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ORIGINAL REPORT

Trends in Racial and Age Disparities in Definitive Local Therapy of Early-Stage Breast Cancer

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The Appendix is included in the full-text version of this article, available online at www.jco.org. It is not included in the PDF version (via Adobe® Reader®).

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ABSTRACT

Purpose
Guidelines recommend breast-conserving surgery (BCS) with radiation or mastectomy for definitive local therapy of stage I/II breast cancers. We assessed receipt of definitive local therapy for early-stage breast cancer by race/ethnicity and age and examined trends over time.

Patients and Methods
We calculated rates of definitive local therapy (mastectomy or BCS with radiation) for 375,547 adult women with stage I or II breast cancer diagnosed during 1988 to 2004 using Surveillance, Epidemiology, and End Results registry data. We assessed the probability of definitive local therapy and trends over time using multivariate logistic regression.

Results
Overall, 85.8% of women had definitive local therapy. As mastectomy rates decreased (76.5% in 1988 to 38.0% in 2004; $P < .001$), definitive local therapy rates also decreased (95.2% in 1988 to 79.2% in 2004; $P < .001$). In adjusted analyses, rates of definitive local therapy were modestly lower for black and Hispanic (*v* white) women and higher for Asian women. Differences for black and Asian women were stable over time ($P = .61$ and $P = .35$ for interaction), but increased for Hispanic women ($P = .0003$). Although age differences narrowed over time, women older than 70 years and women ≤ 60 years had lower rates of definitive local therapy than women 61 to 70 years throughout the study period.

Conclusion
As breast conservation has increasingly substituted mastectomy, our findings suggest fewer women are receiving definitive local breast cancer therapy, with persistent disparities for black and Hispanic women as well as women age ≤ 60 and older than 70 years. Interventions to assure receipt of radiation after BCS are needed to eliminate these disparities.

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INTRODUCTION

Guidelines recommend breast-conserving surgery (BCS) with whole breast radiation or modified radical mastectomy for definitive local therapy for women with stage I and II breast cancers.[1,2] Several randomized trials have demonstrated equivalent long-term survival for BCS with radiation and mastectomy.[3-5] The widespread adoption of BCS with radiation began in the early 1990s, following the National Institutes of Health statement recommending BCS with radiation as the preferred primary therapy for most women with early-stage breast cancers.[6]

BCS without radiation is associated with significantly higher local recurrence rates[3,5,7] and possibly a higher mortality risk.[8] Although some studies suggest that radiation in elderly women may be safely omitted,[7,9-11] decreased local recurrence rates have been observed in women of all ages, and until 2005 guidelines recommended breast radiation for all women who underwent BCS.[12] Despite such guidelines, radiation is often omitted after BCS, particularly in racial/ethnic minorities,[13,14] as well as in the youngest and oldest patients.[15-17]

Although there has been a recent, nationwide emphasis to eliminate disparities in cancer care,[18-20] it is unclear whether definitive local therapy rates (BCS with radiation or mastectomy) are improving over time in vulnerable patients with breast cancer. In a large population-based cohort of women with early-stage breast cancer, we assessed receipt of definitive local therapy for early-stage breast cancer by race/ethnicity and age and examined trends over time.

Table 1. Rates of Definitive Local Therapy by Patient Characteristics (N = 375,547)

