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ORIGINAL ARTICLE – BREAST ONCOLOGY

Trends in Unilateral and Contralateral Prophylactic Mastectomy Use in Ductal Carcinoma In Situ of the Breast: Patterns and Predictors

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ABSTRACT

Background. Increased use of contralateral prophylactic mastectomy (CPM) as treatment for ductal carcinoma in situ (DCIS) in the US was first noted in the early 2000s. Optimization of treatment guidelines for DCIS requires an understanding of current surgical treatment trends, particularly as they may differ by patient sociodemographic and community resource factors.

Objective. The aim of this study was to evaluate surgical treatment trends among US women with DCIS and to assess the impact of sociodemographic and community resource factors on surgical treatment choice.

Methods. The Surveillance, Epidemiology, and End Results dataset was queried for women aged 40 years and older who were diagnosed with unilateral DCIS between 2000 and 2014. Annual mastectomy rates were compared over time by age and race/ethnicity. Multivariable logistic regressions were performed to identify predictors of mastectomy use, with patient sociodemographics, tumor characteristics, and community resource factors (i.e. plastic surgeon density) as covariates.

Results. A total of 130,731 women with DCIS met the inclusion criteria. Overall mastectomy rates remained relatively unchanged over the study period (25–30%). CPM use increased for all age and race/ethnic groups, with the greatest increase exhibited by women aged 40–49 years [relative to 2000; 2014 odds ratio (OR) 10.6]. With respect to community resource factors, CPM use, as opposed to unilateral mastectomy, was associated with counties of higher education level (OR 1.52), higher income level (OR 1.22), and lower plastic surgeon density (OR 1.26).

Conclusion and Relevance. While the popularity of mastectomy in the management of DCIS has remained relatively unchanged since the turn of the century, the use of CPM has risen substantially. Younger women with DCIS have seen the greatest increase in CPM use, a choice that remains influenced by race/ethnicity as well as income, education, and health resource availability. Until clinical risk stratifiers of DCIS are identified, the surgical decision-making paradigm must be improved so that treatment choice remains sensitive to cultural differences but becomes independent of income, education, and health resource availability.

Ductal carcinoma in situ (DCIS) comprises 25% of new breast cancer cases in the US, and its incidence continues to rise.[1,2] Progression to invasive cancer is uncertain, and no prognostic markers currently exist to accurately predict progression. For this reason, most DCIS lesions are treated with either breast-conserving therapy or mastectomy unless part of an active surveillance trial such as the Comparison of Operative to Monitoring and Endocrine Therapy Trial for Low Risk DCIS (COMET; NCT02926911).[3] Recent trends have shown increased use of mastectomy in the treatment of DCIS;[4] however, many of the studies evaluating treatment trends for early breast cancer have combined DCIS and invasive breast cancer. The objectives of the current study were to understand trends in the surgical management of DCIS alone and to determine the impact of health-related community factors on these trends.

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METHODS

Inclusion Criteria

We conducted a retrospective cohort analysis of all women aged 40 years or older in the Surveillance, Epidemiology, and End Results (SEER) public-use dataset who were diagnosed with unilateral DCIS between 2000 and 2014. The SEER program was established by the National Cancer Institute in 1973 to collect cancer incidence and survival data from numerous registries throughout the US. At present, the SEER publishes cancer data, including patient demographics, tumor characteristics, and treatments, from approximately 28% of the US population.[5] In this study, DCIS was defined as behavioral type carcinoma in situ [International Classification of Diseases for Oncology, Third Revision (ICD-O-3) code 2]. Institutional Review Board approval was not required for this retrospective cohort analysis.

Exclusion Criteria

Patients with ICD-O-3 codes 8520/2 (lobular carcinoma in situ), 8522/2 (intraductal and lobular carcinoma in situ), or 8720/2 (melanoma in situ) were excluded from this study. We also excluded women who did not receive DCIS-directed surgery (n = 5267, 3.1%), women whose treatment status was unknown (n = 269, 0.2%), and women for whom DCIS was not their first or only lifetime malignancy as these patients may not have been eligible for breast-conserving surgery (BCS; n = 34,608, 20.3%) (Fig. 1).

