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ORIGINAL ARTICLE – BREAST ONCOLOGY

National Patterns of Breast Reconstruction and Nipple-Sparing Mastectomy for Breast Cancer, 2005–2015

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ABSTRACT

Background. The purpose of this study was to explore national patterns in the uptake of breast reconstruction and nipple-sparing mastectomy (NSM).

Methods. We used the National Cancer Database to identify all women who underwent mastectomy for stage 0–III breast cancer between 2005–2015. Multivariable logistic regression was used to determine factors associated with receipt of reconstruction, with subset analyses performed to determine trends and predictors of NSM in those who underwent mastectomy with reconstruction.

Results. Our cohort consisted of 395,815 women, 238,568 (60.3%) who underwent mastectomy alone and 157,247 (39.7%) who underwent mastectomy followed by reconstruction. The use of breast reconstruction increased from 22.3% of mastectomy cases in 2005 to 49.7% of mastectomy cases in 2015 (odds ratio [OR] 9.7, 95% confidence interval [CI] 7.3–12.8). Among those receiving reconstruction, the use of NSM increased from 1.7% in 2005 to 14.3% in 2015 (OR 9.4, 95% CI 7.1–12.5), with increased utilization among those with early-stage and locally advanced disease, such that by 2015, NSM was performed in 15.3% of mastectomies with reconstruction for DCIS, 14.3% of mastectomies with reconstruction for stage I–II breast cancer, and 10.7% of mastectomies with reconstruction for stage III breast cancer. Factors strongly predicting receipt of NSM included age < 45 years, smaller clinical tumor size, clinically node negative disease, use of neoadjuvant therapy, and facility type.

Conclusions. There has been a dramatic increase in the use of breast reconstruction and NSM between 2005–2015. Further prospective studies evaluating oncologic outcomes of NSM in locally advanced breast cancer are warranted.

Nipple-sparing mastectomy (NSM), a procedure that preserves the nipple-areola complex and skin envelope, is associated with superior cosmetic outcomes and enhanced psychosocial and sexual wellbeing in appropriate candidates and has thus become increasingly attractive to both patients and providers.[1–3] While early guidelines did not endorse the use of NSM outside of a clinical trial, single and multi-institution series have since demonstrated low rates of nipple involvement and comparable local recurrence rates relative to those undergoing skin-sparing mastectomy.[4–9] Based on these studies' findings, the 2015 *National Comprehensive Cancer Network* (NCCN) guidelines evolved to allow the use of NSM in select patients with early stage, biologically favorable, node-negative disease.[10]

As the indications for NSM have continued to expand, several proponents of the procedure have begun to offer NSM to patients with large tumors or locally advanced disease who demonstrate a good response to neoadjuvant chemotherapy.[11,12] A recent 2018 international consensus

This study will be presented as a quickshot oral presentation at the 2019 American Society of Breast Surgeons Annual Meeting, May 2019, Dallas, TX.

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panel of oncoplastic surgeons challenged the notion that tumor size larger than 3 cm and nodal positivity should preclude nipple preservation, whereas in locally advanced breast cancers not treated with neoadjuvant chemotherapy, performing NSM remained controversial.[13] Based on the available retrospective evidence, the most recent 2019 NCCN guidelines state that NSM may be considered for in situ, early-stage, or locally advanced cancers in patients with small-to-moderate breast volume and minimal to moderate ptosis, provided the nipple margin is pathologically assessed.[14] Current contraindications to NSM include evidence of Paget's disease, nipple discharge associated with malignancy, and/or imaging findings suggesting malignant involvement of the nipple or subareolar tissue.[14]

With reconstruction more commonly utilized and NSM now being widely adopted into clinical practice, it has become relevant to obtain an accurate understanding of current use and applied indications for the procedure.[15,16] To achieve this, we used the National Cancer Database (NCDB) to explore population-based trends in the uptake of breast reconstruction and NSM and examined the clinical and demographic factors associated with their use.

METHODS

Data Source and Cohort Ascertainment

The NCDB, a joint initiative between the American College of Surgeons Commission on Cancer and the American Cancer Society, is a nationwide oncology registry that captures approximately 70% of incident cancer cases diagnosed within the United States. From it, we identified all women with a histologically confirmed, first diagnosis of clinical stage 0–III breast cancer who were treated with mastectomy between 2005 and 2015 (Fig. 1). Patients were excluded if they had nonductal or nonlobular histology, Paget's disease, or lobular carcinoma in situ. Our final analytic cohort included 395,815 women who underwent total (simple or skin-sparing) mastectomy, subcutaneous (nipple-sparing) mastectomy, or modified radical mastectomy, with or without reconstruction between 2005 and 2015. Because the study used de-identified data, the protocol was considered exempt by the Brigham and Women's Hospital's Institutional Review Board.

Outcomes of Interest

Our primary outcome of interest was the receipt of reconstruction in patients undergoing mastectomy. In the NCDB, no distinction is made between reconstruction performed immediately (single stage) or in a delayed fashion, as long as reconstruction is planned as part of the first course of therapy. A secondary outcome of interest was the use of NSM, which is coded as "subcutaneous mastectomy." Per NCDB coding rules, subcutaneous mastectomy involves removal of breast tissue without the nipple and areolar complex or overlying skin and considers all such cases as having been performed to facilitate immediate breast reconstruction but does not specify the type of reconstruction or if a contralateral prophylactic mastectomy is performed. Therefore, all cases of NSM were classified in this analysis as having undergone breast reconstruction not otherwise specified.