Characteristic	No.	% Sample	Receiving Definitive Local Therapy		Definitive Local Therapy	
			%	*P**	Adjusted %	*P†*
Overall	375,547	100	85.8		85.8	
Race/ethnicity				< .0001		< .0001
White	297,092	79	86.1		86.0	
Black	28,137	7	82.0		82.8	
Hispanic	24,667	7	83.2		84.5	
Asian/Pacific Islander	24,180	6	89.4		89.2	
Native American	1471	0.4	88.4		84.6	
Age				< .0001		< .0001
≤ 40	25,559	7	86.2		85.4	
41-50	70,345	19	86.0		85.8	
51-60	84,907	23	86.7		87.0	
61-70	85,313	23	88.5		88.3	
71-80	76,729	20	86.5		86.6	
> 80	32,694	9	74.3		75.3	
Marital status				< .0001		< .0001
Married	214,174	57	87.3		86.5	
Single	151,030	40	84.2		85.2	
Unknown	10,343	3	80.2		81.8	
Geographic region				< .0001		< .0001
California	147,985	39	84.0		84.6	
Connecticut	32,699	9	78.5		76.7	
Detroit	34,750	9	86.7		85.5	
Hawaii	10,208	3	90.1		86.4	
Iowa	28,169	8	94.6		93.8	
New Mexico	12,118	3	88.5		87.6	
Seattle	34,867	9	93.6		92.6	
Utah	11,370	3	91.6		90.4	
Atlanta, rural Georgia	19,175	5	86.5		85.6	
Alaska	449	0.1	89.5		91.4	
Kentucky	10,075	3	81.9		86.0	
Louisiana	10,977	3	86.3		89.9	
New Jersey	22,705	6	78.8		83.4	
Year of diagnosis				< .0001		< .0001
1988-1990	32,098	9	94.2		93.4	
1991-1992	28,018	7	91.5		91.9	
1993-1994	32,545	9	90.1		90.5	
1995-1996	34,467	9	88.8		88.9	
1997-1998	39,008	10	86.6		87.1	
1999-2000	60,033	16	84.4		85.0	
2001-2002	77,592	21	82.6		82.7	
2003-2004	71,786	19	80.8		80.1	
Histology				< .0001		< .0001
Ductal	325,924	87	86.0		85.9	
Lobular	30,221	8	87.6		87.6	
Favorable types	19,402	5	80.8		82.3	
Grade				< .0001		< .0001
Well differentiated	64,528	17	83.6		85.4	
Moderately differentiated	137,228	37	85.7		86.2	
Poorly differentiated	115,980	31	85.8		85.7	
Unknown	57,811	15	88.5		85.8	
Tumor size, cm				< .0001		< .0001
≤ 1	106,997	28	84.9		85.6	
1.1-2.0	153,640	41	85.2		85.4	
2.1-3.0	72,166	19	86.4		85.4	
3.1-4.0	25,680	7	88.8		88.0	
> 4.0	17,064	5	91.2		90.3	

(continued on following page)

Table 1. Rates of Definitive Local Therapy by Patient Characteristics (N = 375,547) (continued)

Characteristic	No.	% Sample	Receiving Definitive Local Therapy		Definitive Local Therapy	
			%	P*	Adjusted %	P†
Estrogen receptor				< .0001		< .0001
Positive	236,767	63	86.3		86.5	
Negative	62,841	17	85.4		85.0	
Unknown	75,939	20	84.6		84.5	
Progesterone receptor				< .0001		< .0001
Positive	197,860	53	86.6		86.5	
Negative	92,968	25	85.6		86.2	
Unknown	84,719	23	84.4		83.8	
AJCC stage				< .0001		< .0001
I	208,597	56	84.9		85.3	
IIA	110,870	30	85.7		85.6	
IIB	56,080	15	89.8		88.7	

Abbreviation: AJCC, American Joint Committee on Cancer.
*Using χ^2 tests.
†Using multivariate logistic regression and adjusting for all variables in the Table.

PATIENTS AND METHODS

Data Source and Study Population

We used Surveillance, Epidemiology, and End Results (SEER) registry data from 1988 to 2004. The 17 population-based SEER cancer registries cover areas representing 26% of the United States population and uniformly collect information on patient demographics, tumor characteristics, treatment utilization, and mortality for all incident cancers. Data from the nine original SEER registries were available for the entire study period; data from additional registries were included following SEER expansions in 1992 and 2000.[21]

We included all women age ≥18 years diagnosed with a first breast cancer that was American Joint Committee on Cancer stage I or II during 1988 to 2004 (n = 380,587) who underwent primary surgical therapy (mastectomy or BCS; n = 376,966) and had histologies likely to be treated by standard local therapy guidelines (Appendix Table A1, online only). Women of unknown race were excluded (n = 1,419) because this was a primary variable of interest.