Treatment Rates

Our study evaluated treatment rates over time and by age and race/ethnic groups, at two surgical decision points: (1) mastectomy versus BCS; and (2) contralateral prophylactic mastectomy (CPM) versus unilateral mastectomy alone (in women who chose mastectomy). Women with

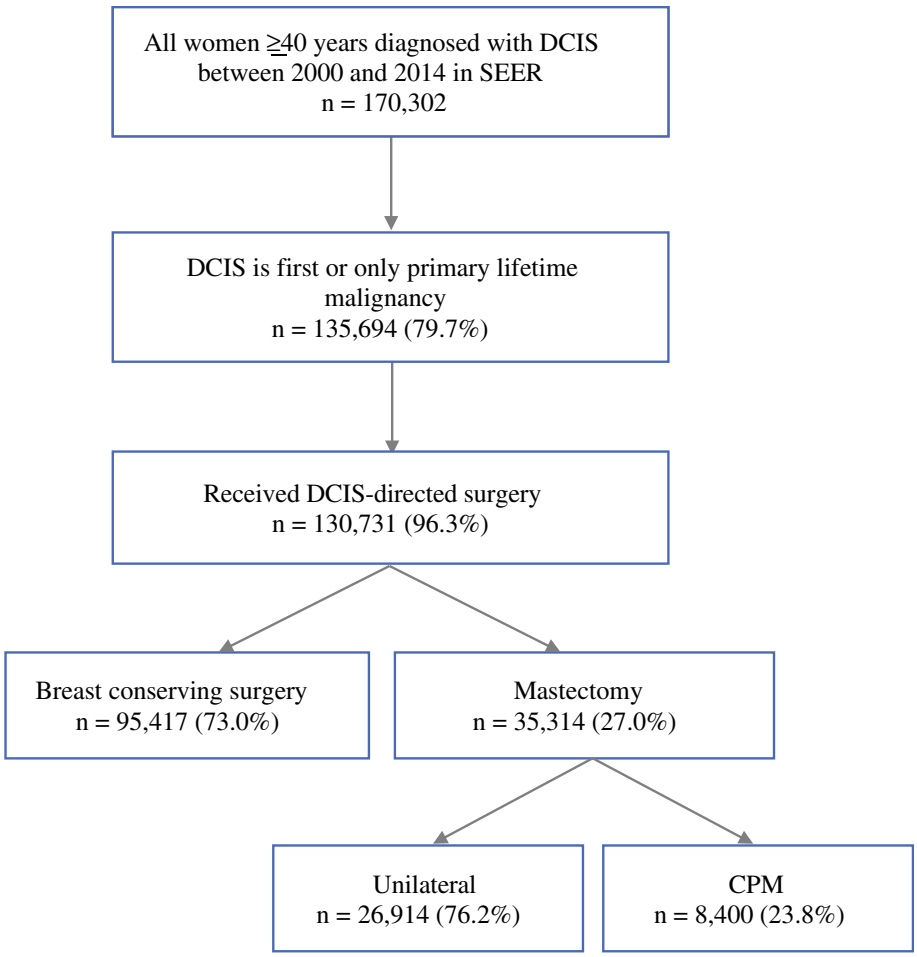


FIG. 1 Study population. *DCIS* ductal carcinoma in situ, *SEER* Surveillance, Epidemiology, and End Results, *CPM* contralateral prophylactic mastectomy

DCIS make these treatment decisions separately, therefore we performed two logistic regression analyses instead of one ordinal regression analysis.

Treatment variables were based on codes for breast-specific surgery at the primary site. BCS was defined as SEER codes for 'partial mastectomy' or 'less than total mastectomy NOS' (including lumpectomy or excisional biopsy, re-excision of the biopsy site for gross or microscopic residual disease, and segmental mastectomy). Mastectomy was defined as SEER codes for 'total (simple) mastectomy NOS', 'modified radical mastectomy', 'radical mastectomy NOS', 'extended radical mastectomy', or 'mastectomy NOS'. CPM was defined as any of the above SEER mastectomy codes plus the addition of 'with removal of uninvolved contralateral breast'.

All logistic regression analyses included analysis of age group, year of diagnosis, race/ethnicity, tumor size, tumor grade, estrogen receptor (ER) status, progesterone receptor (PR) status, health insurance status, and community factors. Age was operationalized as a categorical variable, with three levels chosen based on their clinical relevance: 40–49 years, 50–64 years, and 65 years and older. Race/ethnicity was grouped into mutually exclusive categories: non-Hispanic White (White), non-Hispanic Black (Black), Hispanic, and Asian-Pacific Islander; 2335 patients (1.11%) in this study were of other or unknown race/ethnicity. Tumor size was operationalized as a categorical variable, with levels classified as in a prior study.[6] Insurance status was categorized as a binary variable: insured versus uninsured.

Community factors were defined at the county level using information available in the Area Health Resource Files (AHRF) obtained from the National Bureau of Labor Statistics. The AHRF is a registry containing county, state, and national-level data collected from more than 50 US sources related to health care access.[7] AHRF data were linked to SEER files by the Federal Information Processing Standard county code. Specifically, we evaluated the impact of plastic surgeon density, radiation oncologist density, education level, income, and White population density on mastectomy rates relative to BCS rates. The same community factors were included in multivariable analyses regarding CPM rates relative to unilateral mastectomy rates, except for radiation oncologist density as radiation oncologists are not usually involved in this treatment decision.