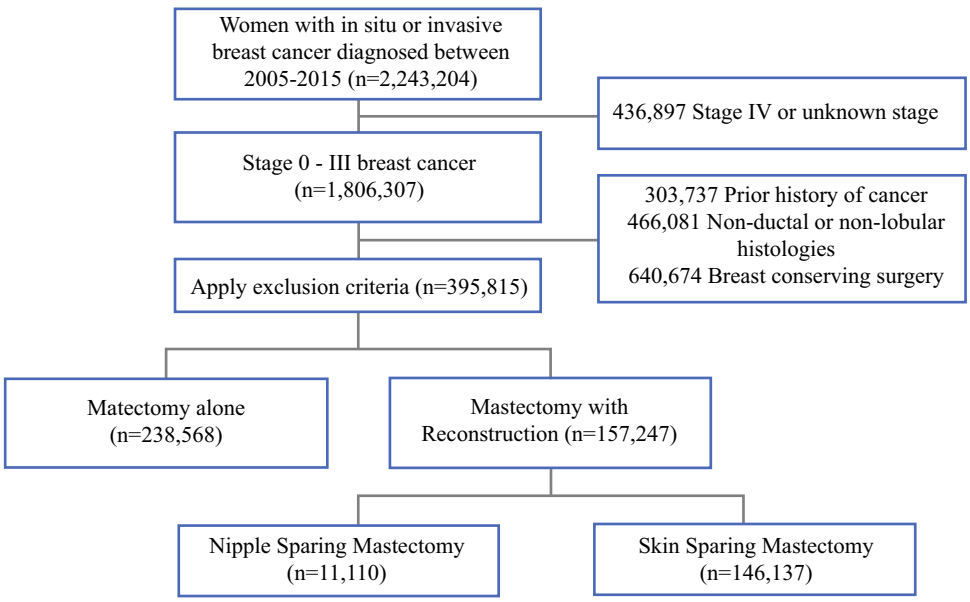

FIG. 1 Cohort selection

Statistical Analysis

We analyzed demographic and clinicopathologic differences across groups using Pearson's Chi-squared test for categorical data, and Student's *t* test for continuous variables. To evaluate unadjusted rates of NSM over time, we calculated the annual proportion of reconstructed patients undergoing NSM for each year between 2005 and 2015 and compared them using the Cochrane–Armitage test for trend. Multivariable logistic regression was then used to determine factors associated with receipt of reconstruction, with subset analyses then performed to determine trends and predictors of NSM in those who underwent reconstruction. To account for temporal trends, year of diagnosis was included as an ordinal variable in the multivariable model. All statistical analyses were performed using SAS version 9.4 (Cary, NJ), with p values < 0.05 used to indicate statistical significance.

RESULTS

Factors Associated with Receipt of Breast Reconstruction

Our cohort consisted of 395,815 women, of whom 238,568 (60.3%) underwent mastectomy alone and 157,247 (39.7%) underwent mastectomy followed by reconstruction. Patient demographic and tumor characteristics according to receipt of reconstruction are shown in Supplemental Table 1. Women undergoing mastectomy with reconstruction were younger, with a mean age at diagnosis of 50.8 years, compared with a mean age of 61.6 years in those undergoing mastectomy alone ($p < 0.001$). On multivariable analysis, those younger than age 45 years at diagnosis were more than twofold likely to undergo breast reconstruction relative to those diagnosed between ages 55–64 years (odds ratio [OR] 2.48, 95% confidence interval [CI] 2.41–2.54). After adjusting for year of treatment, other demographic factors strongly associated with receipt of reconstruction in those undergoing mastectomy included Caucasian race, private insurance, higher income, and treatment at academic/research and integrated network cancer centers (Table 1).

Trends in Reconstruction and Nipple-Sparing Mastectomy

Rates of reconstruction increased from 22.3% of mastectomy cases in 2005 to 49.7% of mastectomy cases in 2015 (Fig. 2a, adjusted OR 9.7, 95% CI 7.3–12.8). Among the 157,247 patients receiving reconstruction during the study period, 11,110 (7.1%) underwent NSM. The use of NSM increased from 1.7% of reconstructive cases in 2005 to 14.3% in 2015 (Fig. 2b, OR 9.6, 95% CI 7.3–12.7). Rising rates of NSM were seen across different age groups, with the largest increase seen in those youngest at diagnosis (Fig. 3a). A trend towards increasing use of NSM was seen across all facility types, with highest rates noted in academic/research centers (Fig. 3b).

Nipple-sparing mastectomy was increasingly employed in both early stage breast cancer and locally advanced disease such that from 2005 to 2015, the use of NSM increased from 1.6 to 15.3% of mastectomies with reconstruction for ductal carcinoma in situ (DCIS) ($p < 0.001$), from 1.6 to 14.3% of mastectomies with reconstruction for stage I–II breast cancer ($p < 0.001$), and from 1.1 to 10.7% of mastectomies with reconstruction for stage III breast cancer ($p < 0.001$; Fig. 3c). Receipt of neoadjuvant chemotherapy was associated with higher rates of NSM in those with larger tumors (Fig. 3d) and clinically node-positive disease.