Dependent Variable

We defined definitive local therapy as receipt of BCS with radiation or mastectomy (with or without radiation). Women undergoing modified radical mastectomy, radical mastectomy, extended radical mastectomy, total (simple) mastectomy, mastectomy not otherwise specified (NOS), and subcutaneous mastectomy were defined as having received mastectomy. Women undergoing partial mastectomy NOS, less than total mastectomy NOS, lumpectomy, and segmental mastectomy were defined as having received BCS. Women who received radiation in addition to BCS were defined as having BCS with radiation. Women for whom radiation was recommended but not received, was unknown to be received, or were refused by the patient according to registry data were categorized as not receiving radiation, although results were similar in sensitivity analyses that considered them to have received radiation (data not shown). Although some recent guidelines recommend postmastectomy radiation, we did not include this in our definition of definitive local therapy because few women had tumors larger than 5 cm and/or more than three positive nodes and consensus is lacking about benefits for other women.

Independent Variables of Interest

Independent variables of interest included race/ethnicity and age at diagnosis. Race/ethnicity (obtained by registrars from medical records and supplemented by Hispanic surname match) was categorized as non-Hispanic white, non-Hispanic black, Native American, Asian/Pacific Islander, or Hispanic. Age was classified as ≤ 40, 41 to 50, 51 to 60, 61 to 70, 71 to 80, and older than 80 years.

Control Variables

Control variables included geographic region, marital status, diagnosis year, histology, tumor size, estrogen receptor status, progesterone receptor status, tumor grade, and American Joint Committee on Cancer stage. Variables were categorized as in Table 1; histology classification is provided in Table A1.

Statistical Analysis

We calculated rates of definitive local therapy by year and compared rates of definitive local therapy, BCS with radiation, and mastectomy at baseline (1988) and at the end of the study period (2004) using χ^2 tests, given the linear trend for each procedure over the study period. We used χ^2 tests to compare rates of definitive local therapy by patient characteristics. We used multivariate logistic regression to assess the probability of definitive local therapy by race/ethnicity and age, controlling for the variables described earlier. We calculated adjusted rates of definitive local therapy for each patient characteristic using a standardized regression approach.[22] To better understand whether differences in rates of definitive local therapy by year of diagnosis, race/ethnicity, age, and geographic region resulted primarily from differences in mastectomy and BCS rates, we used χ^2 tests to assess differences in the rates of mastectomy, BCS with radiation, and BCS without radiation by these characteristics.

In separate logistic regression models, in addition to all of the variables in the first models, we included interaction terms for year by race/ethnicity and for year by age to assess differences in receipt of definitive local therapy over time. We repeated analyses among women who underwent BCS to assess differences in radiation after BCS over time. In a sensitivity analysis, we repeated all analyses after restricting the cohort to women younger than 70 years of age because some recommendations suggest that radiation therapy can be safely omitted in older women.

Because of concerns about under ascertainment of radiation in registry data,[23] we conducted an additional analysis using SEER-Medicare data[24] comparing ascertainment of radiation therapy by registry and Medicare claims data during 1992 to 2002 following the method of Virnig et al.[25] Specifically, we assessed whether agreement varied by patient race and age among women ≥ age 65. All statistical analyses were conducted using SAS version 9.1 (SAS Institute, Cary, NC). Because analyses used preexisting registry data with no identifying patient information, the Partners Human Research Committee granted exemption from review.

RESULTS

Among the 375,547 women in the study cohort, 85.8% underwent definitive local therapy. As mastectomy rates decreased (76.5% in 1988 to 38.0% in 2004; $P < .0001$), rates of definitive local therapy also decreased (95.2% in 1988 to 79.2% in 2004; $P < .0001$). Among women who underwent BCS, rates of radiation decreased over time (79.4% in 1988 to 66.4% in 2004; $P < .0001$). Unadjusted rates of definitive local therapy varied significantly by race/ethnicity and age (Figs 1 and 2). Hispanic women had the highest rates in 1988 with a steady decline over time, resulting in the lowest observed rates of all groups by 2003 (Fig 1). Black women had the lowest rates of definitive local therapy until that time. Asian women had the highest rates throughout the study period. For all years analyzed, women ≥ age 80 had substantially lower rates compared with all other age groups; women ages 61 to 70 had the highest rates (Fig 2).

Unadjusted and adjusted rates of definitive local therapy by patient and tumor characteristics are presented in Table 1. In the adjusted analysis (right columns), black and Hispanic women had lower rates of definitive local therapy than white women, while Asians had higher rates. Women in the youngest and oldest age groups had the lowest rates, while women age 61 to 70 had the highest rates.

