. Proportion of breast cancer patients undergoing CPM by age and year of diagnosis



*Error bars represent Wald 95% confidence intervals, calculated in OpenEpi

Table 2. Proportion of cases receiving CPM by state and year of diagnosis among women with unilateral breast cancer undergoing surgery

State	Total Cases	Year of Diagnosis									
		2004-2006			2007-2009				2010-2012			
	N	Total cases	CPM n (%)		Total cases	CPM n (%)		*P* value for trend*	Total cases	CPM n (%)		*P* value for trend**
Northeast	237,491	75,997	3,166	(4.2)	80,510	5,919	(7.4)	<.0001	80,984	7,961	(9.8)	<.0001
Connecticut	16,262	5,245	249	(4.7)	5,383	445	(8.3)	<.0001	5,634	713	(12.7)	<.0001
Maine	6,689	2,193	150	(6.8)	2,285	226	(9.9)	0.0002	2,211	295	(13.3)	0.0003
Massachusetts	30,980	10,073	331	(3.3)	10,594	583	(5.5)	<.0001	10,313	686	(6.7)	0.0005
New Hampshire	6,175	1,940	64	(3.3)	2,053	138	(6.7)	<.0001	2,182	179	(8.2)	0.0671
New Jersey	36,202	11,812	550	(4.7)	12,420	989	(8.0)	<.0001	11,970	1,163	(9.7)	<.0001
New York	80,723	25,293	1,033	(4.1)	27,552	2,140	(7.8)	<.0001	27,878	2,966	(10.6)	<.0001
Pennsylvania	55,653	17,844	749	(4.2)	18,552	1,316	(7.1)	<.0001	19,257	1,859	(9.7)	<.0001
Rhode Island	4,807	1,597	40	(2.5)	1,671	82	(4.9)	0.0003	1,539	100	(6.5)	0.0516
Midwest	184,266	58,633	2,990	(5.1)	62,730	5,669	(9.0)	<.0001	62,903	7,590	(12.1)	<.0001
Indiana	23,999	7,548	291	(3.9)	8,178	614	(7.5)	<.0001	8,273	800	(9.7)	<.0001
Iowa	13,033	4,196	351	(8.4)	4,338	588	(13.6)	<.0001	4,499	698	(15.5)	0.0090
Michigan	37,524	11,717	532	(4.5)	12,673	1,071	(8.5)	<.0001	13,134	1,492	(11.4)	<.0001
Missouri	25,447	8,072	371	(4.6)	8,479	784	(9.2)	<.0001	8,896	1,382	(15.5)	<.0001
Nebraska	7,504	2,492	242	(9.7)	2,502	406	(16.2)	<.0001	2,510	442	(17.6)	0.1918
North Dakota	2,792	929	39	(4.2)	961	106	(11.0)	<.0001	902	122	(13.5)	0.1005
Ohio	46,471	15,323	698	(4.6)	15,971	1,206	(7.6)	<.0001	15,177	1,443	(9.5)	<.0001
South Dakota	3,510	1,030	117	(11.4)	1,231	201	(16.3)	0.0007	1,249	216	(17.3)	0.5203
Wisconsin	23,986	7,326	349	(4.8)	8,397	693	(8.3)	<.0001	8,263	995	(12.0)	<.0001
South	379,718	114,955	6,213	(5.4)	132,162	12,860	(9.7)	<.0001	132,601	17,427	(13.1)	<.0001
Alabama	17,255	4,797	318	(6.6)	6,472	644	(10.0)	<.0001	5,986	757	(12.6)	<.0001
Arkansas[1]	7,234	3,447	247	(7.2)	3,787	484	(12.8)	<.0001				
Delaware	3,734	1,235	29	(2.3)	1,315	54	(4.1)	0.0124	1,184	83	(7.0)	0.0015
District of Columbia	2,279	719	22	(3.1)	714	22	(3.1)	0.9812	846	40	(4.7)	0.0971