Factors Associated with Receipt of Nipple-Sparing Mastectomy

In adjusted analyses, demographic factors predicting receipt of NSM for those undergoing reconstruction included young age < 45 years at diagnosis (OR 1.16, 95% CI 1.09–1.24), Asian race (OR 1.46, 95% CI 1.29–1.64), and surgery at an academic/research facility (OR 1.95, 95% CI 1.73–2.20; Table 2). Significant geographic variation and temporal trends also were noted, such that when compared with those treated in 2005, patients treated in 2015 were nearly tenfold more likely to receive NSM (OR 9.39, 95% CI 7.07–12.48).

Relative to tumors less than 2 cm and node-negative patients, those with larger tumors (cT3–T4; OR 0.64, 95% CI 0.58–0.71) and clinically node-positive disease (cN1; OR 0.73, 95% CI 0.73–0.68) were less likely to undergo NSM. In contrast, the use of neoadjuvant therapy was associated with a 27–52% increase in the NSM receipt, with increased NSM utilization based on degree of in-breast treatment response (stable disease/no response; OR 1.27, 95% CI 1.16–1.40; partial/complete response; OR 1.52, 95% CI 1.38–1.67). Subgroup analysis restricted to women with locally advanced disease revealed increased NSM receipt in cases of partial or complete in-breast response to therapy (OR 1.63, 95% CI 1.25–2.13), whereas stage III women with stable disease or a lack of response to neoadjuvant treatment saw no increase in NSM receipt (OR 1.08, 95% CI 0.77–1.51).

TABLE 1 Regression analyses of factors associated with receipt of reconstruction in women undergoing mastectomy (n = 395,815)

Characteristic	OR_{RECON}	95% CI	p value
Age group (year)			< 0.001
< 45	**2.48**	**(2.41–2.55)**	
45–55	**1.82**	**(1.78–1.85)**	
55–65	Ref		
65+	**0.38**	**(0.36–0.39)**	
Race			< 0.001
Caucasian	Ref		
Black	**0.79**	**(0.77–0.81)**	
Asian	**0.48**	**(0.45–0.50)**	
Hispanic	**0.90**	**(0.88–0.93)**	
Other	**0.61**	**(0.58–0.63)**	
Insurance status			< 0.001
Not insured	Ref		
Private insurance	**3.36**	**(3.18–3.55)**	
Medicaid	**1.59**	**(1.50–1.69)**	
Medicare	**1.79**	**(1.69–1.90)**	
Other government	**2.77**	**(2.54–3.02)**	
Income			< 0.001
Less than $38,000	Ref		
$38,000–$47,999	**1.17**	**(1.14–1.20)**	
$48,000–$62,999	**1.44**	**(1.40–1.48)**	
$63,000 +	**2.16**	**(2.11–2.21)**	
Facility type			< 0.001
Community cancer center	Ref		
Comprehensive community cancer center	**1.80**	**(1.74–1.86)**	
Academic/research center	**2.41**	**(2.33–2.78)**	
Integrated network cancer center	**2.68**	**(2.58–2.78)**	
Region			< 0.001
New England	Ref		
Middle Atlantic	**1.17**	**(1.12–1.22)**	
South Atlantic	1.03	(0.99–1.07)	
East North Central	**0.92**	**(0.88–0.96)**	
East South Central	**0.78**	**(0.75–0.82)**	
West North Central	**1.06**	**(1.01–1.10)**	
West South Central	**0.82**	**(0.79–0.86)**	
Mountain	**1.09**	**(1.04–1.15)**	
Pacific	**0.73**	**(0.70–0.76)**	
Charlson–Deyo comorbidity score			< 0.001
0	Ref		
1	**0.82**	**(0.80–0.84)**	
2+	**0.53**	**(0.50–0.56)**	
Histology			< 0.001
DCIS	Ref		
Invasive ductal carcinoma	1.01	(0.94–1.09)	
Invasive lobular carcinoma	**1.15**	**(1.11–1.18)**	
Grade			< 0.001
Low/grade I	Ref		
Intermediate/grade II	**0.98**	**(0.95–1.00)**	
High/grade III	**0.92**	**(0.90–0.94)**	

TABLE 1 continued

Characteristic	OR_{RECON}	95% CI	*p* value
Clinical tumor size			< 0.001
cT0	**1.30**	**(1.25–1.35)**	
cT1	Ref		
cT2	**0.84**	**(0.83–0.86)**	
cT3–4	**0.55**	**(0.53–0.56)**	
Hormone receptor			< 0.001
Positive	Ref		
Negative	**0.86**	**(0.84–0.88)**	
Clinical node status			< 0.001
cN0	Ref		
cN1	**0.80**	**(0.78–0.82)**	
cN2–N3	**0.61**	**(0.59–0.64)**	
Neoadjuvant systemic therapy			< 0.001
Not received	Ref		
Received	**1.04**	**(1.01–1.07)**	
Year of diagnosis			< 0.001
2005	Ref		
2006	1.04	(0.73–1.50)	
2007	0.74	(0.51–1.06)	
2008	0.70	(0.50–0.98)	
2009	1.01	(0.75–1.38)	
2010	**1.78**	**(1.33–2.38)**	
2011	**2.68**	**(2.02–3.57)**	
2012	**4.02**	**(3.03–5.32)**	
2013	**5.54**	**(4.19–7.32)**	
2014	**7.94**	**(6.02–10.5)**	
2015	**9.67**	**(7.32–12.8)**	