Other factors significantly associated with not receiving definitive local therapy in adjusted analyses included unmarried or unknown marital status (*v* married), estrogen receptor–negative or unknown estrogen/progesterone receptor status (*v* estrogen/progesterone expressing tumors), and favorable histology subtypes (*v* invasive ductal carcinoma; all $P < .05$). More recent diagnosis was also associated with lower rates of receipt of definitive local therapy. Women with stage IIA and IIB cancers were more likely to undergo definitive local therapy (*v* stage I), as were women with invasive lobular histology (*v* ductal) and larger tumors. Women in Iowa, Seattle, Alaska, and Utah had the highest rates of definitive local therapy, while women in Connecticut had the lowest rates (Table 1).

The high rates of definitive local therapy in Iowa, Alaska, and Utah were primarily driven by high mastectomy rates (66.1%, 67.3%, and 58.6%, respectively), while Seattle and Hawaii had high rates of definitive local therapy, relatively low rates of mastectomy (46.8% and 47.9%, respectively), and high rates of BCS with radiation. Although mastectomy rates were similar for black, Hispanic, and white women (47.9%, 47.8%, and 47.4%, respectively), the rates of definitive local therapy varied because black and Hispanic women had higher rates of BCS without radiation compared with white women (Fig 3). Asian and Native American women had the highest mastectomy rates (53.5% and 53.4%, respectively) and lowest rates of BCS without radiation, leading to the highest overall rates of definitive local therapy (Fig 3). For women of all race/ethnicities, mastectomy rates decreased consistently over time while rates of BCS without radiation increased (all $P < .0001$). As demonstrated in Figure 4, women ≥ age 80 had relatively high rates of mastectomy but more than half of women who underwent BCS did not have radiation after BCS (Fig 4). Despite differences in overall rates of breast conservation for women ≤ age 60 (range, 49.3% to 56.7%), the rates of BCS without radiation were

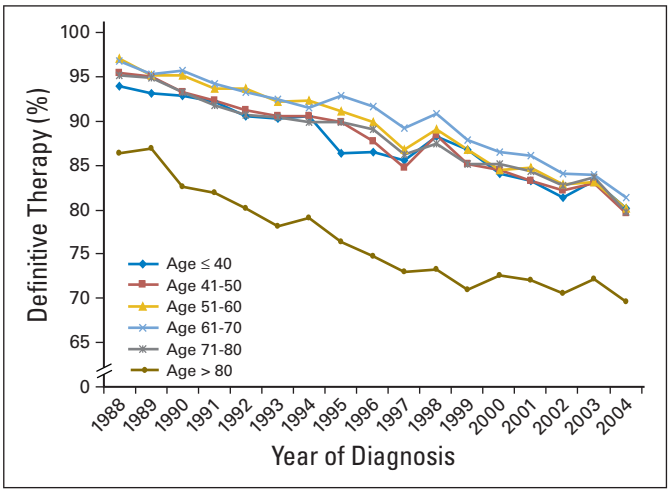

Fig 2. Unadjusted rates of definitive local therapy (%) by age and year. Trends in the rates of definitive local therapy (mastectomy or breast-conserving surgery with radiation) for patients who underwent primary breast surgery by age. Rates decreased significantly over time for all groups ($P < .0001$).

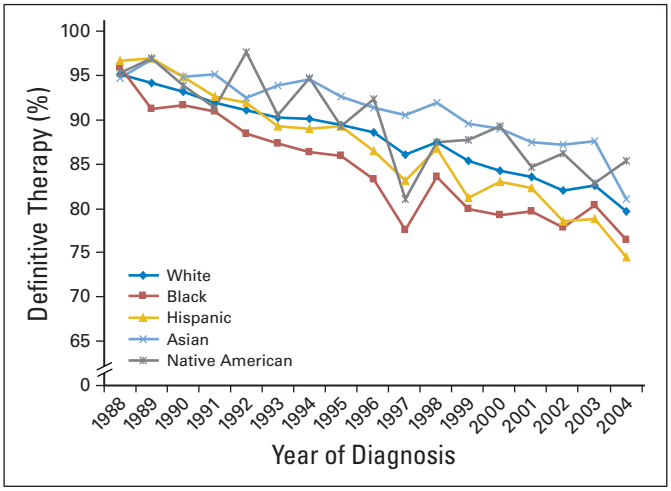

Fig 1. Unadjusted rates (%) of definitive local therapy by race/ethnicity and year. Trends in the rates of definitive local therapy (mastectomy or breast-conserving surgery with radiation) for patients who underwent primary breast surgery by race/ethnicity. Rates decreased significantly over time for all groups ($P < .0001$).