Statistical Analysis

Trends in the rates of mastectomy versus BCS, and rates of CPM versus unilateral mastectomy, were assessed for the general population of all women aged 40 years and older, and then compared by age and race/ethnic group. Univariable associations between demographic or community factors and treatment choices were tested. Multivariable logistic regression analyses were performed to determine associations between treatment choices and patient age, year of diagnosis, race/ethnicity, insurance status, tumor characteristics, and community factors as covariates.

The significance level was set at alpha = 0.05. All statistical analyses were performed using STATA 13/IC (StataCorp LLC, College Station, TX, USA).

RESULTS

A total of 130,731 women with unilateral DCIS met the inclusion and exclusion criteria (Fig. 1). Table 1 details the characteristics of this study population. Overall, 27.0% of all women who received DCIS-directed surgical treatment chose mastectomy over BCS. Among those who underwent mastectomy, 23.8% also chose to have a CPM.

Trends in Mastectomy Rates Over Time

In unadjusted analysis, mastectomy rates remained relatively unchanged, i.e. between 25 and 30%, across the entire study period (Fig. 2a). After adjustment for patient demographics, tumor characteristics, and community factors, mastectomy rates were significantly lower after 2002 than before 2002. The post-2002 era exhibited an approximately 20% reduction in mastectomy rates and remained stable, except for a temporary increase in 2009–2010.

On subset analysis by age, trends after 2002 differed markedly by age group. Mastectomy rates increased significantly over time among women aged 40–49 years, but decreased over time in women aged 65 years and older (Fig. 2c). Mastectomy rates did not change over time in women aged 50–64 years.

Subset analysis by race/ethnicity revealed that all race/ethnicities exhibited trends similar to those observed in the total population, except for the Black race. Black women exhibited decreasing mastectomy rates over time (Fig. 2d).

Predictors of Mastectomy Over Breast-Conserving Surgery

On adjusted multivariable regression analysis, mastectomy was positively associated with age under 65 years [age 40–49 years: odds ratio (OR) 2.14, 95% confidence interval (CI) 2.01–2.29; age 50–64 years: OR 1.29, 95% CI 1.22–1.36], non-Hispanic ethnicity (White: OR 1.09, 95% CI 1.00–1.17; Black: OR 1.17, 95% CI 1.06–1.29; Asian-Pacific Islander: OR 1.24, 95% CI 1.13–1.37) (Table 2), and having health insurance (OR 1.30, 95% CI 1.04–1.63).

TABLE 1 Women aged ≥ 40 years diagnosed with ductal carcinoma in situ as a first or only lifetime malignancy who received surgical treatment—Surveillance, Epidemiology, and End Results 2000–2014

Total	No. of women	%
Demographic factors		
Year of diagnosis		
2000–2001	15,097	11.6
2002–2003	15,723	12.0
2004–2005	16,207	12.4
2005–2006	16,635	12.7
2007–2008	18,373	14.1
2009–2010	18,697	14.3
2011–2012	18,945	14.5
2013–2014	19,193	14.7
Age at diagnosis (year)		
40–49	29,643	22.7
50–64	56,547	43.3
≥ 65	44,541	34.1
Mean (years)		
Race/ethnicity		
White	90,782	69.8
Black	13,755	10.6
Hispanic	11,992	9.2
Asian-Pacific islander	12,852	9.9
Other	765	0.6
Tumor characteristics		
Tumor grade		
Low	15,747	16.0
Intermediate	45,670	46.3
High	37,199	37.7
Unknown	32,115	[a]
Tumor size (mm)		
≤ 15	63,382	67.3
16–40	23,720	25.2
> 40	7123	7.6
Unknown	36,506	[a]
Community factors		
Plastic surgeon density (number/100,000 individuals)		
None	9640	13.4
Lower (< 50th percentile)	19,752	27.5
Higher (> 50th percentile)	42,540	59.1
Radiation oncologist density (number/100,000 individuals)		
None	9118	12.7
Lower (< 25th percentile)	12,186	16.9
Higher (> 25th percentile)	50,628	70.4
Percentage of ≥ 25 year-olds with 4-year college degree		
Lower (< 50th percentile)	6165	4.7
Higher (> 50th percentile)	124,566	95.3
Median income		
Lower (< 25th percentile)	2467	1.9
Higher (> 25th percentile)	128,264	98.1
White population density (number/100,000 individuals)		
Lower (< 50th percentile)	72,173	83.1
Higher (> 50th percentile)	14,647	16.9

[a]Denotes exclusion from percentage calculations

Mastectomy was also positively associated with larger tumor size, higher tumor grade, and negative ER and PR status. With respect to community factors, mastectomy was associated with counties with a higher plastic surgeon density (OR 1.08, 95% CI 1.02–1.15), lower radiation oncologist density (OR 1.27, 95% CI 1.14–1.40), lower education level (OR 1.15, 95% CI 1.07–1.27), and lower income level (OR 1.28, 95% CI 1.12–1.48).