Florida	74,540	22,822	1,310	(5.7)	24,849	2,465	(9.9)	<.0001	26,869	3,698	(13.8)	<.0001
Georgia	34,882	10,372	699	(6.7)	11,943	1,322	(11.1)	<.0001	12,567	1,770	(14.1)	<.0001
Kentucky	17,650	5,465	293	(5.4)	6,014	697	(11.6)	<.0001	6,171	892	(14.5)	<.0001
Louisiana	15,527	4,350	180	(4.1)	5,458	385	(7.1)	<.0001	5,719	599	(10.5)	<.0001
Mississippi	9,825	2,382	168	(7.1)	3,573	413	(11.6)	<.0001	3,870	668	(17.3)	<.0001
North Carolina	38,818	11,811	548	(4.6)	13,020	1,142	(8.8)	<.0001	13,987	1,509	(10.8)	<.0001
Oklahoma	13,526	4,219	241	(5.7)	4,700	457	(9.7)	<.0001	4,607	626	(13.6)	<.0001
South Carolina	19,660	5,843	234	(4.0)	6,759	483	(7.1)	<.0001	7,058	612	(8.7)	0.0009
Tennessee	24,619	7,491	479	(6.4)	8,390	992	(11.8)	<.0001	8,738	1,568	(17.9)	<.0001
Texas	61,172	17,832	997	(5.6)	21,987	2,196	(10.0)	<.0001	21,353	2,895	(13.6)	<.0001
Virginia	31,501	9,808	397	(4.0)	10,720	979	(9.1)	<.0001	10,973	1,468	(13.4)	<.0001
West Virginia	7,496	2,362	51	(2.2)	2,461	125	(5.1)	<.0001	2,673	242	(9.1)	<.0001
West	259,532	80,188	4,360	(5.4)	89,173	7,912	(8.9)	<.0001	90,171	10,854	(12.0)	<.0001
Alaska	2,204	659	31	(4.7)	726	90	(12.4)	<.0001	819	81	(9.9)	0.1170
Arizona	20,045	5,830	437	(7.5)	7,093	764	(10.8)	<.0001	7,122	1,174	(16.5)	<.0001
California	135,216	42,093	1,978	(4.7)	46,060	3,435	(7.5)	<.0001	47,063	4,899	(10.4)	<.0001
Colorado	18,584	5,613	607	(10.8)	6,438	1,062	(16.5)	<.0001	6,533	1,330	(20.4)	<.0001
Hawaii	5,915	1,807	53	(2.9)	1,954	98	(5.0)	0.0012	2,154	126	(5.8)	0.2396
Idaho	5,390	1,546	58	(3.8)	1,864	115	(6.2)	0.0014	1,980	194	(9.8)	<.0001
Montana	4,209	1,292	57	(4.4)	1,441	151	(10.5)	<.0001	1,476	212	(14.4)	0.0015
Nevada[2]	6,261	2,263	67	(3.0)	2,995	219	(7.3)	<.0001	1,003	83	(8.3)	0.3178
New Mexico	6,768	2,033	117	(5.8)	2,270	219	(9.6)	<.0001	2,465	295	(12.0)	0.0104
Oregon	17,059	5,379	409	(7.6)	5,720	733	(12.8)	<.0001	5,960	899	(15.1)	0.0004
Utah	7,412	2,233	58	(2.6)	2,433	186	(7.6)	<.0001	2,746	318	(11.6)	<.0001
Washington	28,574	8,857	455	(5.1)	9,536	766	(8.0)	<.0001	10,181	1,167	(11.5)	<.0001
Wyoming	1,895	583	33	(5.7)	643	74	(11.5)	0.0003	669	76	(11.4)	0.9327

[1]Arkansas missing data for years of diagnosis 2010-2012

[2]Nevada missing data for years of diagnosis 2011-2012

*p-value for Cochran-Armitage test for trend between 2004-2006 diagnosis period and 2007-2009 diagnosis period.

**p-value for Cochran-Armitage test for trend between 2007-2009 diagnosis period and 2010-2012 diagnosis period.

Table 3. Proportion of cases receiving CPM by region, age, and year of diagnosis among women with unilateral breast cancer undergoing surgery

Age Category	Region	Total Cases	Year of Diagnosis									
			2004-2006			2007-2009				2010-2012		
		N	Total cases	CPM n (%)		Total cases	CPM n (%)		*P* value for trend	Total cases	CPM n (%)		*P* value for trend
20-44 years	**Northeast**	30,611	10,617	1,271	(12.0)	10,391	2,201	(21.2)	<.0001	9,603	2,697	(28.1)	<.0001
	Midwest	21,382	7,453	1,022	(13.7)	7,325	1,745	(23.8)	<.0001	6,604	2,224	(33.7)	<.0001
	South	46,816	15,713	1,931	(12.3)	16,131	3,606	(22.4)	<.0001	14,972	4,753	(31.7)	<.0001
	West	31,950	10,577	1,218	(11.5)	10,902	2,227	(20.4)	<.0001	10,471	3,009	(28.7)	<.0001
45 + years	**Northeast**	206,880	65,380	1,895	(2.9)	70,119	3,718	(5.3)	<.0001	71,381	5,264	(7.4)	<.0001
	Midwest	162,884	51,180	1,968	(3.8)	55,405	3,924	(7.1)	<.0001	56,299	5,366	(9.5)	<.0001
	South	332,902	99,242	4,282	(4.3)	116,031	9,254	(8.0)	<.0001	117,629	12,674	(10.8)	<.0001
	West	227,582	69,611	3,142	(4.5)	78,271	5,685	(7.3)	<.0001	79,700	7,845	(9.8)	<.0001

Figure 2. State variation of overall CPM proportion (A-B) and percent increase in CPM proportion between 2004-2006 period and 2010-2012 period (C-D) among women with unilateral breast cancer 20-44 year old (A, C) versus 45 years and older (B, D).