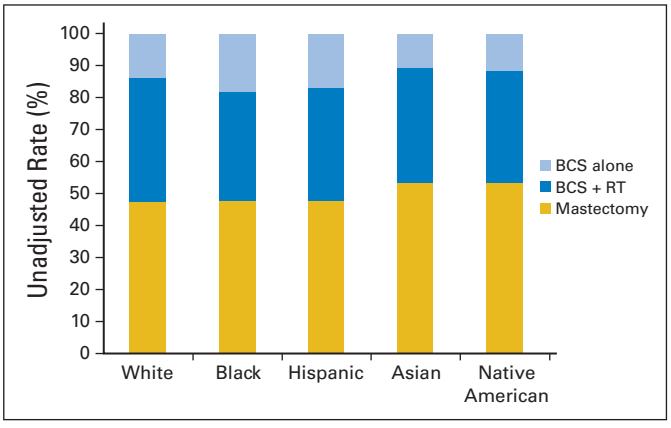

Fig 3. Unadjusted rates of mastectomy, breast-conserving surgery (BCS) with radiation, and BCS without radiation by race/ethnicity. The colored vertical bars represent the total proportion of patients who received mastectomy (yellow), BCS with radiation therapy (RT; dark blue), or BCS alone (light blue) by race/ethnicity; *P* value less than .0001.

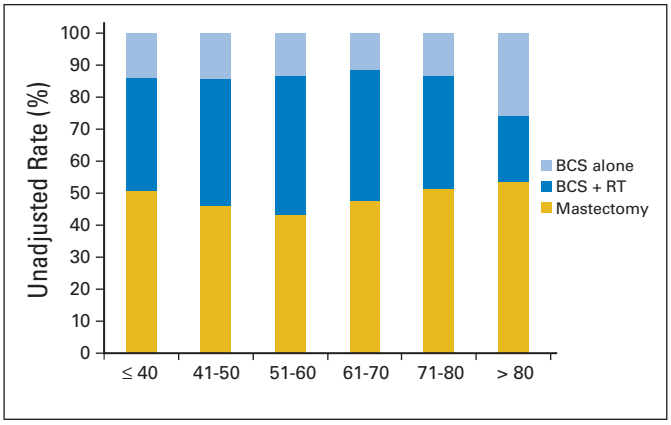

Fig 4. Unadjusted rates of mastectomy, breast-conserving surgery (BCS) with radiation, and BCS without radiation by age. The colored vertical bars represent the total proportion of patients who received mastectomy (yellow), BCS with radiation therapy (RT; dark blue), or BCS alone (light blue) by age; *P* value less than .0001.

similar (range, 13.3% to 14%; Fig 4). For all age groups, mastectomy rates decreased while rates of BCS without radiation increased over time (all $P < .0001$).

Trends in Race/Ethnicity and Age Differences Over Time

The lower rates of definitive local therapy for black versus white women did not change over time ($P = .61$ for interaction; Table 2). The rates for Hispanic women decreased faster than for white women ($P = .0003$) and despite having the highest rates of definitive local therapy in 1988, by the end of the study period, Hispanic women had the lowest rates. Asian women had persistently higher rates compared with white women over time ($P = .35$).

The differences in rates of definitive local therapy for all age groups versus the 61 to 70 age group narrowed significantly over the study period ($P < .0001$ for all interactions; Table 2) with the exception of the 51 to 60 age group, for whom differences remained stable ($P = 1.0$ for interaction). Nevertheless, for older and younger women, differences persisted at the end of the study period. In the model that included interaction terms, multivariate results for other variables were unchanged.