Bold values indicate statistical significance ($p < 0.05$)

DISCUSSION

In this large, population-based cohort of women undergoing mastectomy for DCIS or invasive breast cancer in the NCDB, we found a significant rise in the use of breast reconstruction between 2005 and 2015, which increased to half of patients treated with mastectomy in 2015. In those who received reconstruction, we also observed a significant rise in the utilization of NSM, which represented only 1.7% of all reconstruction cases in 2005 and increased to 14.3% by 2015. The curve demonstrating NSM as a percentage of all mastectomies with reconstruction began to rise more sharply in 2009 and, as of 2015, showed no signs of a plateau. After controlling for temporal trends, we found that demographic and socioeconomic factors, such as age, insurance status, and income, were strongly associated with receipt of breast reconstruction, whereas clinical and treatment-related variables tended to predict receipt of NSM. The use of NSM increased across all age groups and facility types, with highest utilization among patients with in situ or early-stage disease. Interestingly, there also was a growing trend towards application of NSM in those with large tumors and node-positive disease, particularly in patients who underwent neoadjuvant systemic therapy, despite a lack of evidence for safe oncologic outcomes in this group.

Our findings that women younger than 45 years of age are nearly 2.5-fold more likely to undergo reconstruction and, if receiving reconstruction, are 16% more likely to undergo a nipple-sparing procedure compared with those between 55–64 years of age are consistent with prior studies that examined the effect of age at diagnosis on surgical choice.[17–19] In a claims-based cohort of 20,560 women with employment-derived insurance undergoing mastectomy for breast cancer between 1998 and 2008, Jagsi et al. reported receipt of breast reconstruction in 76% of women younger than 40 compared with 67%, 48%, and 33% in women in their forties, fifties, or older than 60 years of age, respectively.[17] Similar age-based trends were seen in a cohort of 1866 women receiving

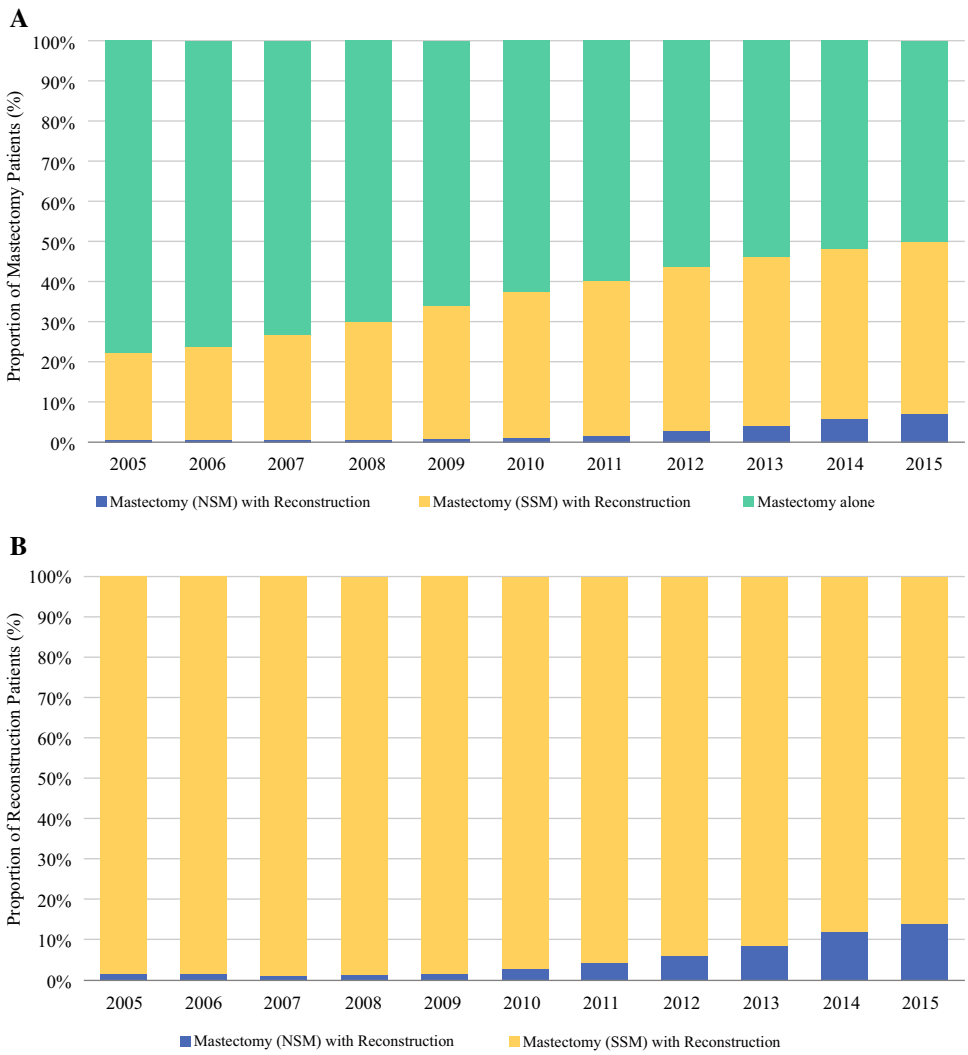

FIG. 2 **a** Trends in all mastectomy patients with and without reconstruction. **b** Trends in mastectomy patients undergoing reconstruction. *NSM* nipple-sparing mastectomy, *SSM* skin-sparing mastectomy