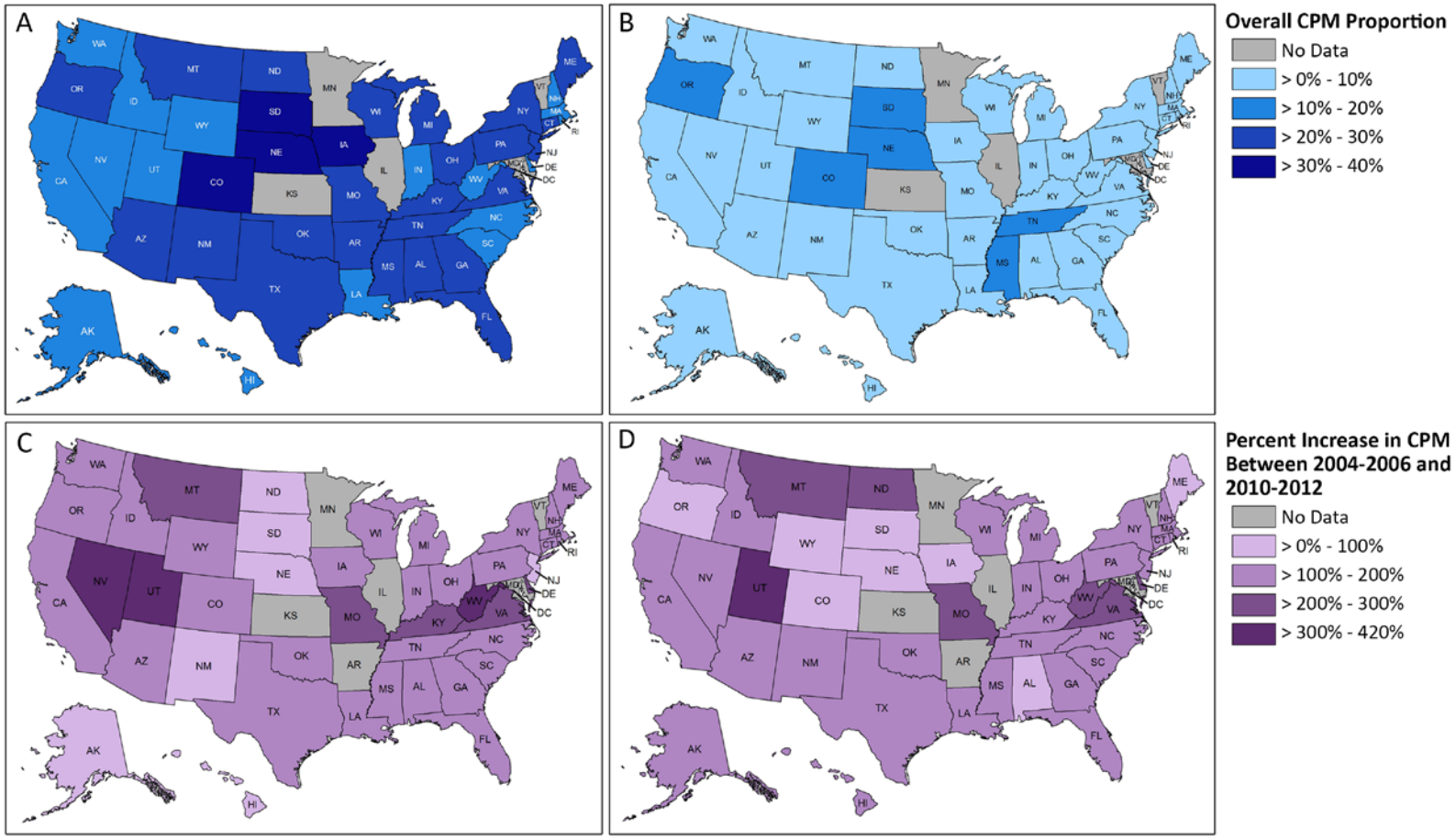