Trends in Contralateral Prophylactic Mastectomy (CPM) Rates Over Time

Among women who chose mastectomy, CPM rates increased from 11% in 2000 to 42% in 2014, representing a nearly fourfold increase throughout the study period (Fig. 3a). After adjusting for patient demographics, tumor characteristics, and community factors, this trend persisted and was even more pronounced, with an eightfold increase over the study period (2014: OR 8.3, 95% CI 6.9–9.9) (Fig. 3b).

On subset analysis by age, all age groups exhibited increases in CPM rates from the years 2000 to 2014 (Fig. 3c). The increase was largest for women aged 40–49 years (2014: OR 10.6, 95% CI 7.9–14.3).

On subset analysis by race/ethnicity, CPM rates increased over time for women of all races/ethnicities (Fig. 3d). The increase was largest for Hispanic women (2014: OR 12.1, 95% CI 4.7–31.0).

Predictors of CPM Over Unilateral Mastectomy

On multivariable regression analysis, CPM, instead of unilateral mastectomy, was positively associated with age younger than 65 years (age 40–49 years: OR 5.59, 95% CI 4.99–6.26; age 50–64 years: OR 3.19, 95% CI 2.86–3.55), White race (OR 2.50, 95% CI 2.18–2.87), and having health insurance (OR 2.32, 95% CI 1.42–3.78) (Table 2). As with the choice of mastectomy over BCS, choosing CPM instead of unilateral mastectomy was positively associated with negative ER status. However, the choice of CPM was associated with positive PR status and smaller tumor size, and there was no association between CPM and