mastectomy and reconstruction at Memorial Sloan Kettering Cancer Center, where Romanoff et al. reported that patients undergoing NSM were on average 4 years younger than those receiving skin-sparing mastectomy ($p < 0.001$).[19]

Our data add to a growing body of literature suggesting significant racial and socioeconomic disparities exist and result in variable access to breast reconstruction.[20–23] In our study, patients of Hispanic, black, and Asian origin were 10%, 21%, and 52% less likely to receive reconstruction compared with Caucasians. In examining socioeconomic status compared with those in the lowest income brackets, those at higher levels of income—more than $63,000 per year—were 2.2-fold more likely to undergo reconstruction, whereas those with private insurance were 3.4-fold more likely to undergo breast reconstruction compared with uninsured individuals. In patients receiving Medicaid and Medicare, the odds of breast reconstruction were 1.6-fold (95% 1.50–1.69) and 1.8-fold (95% CI 1.69–1.90) higher than those who were uninsured, albeit still lower than patients with private insurance, as has been noted in other studies.[21] The association between lower rates of breast reconstruction and lower income has been documented in other countries, including France, as well as in countries with universal coverage of reconstructive procedures, such as Canada and Denmark.[24,25]

Importantly, the racial and socioeconomic disparities present amongst women undergoing mastectomy with and without reconstruction were attenuated when examining factors associated with receipt of NSM. This suggests that once patients have access to breast reconstruction, the decision to preserve the nipple or not instead depends largely on clinical factors. In the group of women undergoing reconstruction, factors most strongly predicting receipt of NSM (after controlling for year of treatment) included smaller clinical tumor size, nodal status, use of neoadjuvant chemotherapy, facility type, and region.