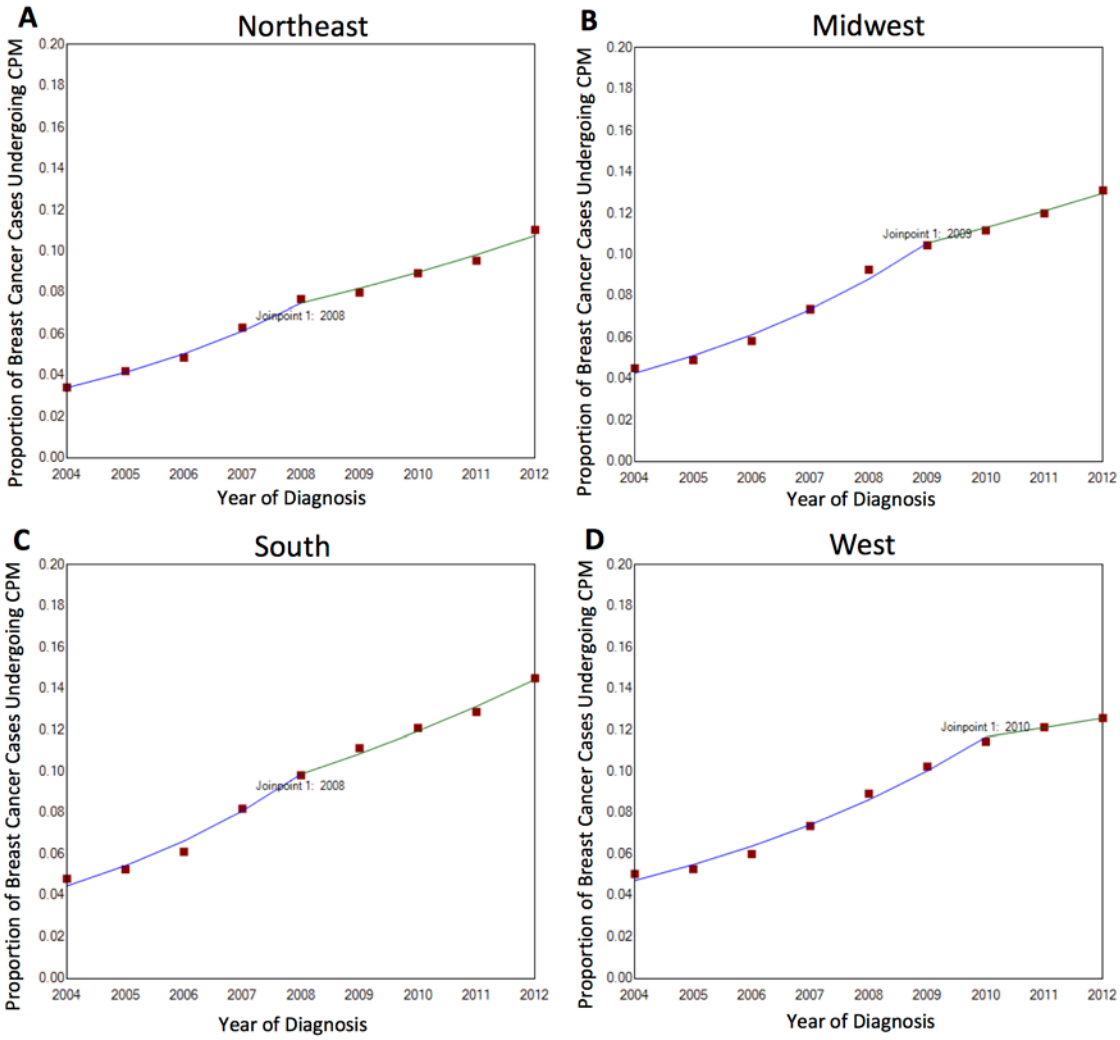