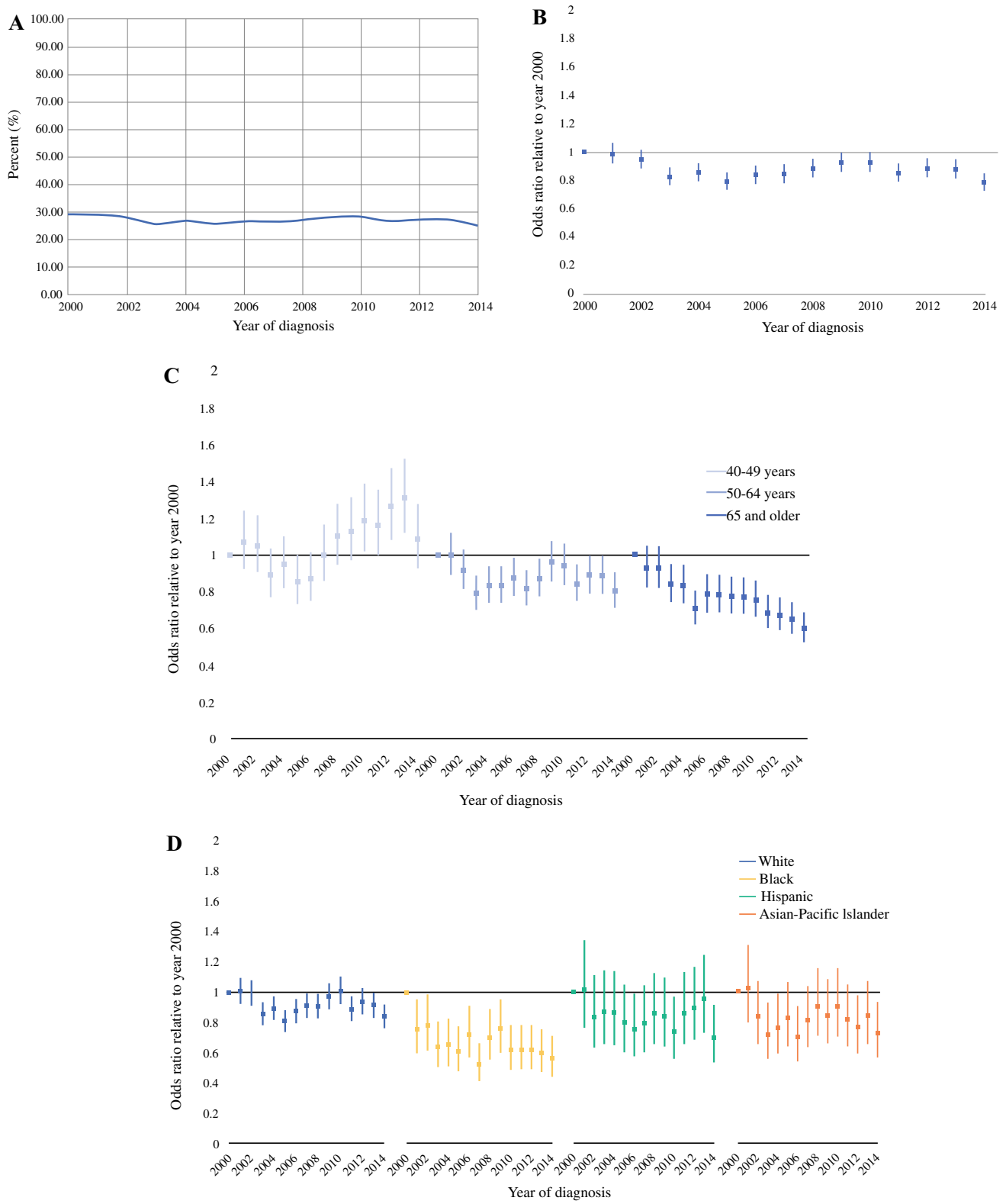


FIG. 2 Proportion of US women aged ≥ 40 years with ductal carcinoma in situ who used mastectomy as surgical treatment—Surveillance, Epidemiology, and End Results 2000–2014 (**a**); adjusted for patient demographics (age, race/ethnicity) and tumor characteristics (tumor size, grade, estrogen receptor status, progesterone receptor status), with odds ratios depicted (**b**); stratified by age with odds ratios depicted, adjusted for patient demographics and tumor characteristics (**c**); stratified by race/ethnicity with odds ratios depicted, adjusted for patient demographics and tumor characteristics (**d**)

TABLE 2 Multivariable analysis of mastectomy outcome among all women who received ductal carcinoma in situ-directed surgery, and contralateral prophylactic mastectomy outcome among all women who received mastectomy

Independent variable	Mastectomy instead of BCS		CPM instead of unilateral mastectomy	
	Odds ratio	95% CI	Odds ratio	95% CI
Demographic factors				
Age at diagnosis (years)				
40–49	2.14	2.01–2.29*	6.18	5.39–7.10*
50–64	1.29	1.22–1.36*	3.48	3.05–3.97*
≥ 65	Reference		Reference	
Race/ethnicity				
White	1.09	1.00–1.17*	2.44	2.08–2.86*
Black	1.17	1.06–1.29*	Reference	
Hispanic	Reference		1.21	0.98–1.50
Asian-Pacific islander	1.24	1.13–1.37*	0.76	0.61–0.95*
Insurance status				
Uninsured	Reference		Reference	
Insured	1.30	1.04–1.63*	2.32	1.42–3.78*
Tumor characteristics				
Tumor size				
1–15 mm	Reference		Reference	
16–40 mm	2.25	2.13–2.38*	0.84	0.75–0.94*
≥ 40 mm	6.59	6.05–7.17*	0.68	0.59–0.78*
Tumor grade				
Low	Reference		Reference	
Intermediate	1.31	1.21–1.42*	1.00	0.84–1.19
High	1.70	1.57–1.84*	0.94	0.79–1.12
ER status				
Positive	Reference		Reference	
Negative	1.18	1.08–1.28*	1.19	1.01–1.41*
Borderline	1.40	0.74–2.65	0.73	0.19–2.82
PR status				
Positive	Reference		1.25	1.08–1.45*
Negative	1.24	1.15–1.34*	Reference	
Borderline	0.74	0.44–1.24	0.46	0.10–2.14
Community factors				
Plastic surgeon density				
Lower (< 50th percentile)	Reference		1.26	1.11–1.43*
Higher (> 50th percentile)	1.08	1.02–1.15*	Reference	
Radiation oncologist density			Not included in analysis	
Lower (< 25th percentile)	1.27	1.14–1.40*		
Higher (25th percentile)	Reference			
Percentage of ≥ 25 year-olds with 4-year college degree				
Lower (< 50th percentile)	1.15	1.07–1.27*	Reference	
Higher (> 50th percentile)	Reference		1.52	1.24–1.87*

TABLE 2 continued

Independent variable	Mastectomy instead of BCS		CPM instead of unilateral mastectomy	
	Odds ratio	95% CI	Odds ratio	95% CI
Median income				
Lower (< 25th percentile)	1.28	1.12–1.48*	Reference	1.04–1.44*
Higher (> 25th percentile)	Reference		1.22	
White population density				
Lower (< 25th percentile)	Reference		Reference	
Higher (> 25th percentile)	1.04	0.99–1.10	1.02	0.92–1.12