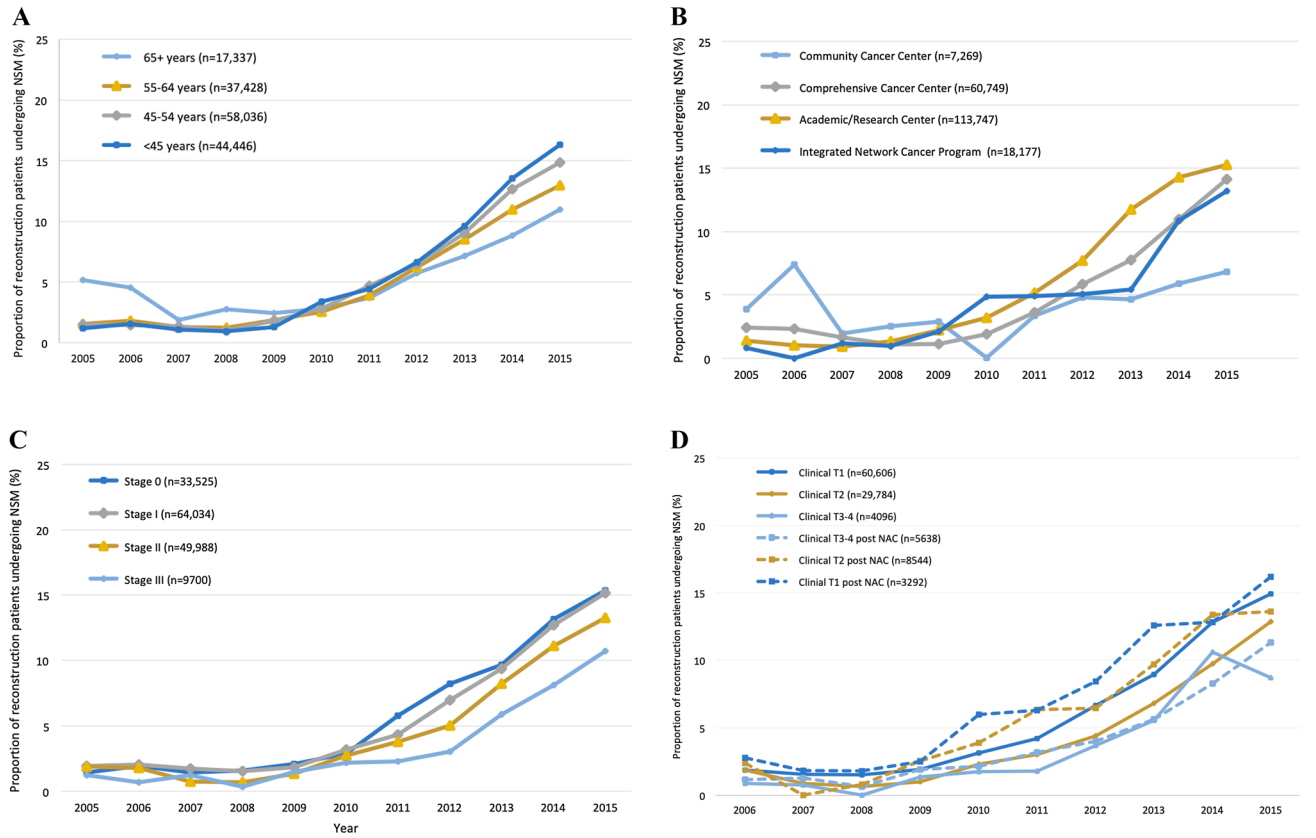

FIG. 3 Trends in nipple-sparing mastectomy stratified by **a** age, **b** treatment facility type, **c** clinical stage, **d** tumor size in those undergoing upfront surgery or neoadjuvant chemotherapy. *NAC* neoadjuvant chemotherapy, *NSM* nipple-sparing mastectomy

Women with tumors between 2–5 cm and > 5 cm were 18% and 35% less likely to undergo NSM, whereas women with clinically node-positive disease were 27–43% less likely to undergo the procedure. These trends likely reflect guideline-concordant care, as the NCCN clinical practice guidelines at the time of study recommended NSM be selectively adopted for women with early-stage, node-negative disease who have the lowest risk for occult nipple involvement.[10,26]

The rising rates of NSM that we report across all age groups, facility types, and clinical stages are presumably the result of both expanding indications for the procedure, as well as gradual adoption of the technique across the larger community of breast surgeons in the United States.[11,12,27–29] In an early analysis from the *Surveillance, Epidemiology and End Results* database, Agarwal et al. found that between 2005 and 2009, the absolute number of patients undergoing NSM for tumors larger than 2 cm increased substantially, and more than 10% of patients had one or more involved nodes on final pathology.[30] Similarly, Sisco et al. examined trends of NSM in the NCDB between 2010 and 2013 and reported that 23% of all NSM patients had tumors larger than 2 cm, whereas 10% of patients had clinically node-positive disease.[16] Our findings further extend these results, with 31.3% and 12.5% of NSM patient treated in 2015 reported as having clinical T2–T4 tumors or clinically node-positive disease respectively. Because NSM is increasingly performed for more advanced T and N stages, it is reassuring that prior studies have demonstrated no delay in initiation of chemotherapy or postmastectomy radiation therapy following NSM.[31]

The use of NSM in patients who have received neoadjuvant chemotherapy is an area of growing interest. One series from the Mayo Clinic reported an 8% to 21% increase in the proportion of NSM patients treated with preoperative systemic therapy over the 5 years of study.[28] Leveraging response to preoperative therapy to downstage locally advanced disease and optimize candidacy for NSM has been the focus of several recent studies; single-institution retrospective studies reported comparable complication and locoregional recurrence rates between nipple-sparing and skin-sparing mastectomy patients in this high-risk group.[11,12] In our analysis, in-breast response to neoadjuvant therapy—defined as a 50% or greater reduction between clinical and pathologic tumor size—was associated with a 52% increase in NSM receipt in all patients. Interestingly, receipt of NSM was still 27% higher in those undergoing neoadjuvant treatment without response compared with

TABLE 2 Regression analyses of factors associated with receipt of nipple-sparing mastectomy relative to skin-sparing mastectomy in those undergoing mastectomy with reconstruction (n = 157,247)

Characteristic	OR_{NSM}	95% CI	p value
Age group (year)			< 0.001
< 45	**1.16**	**(1.09–1.24)**	
45–55	**1.09**	**(1.04–1.15)**	
55–65	Ref		
65–75	**0.84**	**(0.76–0.94)**	
75+	**1.23**	**(1.01–1.49)**	
Race			< 0.001
Caucasian	Ref		
Black	0.96	(0.89–1.03)	
Asian	**1.46**	**(1.29–1.64)**	
Hispanic	**1.12**	**(1.03–1.20)**	
Other	1.03	(0.93–1.14)	
Insurance status			< 0.001
Not insured	Ref		
Private insurance	1.01	(0.84–1.22)	
Medicaid	0.91	(0.74–1.11)	
Medicare	1.02	(0.83–1.26)	
Other government	1.26	(0.99–1.60)	
Income			0.23
Less than $38,000	Ref		
$38,000–$47,999	1.08	(1.00–1.18)	
$48,000–$62,999	1.05	(0.97–1.14)	
$63,000 +	1.08	(1.00–1.17)	
Facility type			< 0.001
Community cancer center	Ref		
Comprehensive community cancer center	**1.42**	**(1.26–1.60)**	
Academic/research center	**1.95**	**(1.73–2.20)**	
Integrated network cancer center	**1.49**	**(1.31–1.70)**	
Region			< 0.001
New England	Ref		
Middle Atlantic	**1.13**	**(1.01–1.27)**	
South Atlantic	**1.54**	**(1.38–1.71)**	
East North Central	**0.87**	**(0.77–0.97)**	
East South Central	**0.38**	**(0.31–0.45)**	
West North Central	**1.37**	**(1.21–1.55)**	
West South Central	**1.09**	**(0.96–1.24)**	
Mountain	**1.21**	**(1.05–1.39)**	
Pacific	**2.06**	**(1.83–2.31)**	
Charlson–Deyo comorbidity score			< 0.001
0	Ref		
1	**0.81**	**(0.75–0.87)**	
2+	**0.78**	**(0.64–0.95)**	
Histology			0.007
Ductal carcinoma	Ref		
Lobular carcinoma	**1.06**	**(0.96–1.18)**	
Mixed invasive ductal/lobular carcinoma	**0.92**	**(0.85–0.99)**	
Grade			0.001
Low/grade I	Ref		
Intermediate/grade II	**0.92**	**(0.87–0.98)**	
High/grade III	**0.93**	**(0.87–0.99)**	