Figure 3. Joinpoint Analysis of CPM proportion in each region by year of diagnosis



The APCs for the Northeast (A) before and after the 2008 joinpoint are 21.8 and 9.5, respectively. The APCs for the Midwest (B) before and after the 2009 joinpoint are 19.8 and 7.1, respectively. The APCs for the South (C) before and after the 2008 joinpoint are 22.0 and 10.0, respectively. And the APCs for the West (D) before and after the 2010 joinpoint are 16.3 and 3.8[1] respectively.

[1]Not statistically significant at the p=0.05 level.

Table 4. Multivariate association between receipt of CPM and patient demographic and clinical characteristics

	CPM vs. Other Surgery aOR (95% CI)	CPM vs. UM aOR (95% CI)
Age at Diagnosis		
20-29 years	4.7 (4.44 5.03)	3.7 (3.41 3.94)
30-39 years	3.6 (3.50 3.68)	2.8 (2.75 2.91)
40-49 years	1.8 (1.79 1.85)	1.6 (1.59 1.65)
50-59 years	1 Reference	1 Reference
60-69 years	0.6 (0.59 0.61)	0.6 (0.60 0.63)
70+ years	0.2 (0.23 0.25)	0.2 (0.21 0.23)
Year of Diagnosis		
2004-2006	1 Reference	1 Reference
2007-2009	1.9 (1.90 1.98)	1.9 (1.85 1.94)
2010-2012	2.9 (2.84 2.95)	2.9 (2.84 2.96)
Summary Stage[1]		
L	1 Reference	1 Reference
RE	0.9 (0.89 1.00)[2]	0.7 (0.63 0.71)
RN	1.3 (1.27 1.32)	0.8 (0.83 0.86)
RE + RN	1.3 (1.26 1.36)	0.7 (0.65 0.70)
Histology		
Ductal	1 Reference	1 Reference
Lobular	1.8 (1.73 1.81)	1.4 (1.37 1.44)
Tumor Grade		
Well Differentiated	1 Reference	1 Reference
Moderately Differentiated	1.1 (1.10 1.15)	1 (0.94 0.99)
Poorly Differentiated	1.2 (1.18 1.23)	1 (0.99 1.04)[2]
Undifferentiated	1.2 (1.11 1.33)	1 (0.87 1.06)[2]
Tumor size, cm		
< 2	1 Reference	1 Reference
2-4.9	1.2 (1.19 1.23)	0.8 (0.78 0.81)
≥ 5[3]	1.6 (1.53 1.61)	0.7 (0.69 0.73)
Race		
Non-Hispanic White	1 Reference	1 Reference
Non-Hispanic Black	0.4 (0.41 0.43)	0.4 (0.42 0.45)
Non-Hispanic Other	0.5 (0.47 0.51)	0.4 (0.37 0.40)
Hispanic	0.5 (0.52 0.55)	0.5 (0.47 0.50)
Insurance Status		
Private	1 Reference	1 Reference
Medicaid	0.6 (0.57 0.61)	0.5 (0.49 0.53)
Medicare	0.8 (0.78 0.83)	0.7 (0.68 0.72)
Other	0.8 (0.82 0.86)	0.8 (0.78 0.82)
Uninsured	0.5 (0.46 0.52)	0.4 (0.41 0.46)
Unknown	0.8 (0.80 0.83)	0.7 (0.73 0.76)

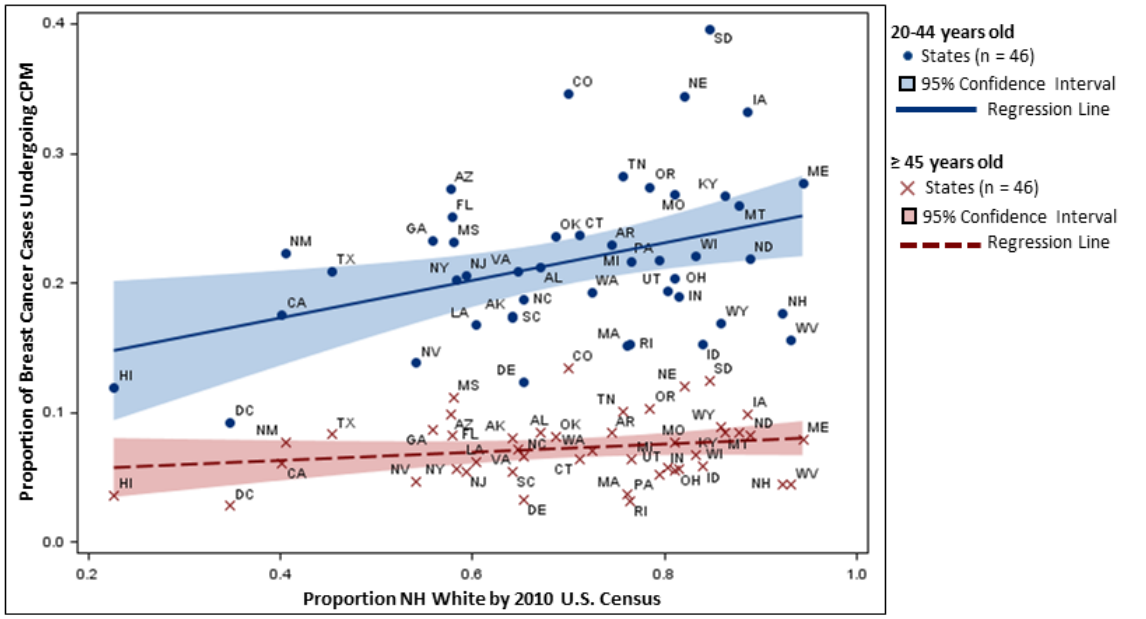
Region						
Northeast	1	Reference		1	Reference	
Midwest	1.2	(1.21	1.27)	1.1	(1.08	1.14)
South	1.5	(1.46	1.52)	1.2	(1.20	1.25)
West	1.4	(1.33	1.39)	1.3	(1.24	1.30)

[1]Summary stage abbreviations: L=Localized, RE=Regional by direct extension only, RN=Regional by lymph node involvement, RE+RN=Regional by both direct extension and lymph node involvement

[2]p-value > 0.05

[3]Excluded cases with tumor size greater than 20 cm due to implausibility

Figure 4. The correlation between the proportion of breast cancer patients diagnosed 2004-2012 undergoing CPM and the proportion of NH whites according to the 2010 U.S. census by state and age category.



The β-coefficient for the linear regression of CPM proportion on the proportion of NH Whites per state according to the 2010 census is 0.145 (SE=0.05, p=0.0091) for patients 20-44 years old and 0.032 (SE=0.02, p=0.1669) for patients ≥ 45 years old. The adjusted correlation coefficient (R^2) for the statistically significant regression among 20-44 year old women is 0.125.