BCS breast-conserving surgery, *CI* confidence interval, *ER* estrogen receptor, *PR* progesterone receptor, *CPM* contralateral prophylactic mastectomy

*Denotes statistical significance

tumor grade. With respect to community factors, CPM was positively associated with counties with a higher education level (OR 1.52, 95% CI 1.24–1.87), higher income level (OR 1.22, 95% CI 1.04–1.44), and lower plastic surgeon density (OR 1.26, 95% CI 1.11–1.43). This inverse relationship between CPM and plastic surgeon density was contrary to our initial hypothesis, and, as such, an additional analysis was devised to test whether the CPM patients included might have opted out of reconstruction. Additionally extracted data from the SEER dataset revealed that CPM patients have utilized reconstructive surgery, and at a higher rate than unilateral mastectomy patients (61 vs. 39%, $p < 0.01$). Among CPM patients, those living in counties of higher plastic surgeon density exhibited a higher rate of reconstructive surgery relative to those living in counties with lower plastic surgeon density (66 vs. 59%, $p < 0.01$).

DISCUSSION

The introduction of mammography screening has led to a rise in the incidence rates of DCIS in the US population.[2,8] Currently, approximately 25% of all new early breast cancer diagnoses are DCIS.[1] Analysis of treatment trends in women with DCIS alone is important as the increasing number of women diagnosed with DCIS is expected to drive treatment trends for early breast cancer. The current study evaluated trends in the surgical management of DCIS and the effects of health-related factors on surgical treatment choice.

After release of the 1991 National Institutes of Health consensus statement indicating that breast-conserving therapy is the 'preferable' treatment for early-stage breast cancer,[9] BCS has outpaced mastectomy as the most popular treatment among women with early breast cancer. This trend was observed in our study. While older studies showed lower rates of BCS among African American women,[10,11] more recent studies have shown that compared with White women, BCS rates were higher in African American women and lower in Asian-Pacific Islander women.[12] However, many of these studies included management of invasive breast cancer, as well as DCIS. Our findings in patients with DCIS alone are consistent with the results of recent studies, with higher BCS rates observed in Black women than in White women (Fig. 2d).[12]

Overall mastectomy rates remained relatively constant throughout the study period, although the rates differed substantially by patient age, race, and ethnicity. We observed clear age-related shifts over time, with younger women increasingly choosing mastectomy and older women increasingly choosing BCS during the study. The preference for BCS in older women will likely continue to increase, with recent data indicating that radiation may be omitted in women aged 70 years and older undergoing BCS.[13] In addition, data from the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) revealed that for women older than 50 years of age undergoing BCS, radiation resulted in a larger proportional reduction of an ipsilateral breast recurrence than for women younger than 50 years of age.[14]

However, for CPM, we found an overall increase in CPM rates over time, which is consistent with the results of prior studies.[4,8,15,16] There was a nearly fourfold increase in CPM rates between the years 2000 and 2014. This rise was likely driven by increased preference for CPM, rather than changes in disease presentation, such as an increase in patients with bilateral DCIS or genetic mutations.[17] Our results reflect a growing trend in favor of CPM among younger women. The decision to undergo CPM is multifactorial and may be influenced by anxiety regarding contralateral breast cancer, fear of recurrence, and impressions of improved survival with more aggressive surgery despite counseling negating these impressions.[18–20] Many considerations are non-clinical and unrelated to