When we repeated analyses examining receipt of radiation after BCS among women who underwent BCS (n = 195,752), results were similar to those for definitive local therapy (data not shown) with the exceptions that the disparity for black versus white women narrowed slightly over time (β coefficient = .01; $P = .05$ for interaction) and disparities for women ≤ age 50 to versus 61 to 70 remained stable over time (both $P > .20$).

In a sensitivity analysis excluding 109,423 women ≥ age 70 from the cohort, results were similar. Women age ≤ 40, 41 to 50, and 51 to 60 had lower odds of definitive local treatment compared with women aged 61 to 70 and differences by race/ethnicity persisted (data not shown). Trends over time confirmed narrowing of differences for women age ≤ 40 and 41 to 50 versus age 61 to 70 ($P < .0001$ for interactions) with stable rates over time for women age 51 to 60 ($P = .81$ for interaction). Rates of definitive local therapy for younger women remained significantly lower at the end of the study period.

When we compared ascertainment of radiation therapy in registry data versus Medicare claims data among women older than 65, we found excellent agreement between the two sources of data (91%).

Table 2. Race/Ethnicity and Age Differences in Definitive Local Therapy Over Time*

Race/Ethnicity and Age Changes Over Time and Interactions	β Coefficient	*P*†
Race/ethnicity		
White	Reference	—
Black	−.28	< .0001
Hispanic	.10	.13
Asian/Pacific Islander	.38	< .0001
Native American	−.19	.45
Interaction of race/ethnicity by year of diagnosis*		
Black	.00	.61
Hispanic	−.02	.0003
Asian	−.01	.35
Native American	.01	.75
Age		
≤ 40	−.58	< .0001
41-50	−.44	< .0001
51-60	−.12	.01
61-70	Reference	—
71-80	−.41	< .0001
> 80	−1.55	< .0001
Interaction of age by year of diagnosis*		
≤ 40	.03	< .0001
41-50	.02	< .0001
51-60	.00	1.0
71-80	.02	< .0001
> 80	.05	< .0001

*Results from multivariate model with main effects and interaction terms. Findings for other independent variables were unchanged from Table 1.
†Using multivariate logistic regression controlling for all variables in the table as well as the variables in Table 1.

Moreover, we found similar rates of agreement by race/ethnicity and increasing rates of agreement with increasing patient age (Appendix Table A2, online only). These findings suggest that the differences we observed in rates of radiation after BCS for black and Hispanic women and older women are likely not explained by differences in ascertainment of radiation therapy in these groups by the registries.

DISCUSSION

We assessed the receipt of definitive local therapy by race/ethnicity and age over time and observed that as rates of BCS steadily increased, rates of definitive local therapy decreased for all women. Lower rates of definitive local therapy and omission of radiation after BCS were unexpectedly not limited to those with favorable prognostic features but were seen in the youngest and oldest women, black and Hispanic (*v* white) women, and women with estrogen receptor–negative tumors. Although the differences between subgroups were relatively small, black women had persistently lower rates of definitive local therapy than white women over the entire study period, and despite the highest rates at the start of the study period, Hispanic women had the lowest rates by 2004. The oldest and youngest patients, versus women age 61 to 70 years, also had lower rates of definitive local therapy throughout the study period. Although the lower rates in elderly women were expected and may have been appropriate, the lower rates among the youngest patients were surprising because they may have the greatest long-term benefits.

Lack of definitive local therapy was due primarily to increasing rates of BCS without radiation in the setting of increases in BCS and decreases in mastectomy. The reasons for omission of radiation among women undergoing BCS are unclear but are likely multifactorial. Some women may find it difficult to make daily radiation visits, either because of distance or other responsibilities, such as employment or childcare. This may be particularly relevant for younger, employed women with small children or limited transportation, resources, and social supports. Some patients may choose to forgo radiation, perhaps perceiving that the benefit is not worth the perceived risks or inconvenience. However, it is also possible that physicians have not sufficiently communicated the importance of radiation after BCS for long-term outcomes comparable to mastectomy. For patients of advanced age, physicians may not have recommended radiation due to minimal perceived benefit; however, our findings of disparities for black and Hispanic women as well as younger women persisted even when women age $\geq$ 70 years were excluded.