APPENDIX:

Table 1A. Proportion of cases receiving CPM by state and year of diagnosis among women ages 20-44 years with unilateral breast cancer undergoing surgery

State	Total Cases	Year of Diagnosis										
		2004-2006			2007-2009				2010-2012			
	N	Total cases	CPM n (%)		Total cases	CPM n (%)		*P* value for trend	Total cases	CPM n (%)		*P* value for trend
Northeast	30,611	10,617	1,271	(12.0)	10,391	2,201	(21.2)	<.0001	9,603	2,697	(28.1)	<.0001
Connecticut	2,109	712	89	(12.5)	704	161	(22.9)	<.0001	693	249	(35.9)	<.0001
Maine	710	245	46	(18.8)	250	62	(24.8)	0.1047	215	89	(41.4)	0.0001
Massachusetts	4,005	1,363	124	(9.1)	1,419	232	(16.3)	<.0001	1,223	249	(20.4)	0.0077
New Hampshire	789	295	25	(8.5)	235	50	(21.3)	<.0001	259	64	(24.7)	0.3656
New Jersey	5,062	1,788	256	(14.3)	1,757	400	(22.8)	<.0001	1,517	380	(25.0)	0.1262
New York	11,039	3,760	415	(11.0)	3,703	789	(21.3)	<.0001	3,576	1,027	(28.7)	<.0001
Pennsylvania	6,342	2,247	299	(13.3)	2,134	477	(22.4)	<.0001	1,961	601	(30.6)	<.0001
Rhode Island	555	207	17	(8.2)	189	30	(15.9)	0.0186	159	38	(23.9)	0.0600
Midwest	21,382	7,453	1,022	(13.7)	7,325	1,745	(23.8)	<.0001	6,604	2,224	(33.7)	<.0001
Indiana	2,779	929	100	(10.8)	985	192	(19.5)	<.0001	865	234	(27.1)	0.0001
Iowa	1,481	548	121	(22.1)	496	167	(33.7)	<.0001	437	203	(46.5)	<.0001
Michigan	4,453	1,545	191	(12.4)	1,530	345	(22.5)	<.0001	1,378	428	(31.1)	<.0001
Missouri	2,987	1,044	133	(12.7)	989	249	(25.2)	<.0001	954	419	(43.9)	<.0001
Nebraska	845	302	66	(21.9)	302	120	(39.7)	<.0001	241	105	(43.6)	0.3676
North Dakota	289	87	11	(12.6)	101	27	(26.7)	0.0165	101	25	(24.8)	0.7476
Ohio	5,371	1,961	242	(12.3)	1,818	393	(21.6)	<.0001	1,592	454	(28.5)	<.0001
South Dakota	366	119	36	(30.3)	129	51	(39.5)	0.1259	118	58	(49.2)	0.1284
Wisconsin	2,811	918	122	(13.3)	975	201	(20.6)	<.0001	918	298	(32.5)	<.0001
South	46,816	15,713	1,931	(12.3)	16,131	3,606	(22.4)	<.0001	14,972	4,753	(31.7)	<.0001
Alabama	1,989	650	86	(13.2)	752	153	(20.3)	0.0004	587	182	(31.0)	<.0001
Arkansas[1]	844	432	70	(16.2)	412	123	(29.9)	<.0001				