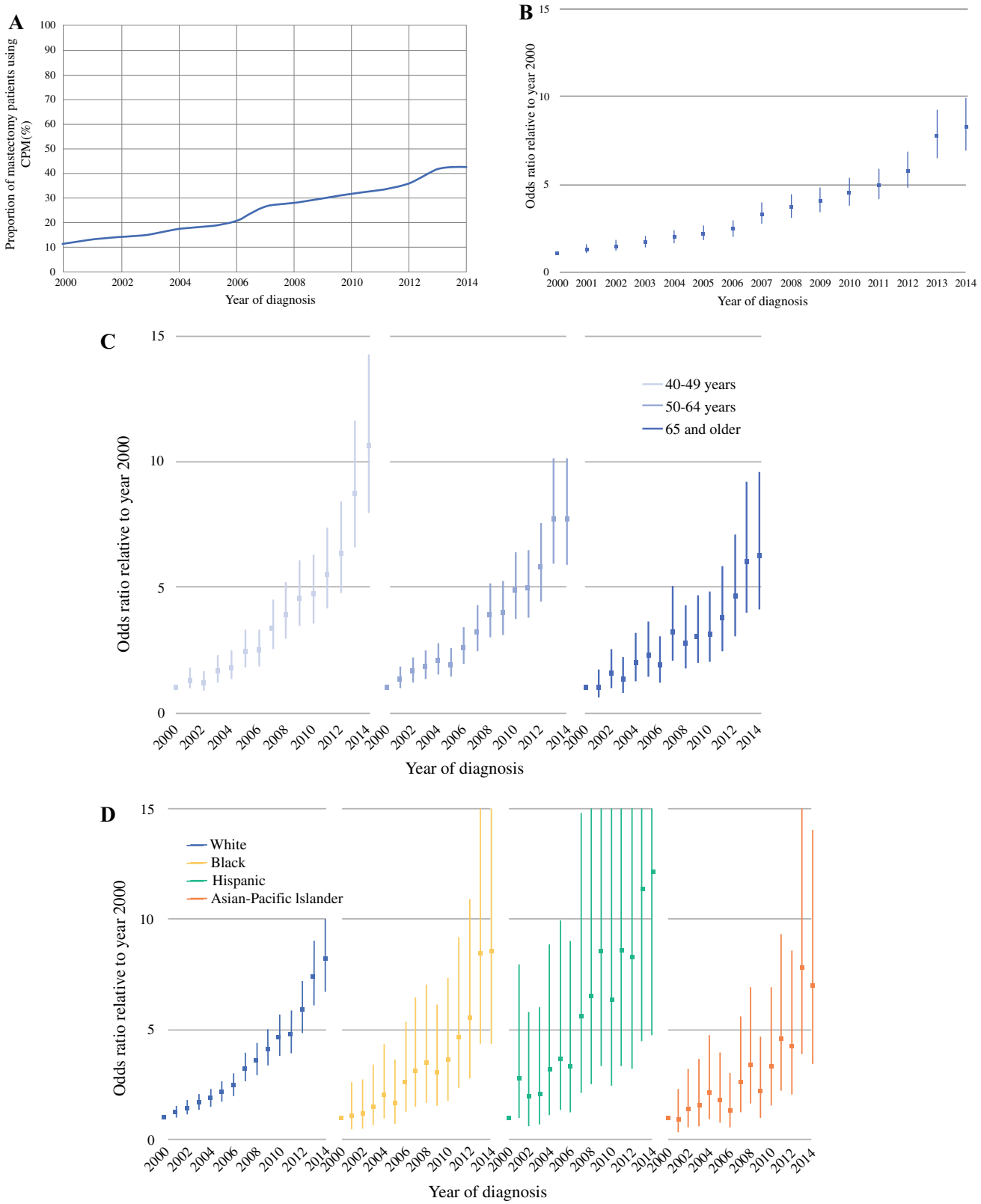
tumor characteristics or disease presentation. This is exemplified by our finding that women with larger tumors were less likely to choose CPM than those with smaller tumors. Regardless, age younger than 50 years is the most important risk factor for recurrence in women undergoing BCS.[14,21,22] This combined with the risk of having a contralateral breast cancer, an estimated 0.5–0.75% per year, may be driving the popularity of CPM in a younger demographic.[23–25] While our data do not support choosing one treatment modality over another, the disparity in treatment choice seen among younger women does raise the question of possible causes. The data forces us to consider that CPM is disfavored among lower income and non-Caucasian women. Unique to our study, we evaluated non-clinical factors that might impact care. Studies have shown that implicit bias has an impact on health care professionals, and, despite surgeons' best attempts at educating patients regarding their choices, implicit bias may influence these interactions and affect treatment choice.

Greater availability of nipple-sparing mastectomy and reconstructive options has also popularized mastectomy among younger women concerned about cosmesis. We found that mastectomy rates were associated with counties of high plastic surgeon density. Nevertheless, among younger women, there were differences in CPM rates between White and non-White women. The differences may be at least partly attributable to health insurance status as women with health insurance were more likely to choose mastectomy over BCS and to choose CPM over mastectomy. Recent changes in the US healthcare landscape with the implementation of the Affordable Care Act, which expanded coverage for younger women, may reduce race/ethnicity-related differences and influence overall trends in this age group in the future. The disparity in CPM rates according to race/ethnicity may also reflect differences in health care literacy and cultural perceptions. CPM rates were higher in counties with a higher income level, higher education level, and, unexpectedly, lower plastic surgeon density. Overall, our observations that associations exist between community factors and surgical treatment choices mirror the findings of previous studies, which have reported that patient treatment choice is influenced by the availability of reconstructive surgery.[26,27] The association between CPM and low plastic surgeon density may at first seem counterintuitive, but it may be explained by related data; our data show that CPM rates are positively associated with income and education level, which may reflect higher community health literacy. Patients' baseline knowledge of breast cancer and treatment options in high-income and high-education communities may be more important than provider availability. Despite the common perception that the public is oversaturated with information about breast cancer, the ubiquity of the topic in the mainstream media may have actually led to disinformation. There is a clear need for decision-making tools in DCIS, and investigators are currently devising aids that would be readily usable by our patient population. In lower-income communities, treatment decisions may be driven more by provider availability, as well as by referral to specialists. Race and ethnicity have been shown to directly impact whether referral or reconstruction is offered.[28]