TABLE 2 continued

Characteristic	OR_{NSM}	95% CI	*p* value
Clinical tumor size			< 0.001
cT0	0.95	(0.86–1.04)	
cT1	Ref		
cT2	**0.82**	**(0.78–0.86)**	
cT3–T4	**0.65**	**(0.58–0.72)**	
Hormone receptor			< 0.001
Positive	Ref		
Negative	**0.85**	**(0.80–0.91)**	
Clinical node status			< 0.001
cN0	Ref		
cN1	**0.73**	**(0.68–0.78)**	
cN2–N3	**0.57**	**(0.48–0.68)**	
Neoadjuvant systemic therapy (NST)			< 0.001
Not received	Ref		
NST with stable disease/minimal response	**1.27**	**(1.16–1.40)**	
NST with partial/complete response	**1.52**	**(1.38–1.67)**	
Year of diagnosis			< 0.001
2005	Ref		
2006	1.09	(0.75–1.57)	
2007	0.73	(0.51–1.07)	
2008	0.71	(0.51–1.00)	
2009	1.02	(0.74–1.39)	
2010	**1.73**	**(1.28–2.33)**	
2011	**2.56**	**(1.91–3.43)**	
2012	**3.83**	**(2.87–5.11)**	
2013	**5.25**	**(3.94–6.98)**	
2014	**7.59**	**(5.71–10.10)**	
2015	**9.39**	**(7.07–12.48)**	

Bold values indicate statistical significance ($p < 0.05$)

those undergoing upfront surgery. In stage III women treated with mastectomy in 2015, NSM was used in 11.6% of patients who underwent neoadjuvant systemic therapy, compared with only 7.9% of patients who underwent upfront surgery. Multivariable analyses in this subset of patients revealed that partial or complete response to neoadjuvant treatment increased the likelihood of NSM by 63%, whereas stable disease/minimal response in the breast resulted in no such increase. Together, these data suggest that overall, centers more likely to recommend neoadjuvant treatment also may be more likely to offer NSM, whereas in locally advanced cases, response to neoadjuvant therapy is strongly associated with NSM receipt.

Limitations of this study include the absence of information on tumor-to-nipple distance, multicentricity, and other factors that affect candidacy for NSM, including breast size, degree of ptosis, history of smoking, and body mass index, all of which may explain some of the racial, socioeconomic, and age-related differences in our findings. As with all large database studies, this analysis was subject to coding and misclassification error, particularly with respect to the accurate identification of patients undergoing NSM, which may be underreported in the NCDB. Finally, we lacked details on type, laterality, or timing of breast reconstruction and did not have information on cases performed for prophylaxis, limiting our ability to explore global trends in breast reconstruction for women treated with breast cancer or undergoing surgery for risk reduction.

Despite the stated limitations, this study demonstrates the increased utilization of both breast reconstruction and NSM in women undergoing surgery for DCIS or invasive breast cancer. While efforts to minimize variations in patterns of care and standardize selection criteria for NSM are underway, further prospective studies that serve to evaluate oncologic outcomes of NSM in locally advanced breast cancer and following neoadjuvant treatment are warranted.

DISCLOSURE The authors have no relevant conflict of interest to disclose.