Delaware	479	170	12	(7.1)	178	18	(10.1)	0.3103	131	29	(22.1)	0.0036
District of Columbia	315	83	4	(4.8)	114	8	(7.0)	0.5241	118	17	(14.4)	0.0696
Florida	8,032	2,817	425	(15.1)	2,627	661	(25.2)	<.0001	2,588	933	(36.1)	<.0001
Georgia	5,148	1,720	241	(14.0)	1,739	417	(24.0)	<.0001	1,689	535	(31.7)	<.0001
Kentucky	2,131	752	96	(12.8)	715	209	(29.2)	<.0001	664	264	(39.8)	<.0001
Louisiana	1,903	607	61	(10.0)	650	97	(14.9)	0.0092	646	161	(24.9)	<.0001
Mississippi	1,258	344	40	(11.6)	439	101	(23.0)	<.0001	475	149	(31.4)	0.0046
North Carolina	5,134	1,706	180	(10.6)	1,749	353	(20.2)	<.0001	1,679	429	(25.6)	0.0002
Oklahoma	1,446	508	71	(14.0)	476	115	(24.2)	<.0001	462	155	(33.5)	0.0015
South Carolina	2,258	720	70	(9.7)	793	141	(17.8)	<.0001	745	180	(24.2)	0.0021
Tennessee	3,031	1,027	152	(14.8)	1,046	289	(27.6)	<.0001	958	415	(43.3)	<.0001
Texas	7,872	2,507	267	(10.7)	2,773	594	(21.4)	<.0001	2,592	786	(30.3)	<.0001
Virginia	4,211	1,422	143	(10.1)	1,408	291	(20.7)	<.0001	1,381	448	(32.4)	<.0001
West Virginia	765	248	13	(5.2)	260	36	(13.8)	0.0010	257	70	(27.2)	0.0002
West	31,950	10,577	1,218	(11.5)	10,902	2,227	(20.4)	<.0001	10,471	3,009	(28.7)	<.0001
Alaska	282	88	10	(11.4)	90	16	(17.8)	0.2257	104	23	(22.1)	0.4522
Arizona	2,246	709	119	(16.8)	812	221	(27.2)	<.0001	725	272	(37.5)	<.0001
California	17,580	5,969	616	(10.3)	5,899	997	(16.9)	<.0001	5,712	1,471	(25.8)	<.0001
Colorado	2,425	766	165	(21.5)	840	301	(35.8)	<.0001	819	374	(45.7)	<.0001
Hawaii	793	255	21	(8.2)	277	35	(12.6)	0.0985	261	38	(14.6)	0.5149
Idaho	550	152	13	(8.6)	204	31	(15.2)	0.0596	194	40	(20.6)	0.1578
Montana	385	130	14	(10.8)	129	39	(30.2)	0.0001	126	47	(37.3)	0.2326
Nevada[2]	816	286	16	(5.6)	401	68	(17.0)	<.0001	129	29	(22.5)	0.1582
New Mexico	743	262	39	(14.9)	258	61	(23.6)	0.0113	223	66	(29.6)	0.1397
Oregon	1,688	550	81	(14.7)	540	174	(32.2)	<.0001	598	207	(34.6)	0.3930
Utah	1,021	317	19	(6.0)	337	68	(20.2)	<.0001	367	111	(30.2)	0.0022
Washington	3,243	1,038	100	(9.6)	1,063	205	(19.3)	<.0001	1,142	317	(27.8)	<.0001
Wyoming	178	55	5	(9.1)	52	11	(21.2)	0.0803	71	14	(19.7)	0.8450

[1] Arkansas missing data for years of diagnosis 2010-2012

[2] Nevada missing data for years of diagnosis 2011-2012

Table 2A. Proportion of cases receiving CPM by state and year of diagnosis among women ages ≥ 45 years with unilateral breast cancer undergoing surgery

State	Total Cases	Year of Diagnosis										
		2004-2006			2007-2009				2010-2012			
	N	Total cases	CPM n (%)		Total cases	CPM n (%)		*P* value for trend	Total cases	CPM n (%)		*P* value for trend
Northeast	206,880	65,380	1,895	(2.9)	70,119	3,718	(5.3)	<.0001	71,381	5,264	(7.4)	<.0001
Connecticut	14,153	4,533	160	(3.5)	4,679	284	(6.1)	<.0001	4,941	464	(9.4)	<.0001
Maine	5,979	1,948	104	(5.3)	2,035	164	(8.1)	0.0006	1,996	206	(10.3)	0.0129
Massachusetts	26,975	8,710	207	(2.4)	9,175	351	(3.8)	<.0001	9,090	437	(4.8)	0.0011
New Hampshire	5,386	1,645	39	(2.4)	1,818	88	(4.8)	0.0001	1,923	115	(6.0)	0.1240
New Jersey	31,140	10,024	294	(2.9)	10,663	589	(5.5)	<.0001	10,453	783	(7.5)	<.0001
New York	69,684	21,533	618	(2.9)	23,849	1,351	(5.7)	<.0001	24,302	1,939	(8.0)	<.0001
Pennsylvania	49,311	15,597	450	(2.9)	16,418	839	(5.1)	<.0001	17,296	1,258	(7.3)	<.0001
Rhode Island	4,252	1,390	23	(1.7)	1,482	52	(3.5)	0.0018	1,380	62	(4.5)	0.1786
Midwest	162,884	51,180	1,968	(3.8)	55,405	3,924	(7.1)	<.0001	56,299	5,366	(9.5)	<.0001
Indiana	21,220	6,619	191	(2.9)	7,193	422	(5.9)	<.0001	7,408	566	(7.6)	<.0001
Iowa	11,552	3,648	230	(6.3)	3,842	421	(11.0)	<.0001	4,062	495	(12.2)	0.0882
Michigan	33,071	10,172	341	(3.4)	11,143	726	(6.5)	<.0001	11,756	1,064	(9.1)	<.0001
Missouri	22,460	7,028	238	(3.4)	7,490	535	(7.1)	<.0001	7,942	963	(12.1)	<.0001
Nebraska	6,659	2,190	176	(8.0)	2,200	286	(13.0)	<.0001	2,269	337	(14.9)	0.0739
North Dakota	2,503	842	28	(3.3)	860	79	(9.2)	<.0001	801	97	(12.1)	0.0530
Ohio	41,100	13,362	456	(3.4)	14,153	813	(5.7)	<.0001	13,585	989	(7.3)	<.0001
South Dakota	3,144	911	81	(8.9)	1,102	150	(13.6)	0.0009	1,131	158	(14.0)	0.8061
Wisconsin	21,175	6,408	227	(3.5)	7,422	492	(6.6)	<.0001	7,345	697	(9.5)	<.0001
South	332,902	99,242	4,282	(4.3)	116,031	9,254	(8.0)	<.0001	117,629	12,674	(10.8)	<.0001
Alabama	15,266	4,147	232	(5.6)	5,720	491	(8.6)	<.0001	5,399	575	(10.7)	0.0002
Arkansas[1]	6,390	3,015	177	(5.9)	3,375	361	(10.7)	<.0001				
Delaware	3,255	1,065	17	(1.6)	1,137	36	(3.2)	0.0163	1,053	54	(5.1)	0.0208