FIG. 3 Proportion of US women aged ≥ 40 years with ductal carcinoma in situ who used CPM among all mastectomy users—Surveillance, Epidemiology, and End Results 2000–2014 (**a**); adjusted for patient demographics and tumor characteristics, with odds ratios depicted (**b**); stratified by age with odds ratios depicted, adjusted for patient demographics and tumor characteristics (**c**); stratified by race/ethnicity with odds ratios depicted, adjusted for patient demographics and tumor characteristics (**d**). *CPM* contralateral prophylactic mastectomy ▶

Collectively, our analyses reveal that surgical decision making in DCIS is multifactorial and largely due to non-clinical factors. DCIS is a non-obligatory pre-invasive breast lesion that is associated with excellent survival rates.[29] In national campaigns focused on raising awareness for breast cancer and rallying public support for the fight against cancer, this fact has been lost. As DCIS becomes a more common diagnosis among younger women, breast oncologists must rise to the challenge of helping patients understand their risk of disease progression and their high likelihood of survival.

Our study is unique in that it evaluated recent trends in the surgical management of DCIS alone and with explicit consideration of health resource factors that affect treatment outcomes. However, the study does have limitations. The SEER database is a good representation of women across the US, but it does not include all women in the country. It was not possible to determine the impact of family history and pathogenic mutations on treatment choice for our study cohort. In addition, no data were available regarding actual referrals to radiation oncologists


A
Proportion of mastectomy patients using CPM(%)
Year of diagnosis
B
Odds ratio relative to year 2000
Year of diagnosis
C
40-49 years
50-64 years
65 and older
Odds ratio relative to year 2000
Year of diagnosis
D
White
Black
Hispanic
Asian-Pacific Islander
Odds ratio relative to year 2000
Year of diagnosis

and plastic surgeons in our cohort. We were not able to assess the use of preoperative MRI, which has been shown to increase CPM rates.

CONCLUSIONS

Overall, the proportion of US women choosing mastectomy over BCS as surgical treatment for DCIS has remained relatively unchanged since the turn of the century. However, this is not true for all subgroups of US women: younger women (aged 40–49 years) have increasingly favored mastectomy and, in particular, CPM. The choice of CPM appears to be influenced by race/ethnicity and health resource factors, and may also be influenced by cultural norms, among non-Caucasian women, that make CPM a less favorable choice. Given the rising incidence of DCIS, especially among younger women, surgical treatment trends for DCIS are likely to drive trends in breast cancer treatment as a whole. Surgical decision-making paradigms must be improved so that treatment choice remains sensitive to cultural differences but becomes independent of income, education, and health resource availability.

AUTHOR'S CONTRIBUTIONS With regard to Sect. 1 of the journal guidelines, the authors made significant contributions in the following areas: Biqi Zhang, BS: (1) Study conception and design, data acquisition, data interpretation/analysis; (2) drafting the article and revising it critically for important intellectual content; and (3) gave final approval of the version to be published. Suzanne B. Coopey, MD: (1) Data interpretation/analysis; (2) revising the article critically for important intellectual content; and (3) gave final approval of the version to be published. Michele A. Gadd, MD: (1) Data interpretation/analysis; (2) revising the article critically for important intellectual content; and (3) gave final approval of the version to be published. Kevin S. Hughes, MD: (1) Data interpretation/analysis; (2) revising the article critically for important intellectual content; and (3) gave final approval of the version to be published. David C. Chang, PhD, MPH, MBA: (1) Study conception and design, data acquisition, data interpretation/analysis;(2) drafting the article and revising it critically for important intellectual content; and (3) gave final approval of the version to be published. Tawakalitu O. Oseni, MD: (1) Study conception and design, data interpretation/analysis; (2) drafting the article and revising it critically for important intellectual content; and (3) gave final approval of the version to be published.

DISCLOSURES Biqi Zhang, Suzanne B. Coopey, Michele A. Gadd, Kevin S. Hughes, David C. Chang, and Tawakalitu O. Oseni have no conflicts of interest to declare.

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