Although recent controversy exists regarding whether women over age 70 benefit from optimized local control as much as younger women, receipt of mastectomy or BCS with radiation therapy was the standard of care for women of all ages with early-stage breast cancer during the study period. The landmark randomized trials comparing BCS, BCS with radiation, and mastectomy had few patients older than age 65, and these studies are unable to inform the decision to avoid radiation in elderly women.[26] We observed decreased rates of definitive local therapy (and radiation after BCS) in elderly women at the start of our study, when radiation was considered standard of care for all women undergoing BCS, and for many years before the first publications suggesting acceptable omission of radiation in older women (1999 and 2001).[7,11,27] The evolving data regarding elderly women may have impacted rates of definitive local therapy in later years but are unlikely to explain the lower rates noted earlier in the study period.

Our analysis was limited by lack of comorbidity information, but other analyses have found that lower rates of radiation after BCS in older women are evident even when patients are matched for comorbidity.[16] In addition, the extent of comorbidity is likely to be stable over time across the population, but rates of definitive local therapy still decreased for all patients over the study period.

The geographic differences in rates of definitive local therapy were due, in part, to differences in underlying rates of mastectomy versus breast conservation, with regions with the highest mastectomy rates typically also having the highest rates of definitive local therapy. The high rates of mastectomy in areas such as Iowa, Alaska, and Utah may be due to provider beliefs about the different therapies or a lack of adoption of breast conservation due to less availability of radiation in rural areas. Nevertheless, the high rates of definitive local therapy in regions such as Seattle and Hawaii suggest that it is possible to obtain high rates of definitive local therapy even in areas that perform fewer mastectomies.

Other investigators have reported that rates of BCS without radiation vary by race/ethnicity, age, geographic region, tumor characteristics, and treating institution, but have not looked at trends in definitive local therapy rates.[28,29] Bickell et al reported underutilization of various adjuvant therapies in a New York City based medical record review during 1999 to 2000 and found that black women were significantly less likely to have adjuvant radiation compared with white women.[13] More recently, Gross et al examined a SEER-Medicare patient population during 1992 to 2002 and reported significant differences in the percentage of age-matched women who received radiation after BCS but did not analyze mastectomy rates, women $\leq$ age 65, or other race/ethnicities.[16]

Our study has several limitations. We had no information about patients' socioeconomic status, comorbidity, treatment preferences, or insurance status, nor did we have information about facility characteristics or provider reasoning, all of which could influence treatment decision making and recommendations. In addition, non-SEER geographic areas are not represented in our analysis. Finally, because some data suggest that cancer registries may incompletely ascertain receipt of radiation therapy,[23] we assessed whether this possibility would be likely to alter our conclusions by examining agreement between SEER registry data and Medicare claims data. Although these analyses were limited to women older than 65 years of age, because we found similar rates of agreement between these sources by race/ethnicity and increasing agreement with increasing age, we believe it is unlikely that our findings would be explained by problems ascertaining radiation therapy by the SEER registries.

In conclusion, although the ability to preserve the breast has improved over recent decades with the emergence of breast conservation, an opportunity for disparities has arisen as women who choose breast conservation must complete two steps, surgery followed by radiation, for definitive local therapy. Despite recent nationwide efforts to eliminate disparities in cancer care by race/ethnicity and age, our findings suggest persistent, modest disparities in receipt of definitive local therapy among breast cancer patients of differing race/ethnicity and age. Although the lower rates in elderly women may be appropriate, this is of particular concern in young women, who had high rates of BCS as primary surgery and are at most risk for long-term inferior outcomes. Further studies examining factors contributing to these disparities are needed to allow for development of targeted interventions to improve receipt of definitive local therapy. Ensuring completion of primary therapy should be a priority in order to improve the quality of breast cancer care.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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Administrative support: Rachel A. Freedman, Eric P. Winer, Nancy L. Keating
Provision of study materials or patients: Rachel A. Freedman, Nancy L. Keating
Collection and assembly of data: Rachel A. Freedman, Nancy L. Keating
Data analysis and interpretation: Rachel A. Freedman, Yulei He, Eric P. Winer, Nancy L. Keating
Manuscript writing: Rachel A. Freedman, Yulei He, Eric P. Winer, Nancy L. Keating
Final approval of manuscript: Rachel A. Freedman, Yulei He, Eric P. Winer, Nancy L. Keating

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