District of Columbia	1,964	636	18	(2.8)	600	14	(2.3)	0.5825	728	23	(3.2)	0.3627
Florida	66,508	20,005	885	(4.4)	22,222	1,804	(8.1)	<.0001	24,281	2,765	(11.4)	<.0001
Georgia	29,734	8,652	458	(5.3)	10,204	905	(8.9)	<.0001	10,878	1,235	(11.4)	<.0001
Kentucky	15,519	4,713	197	(4.2)	5,299	488	(9.2)	<.0001	5,507	628	(11.4)	0.0002
Louisiana	13,624	3,743	119	(3.2)	4,808	288	(6.0)	<.0001	5,073	438	(8.6)	<.0001
Mississippi	8,567	2,038	128	(6.3)	3,134	312	(10.0)	<.0001	3,395	519	(15.3)	<.0001
North Carolina	33,684	10,105	368	(3.6)	11,271	789	(7.0)	<.0001	12,308	1,080	(8.8)	<.0001
Oklahoma	12,080	3,711	170	(4.6)	4,224	342	(8.1)	<.0001	4,145	471	(11.4)	<.0001
South Carolina	17,402	5,123	164	(3.2)	5,966	342	(5.7)	<.0001	6,313	432	(6.8)	0.0114
Tennessee	21,588	6,464	327	(5.1)	7,344	703	(9.6)	<.0001	7,780	1,153	(14.8)	<.0001
Texas	53,300	15,325	730	(4.8)	19,214	1,602	(8.3)	<.0001	18,761	2,109	(11.2)	<.0001
Virginia	27,290	8,386	254	(3.0)	9,312	688	(7.4)	<.0001	9,592	1,020	(10.6)	<.0001
West Virginia	6,731	2,114	38	(1.8)	2,201	89	(4.0)	<.0001	2,416	172	(7.1)	<.0001
West	227,582	69,611	3,142	(4.5)	78,271	5,685	(7.3)	<.0001	79,700	7,845	(9.8)	<.0001
Alaska	1,922	571	21	(3.7)	636	74	(11.6)	<.0001	715	58	(8.1)	0.0295
Arizona	17,799	5,121	318	(6.2)	6,281	543	(8.6)	<.0001	6,397	902	(14.1)	<.0001
California	117,636	36,124	1,362	(3.8)	40,161	2,438	(6.1)	<.0001	41,351	3,428	(8.3)	<.0001
Colorado	16,159	4,847	442	(9.1)	5,598	761	(13.6)	<.0001	5,714	956	(16.7)	<.0001
Hawaii	5,122	1,552	32	(2.1)	1,677	63	(3.8)	0.0044	1,893	88	(4.6)	0.1863
Idaho	4,840	1,394	45	(3.2)	1,660	84	(5.1)	0.0122	1,786	154	(8.6)	<.0001
Montana	3,824	1,162	43	(3.7)	1,312	112	(8.5)	<.0001	1,350	165	(12.2)	0.0018
Nevada[2]	5,445	1,977	51	(2.6)	2,594	151	(5.8)	<.0001	874	54	(6.2)	0.6984
New Mexico	6,025	1,771	78	(4.4)	2,012	158	(7.9)	<.0001	2,242	229	(10.2)	0.0075
Oregon	15,371	4,829	328	(6.8)	5,180	559	(10.8)	<.0001	5,362	692	(12.9)	0.0008
Utah	6,391	1,916	39	(2.0)	2,096	118	(5.6)	<.0001	2,379	207	(8.7)	<.0001
Washington	25,331	7,819	355	(4.5)	8,473	561	(6.6)	<.0001	9,039	850	(9.4)	<.0001
Wyoming	1,717	528	28	(5.3)	591	63	(10.7)	0.0011	598	62	(10.4)	0.8696

[1] Arkansas missing data for years of diagnosis 2010-2012

[2] Nevada missing data for years of diagnosis 2011-2012