REFERENCES

1. Didier F, Radice D, Gandini S, et al. Does nipple preservation in mastectomy improve satisfaction with cosmetic results, psychological adjustment, body image and sexuality? *Breast Cancer Res Treat*. 2009;118:623–33.
2. Satteson ES, Brown BJ, Nahabedian MY. Nipple-areolar complex reconstruction and patient satisfaction: a systematic review and meta-analysis. *Gland Surg*. 2017;6:4–13.
3. Wei CH, Scott AM, Price AN, et al. Psychosocial and sexual well-being following nipple-sparing mastectomy and reconstruction. *Breast J*. 2016;22:10–7.
4. Hartmann LC, Schaid DJ, Woods JE, et al: Efficacy of bilateral prophylactic mastectomy in women with a family history of breast cancer. *N Engl J Med*. 1999;340:77–84.
5. Jakub JW, Peled AW, Gray RJ, et al. Oncologic safety of prophylactic nipple-sparing mastectomy in a population with BRCA mutations: a multi-institutional study. *JAMA Surg*. 2018;153:123–9.
6. Mitchell SD, Willey SC, Beitsch P, et al. Evidence based outcomes of the American Society of Breast Surgeons Nipple Sparing Mastectomy Registry. *Gland Surg*. 2018;7:247–57.
7. Petit JY, Veronesi U, Rey P, et al. Nipple-sparing mastectomy: risk of nipple-areolar recurrences in a series of 579 cases. *Breast Cancer Res Treat*. 2009;114:97–101.
8. Smith BL, Tang R, Rai U, et al. Oncologic safety of nipple-sparing mastectomy in women with breast cancer. *J Am Coll Surg*. 2017;225:361–5.
9. Yao K, Liederbach E, Tang R, et al. Nipple-sparing mastectomy in BRCA1/2 mutation carriers: an interim analysis and review of the literature. *Ann Surg Oncol*. 2015;22:370–6.
10. Gradishar WJ, Anderson BO, Balassanian R, et al. Breast Cancer Version 2.2015. *J Natl Compr Canc Netw*. 2015;13:448–75.
11. Burdge EC, Yuen J, Hardee M, et al. Nipple skin-sparing mastectomy is feasible for advanced disease. *Ann Surg Oncol*. 2013;20:3294–302.
12. Peled AW, Wang F, Foster RD, et al. Expanding the indications for total skin-sparing mastectomy: is it safe for patients with locally advanced disease? *Ann Surg Oncol*. 2016;23:87–91.
13. Weber WP, Haug M, Kurzeder C, et al. Oncoplastic Breast Consortium consensus conference on nipple-sparing mastectomy. *Breast Cancer Res Treat*. 2018;172:523–37.
14. NCCN Guidelines Version 3.2018 Breast cancer. Published October 25, 2018. Accessed 11 Nov 2018. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.
15. Jonczyk MM, Jean J, Graham R, et al. Surgical trends in breast cancer: a rise in novel operative treatment options over a 12-year analysis. *Breast Cancer Res Treat*. 2019;173:267–74.
16. Sisco M, Kyrillos AM, Lapin BR, et al. Trends and variation in the use of nipple-sparing mastectomy for breast cancer in the United States. *Breast Cancer Res Treat*. 2016;160:111–20.
17. Jagsi R, Jiang J, Momoh AO, et al. Trends and variation in use of breast reconstruction in patients with breast cancer undergoing mastectomy in the United States. *J Clin Oncol*. 2014;32:919–26.
18. O'Halloran N, Lowery A, Kalinina O, et al. Trends in breast reconstruction practices in a specialized breast tertiary referral centre. *BJS Open*. 2017;1:148–57.
19. Romanoff A, Zabor EC, Stempel M, et al. A comparison of patient-reported outcomes after nipple-sparing mastectomy and conventional mastectomy with reconstruction. *Ann Surg Oncol*. 2018;25:2909–16.
20. Sisco M, Du H, Warner JP, et al. Have we expanded the equitable delivery of postmastectomy breast reconstruction in the new millennium? Evidence from the national cancer data base. *J Am Coll Surg*. 2012;215:658–66; **discussion 666**.
21. Yang RL, Newman AS, Lin IC, et al. Trends in immediate breast reconstruction across insurance groups after enactment of breast cancer legislation. *Cancer*. 2013;119:2462–8.
22. Epstein S, Tran BN, Cohen JB, et al. Racial disparities in post-mastectomy breast reconstruction: National trends in utilization from 2005 to 2014. *Cancer*. 2018;124:2774–84.
23. Schumacher JR, Taylor LJ, Tucholka JL, et al. Socioeconomic factors associated with post-mastectomy immediate reconstruction in a contemporary cohort of breast cancer survivors. *Ann Surg Oncol*. 2017;24:3017–23.
24. Regis C, Le J, Chauvet MP, et al. Variations in the breast reconstruction rate in France: a nationwide study of 19,466 patients based on the French medico-administrative database. *Breast*. 2018;42:74–80.
25. Retrouvey H, Solaja O, Gagliardi AR, et al. Barriers of access to breast reconstruction: a systematic review. *Plast Reconstr Surg*. 2019;143:465e–76e.
26. Tang R, Coopey SB, Merrill AL, et al. Positive nipple margins in nipple-sparing mastectomies: rates, management, and oncologic safety. *J Am Coll Surg*. 2016;222:1149–55.
27. de Alcantara Filho P, Capko D, Barry JM, et al. Nipple-sparing mastectomy for breast cancer and risk-reducing surgery: the Memorial Sloan-Kettering Cancer Center experience. *Ann Surg Oncol*. 2011;18:3117–22.
28. Krajewski AC, Boughey JC, Degnim AC, et al: Expanded indications and improved outcomes for nipple-sparing mastectomy over time. *Ann Surg Oncol*. 2015;22:3317–23.
29. Orcutt ST, O'Donoghue C, Smith P, et al: Expanding eligibility criteria for nipple-sparing mastectomy. *South Med J*. 2017;110:654–9.
30. Agarwal S, Agarwal S, Neumayer L, et al. Therapeutic nipple-sparing mastectomy: trends based on a national cancer database. *Am J Surg*. 2014;208:93–8.
31. Albright EL, Schroeder MC, Foster K, et al. Nipple-sparing mastectomy is not associated with a delay of adjuvant treatment. *Ann Surg Oncol*. 2018;25:1928–35.