

Age-Related Radiotherapy Utilization Patterns and Associated Survival by Surgical Approach in Stage I–III Breast Cancer

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Abstract

Purpose

Age-related patterns of radiotherapy utilization and associations between radiotherapy (RT) receipt and overall survival (OS) across surgical settings remain understudied. We evaluated age-specific associations between postoperative radiotherapy receipt and OS and characterized age-related radiotherapy utilization and documented reasons for omission among women with stage I–III breast cancer undergoing breast-conserving surgery (BCS) or mastectomy (Mx) with indications for postmastectomy radiotherapy (PMRT).

Methods

We conducted a retrospective National Cancer Database cohort study (2004–2021), with follow-up through 2022. Overlap-weighted Kaplan–Meier and Cox models evaluated surgery-radiotherapy comparisons across age strata. Time-varying models assessed immortal-time bias. Marginally standardized logistic regressions estimated adjusted radiotherapy probabilities by age group.

Results

Among 1,457,243 patients, weighted 5-year OS was 93.2% (95% CI, 93.1–93.3) with BCS + RT and 89.3% (95% CI, 89.2–89.4) with Mx – RT. Corresponding estimates were 89.5% (95% CI, 89.3–89.6) versus 82.6% (95% CI, 82.4–82.9) for radiotherapy versus no radiotherapy after BCS and 82.9% (95% CI, 82.6–83.1) versus 80.5% (95% CI, 80.3–80.8) among PMRT-indicated patients. Age-stratified hazard ratios for radiotherapy ranged from 0.49 to 0.71 after BCS and from 0.77 to 0.94 among PMRT-indicated patients. At age ≥ 75 years, observed RT receipt was 58.6% after BCS and 41.6% among PMRT-indicated patients; adjusted probabilities were 72.1% and 57.1%, respectively. Treatment nonselection and patient refusal predominated among reasons for omission.

Conclusion

Radiotherapy receipt was associated with higher overall survival across age groups, whereas radiotherapy utilization declined independently with age, supporting individualized radiotherapy decisions beyond chronological age alone.

INTRODUCTION

Seminal randomized clinical trials have shown long-term survival equivalence between breast-conserving surgery (BCS) with adjuvant radiotherapy (RT) and mastectomy (Mx) alone among patients with early-stage breast cancer [1–3]. More recently, large observational studies have reported improved

overall and breast cancer-specific survival among early-stage patients treated with BCS and radiotherapy compared with Mx [4–9].

Adjuvant radiotherapy plays a central role in the management of early-stage breast cancer, with its indication closely tied to the surgical approach. Radiotherapy is a standard component of breast conservation therapy and is also recommended for selected patients undergoing Mx, particularly those with higher-risk disease features such as nodal involvement or positive margins [10]. Randomized trials have demonstrated that radiotherapy reduces breast cancer recurrence and mortality in these populations [11, 12].

Despite the established role of adjuvant radiotherapy, real-world patterns of radiotherapy utilization among patients for whom it is indicated remain an important knowledge gap. Radiotherapy omission may occur for numerous reasons, including variations in physician recommendation [13, 14], patient preference [15], and medical contraindications [16]. Age may be a particularly influential factor in radiotherapy treatment decision-making. Although randomized trials support radiotherapy omission among selected older women with hormone receptor–positive, node-negative breast cancer receiving endocrine therapy who underwent BCS [17, 18], prior studies have suggested that increasing chronological age may be independently associated with lower radiotherapy utilization among breast cancer patients who are otherwise eligible for postoperative radiotherapy [14, 19, 20]. These findings raise concern that age-based treatment de-escalation may extend beyond populations for whom omission is supported by evidence [21], resulting in the underutilization of adjuvant radiotherapy among older patients who may still benefit from treatment in the general population. Furthermore, the evidence supporting radiotherapy omission in BCS patients may not be generalizable to Mx patients with higher-risk disease or postmastectomy radiotherapy (PMRT) indications. Whether radiotherapy omission in these populations is associated with comparable survival remains unclear.

Using the National Cancer Database (NCDB), we aimed to estimate age-specific associations between radiotherapy receipt and overall survival among women with stage I–III invasive breast cancer, particularly within patients undergoing BCS and those with guideline-based indications for PMRT. We also aimed to characterize patterns of radiotherapy omission, including reasons for non-receipt and whether increasing age was independently associated with lower radiotherapy utilization. This study will enhance understanding of age-dependent survival implications in both BCS and PMRT-indicated patients, patterns of radiotherapy utilization by age, and whether utilization patterns parallel the survival associations.

METHODS

This retrospective study used data from the NCDB, a hospital-based oncology registry capturing approximately 70% of newly diagnosed U.S. cancer cases from Commission on Cancer (CoC)–accredited hospitals. The NCDB is 82% complete for breast cancer and has 94% compliance on re-

abstracting and recording [22]. The database includes 4,230,678 patients diagnosed with breast cancer between 2004 and 2021.

Study Population and Treatment Definitions

We identified adult female patients with clinical and pathological stage I-III invasive breast cancer using International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3), topographic codes C50.0 to C50.9. Patients were diagnosed between 2004 and 2021 and followed through December 31, 2022. BCS was defined as partial mastectomy with or without nipple-areola resection, lumpectomy, excisional biopsy upgraded to cancer, and segmental mastectomy. Mx was defined as skin sparing, nipple/areola sparing, total, modified radical, radical, and extended radical mastectomies (with or without contralateral Mx). Analyses included patients who underwent BCS or Mx, as defined above. Exclusion criteria included clinical or pathological M1 disease, neoadjuvant radiotherapy receipt ($n = 7,179$), unknown survival status, follow-up time, primary surgery information, primary tumor size, or radiotherapy receipt. Patients were also excluded if they had a prior or subsequent second primary malignancy or non-analytic cases in the NCDB.

Postoperative radiotherapy receipt was determined using two variables: location of radiotherapy treatment facility and the reason for no radiotherapy. To minimize misclassification, patients were classified as having received radiotherapy only when both variables confirmed radiotherapy receipt, and as not having received radiotherapy only when both variables indicated no radiotherapy. This definition was used in all primary analyses (i.e., radiotherapy receipt yes vs no).

We evaluated three clinically motivated comparisons. First, patients receiving BCS + RT were compared to those undergoing Mx – RT, contextualizing established locoregional treatment strategies. Second, among patients treated with BCS, outcomes were compared between those who received adjuvant radiotherapy and those who did not. Third, because patients receiving PMRT often have worse baseline prognostic features, we identified patients undergoing Mx who were indicated for PMRT, including those with pathologically node-positive disease or positive margins, based on the American Society for Radiation Oncology–American Society of Clinical Oncology–Society of Surgical Oncology guideline for PMRT [10]. Among this group, we compared those who received PMRT and those who did not.

Clinical covariates included tumor stage group (based on clinical and pathological TNM), breast subtype (hormone receptor [ER, PR] and human epidermal growth factor receptor 2 status [HER2]), tumor size, number of positive lymph nodes, tumor grade, histology, lymphovascular invasion, and systemic therapies including chemotherapy, endocrine treatment, and immunotherapy. Histologic subtype was coded by ICD-O-3 and collapsed into ductal, lobular, and other categories. Systemic therapy variables were coded as yes, no, or unknown. Age at diagnosis was categorized into 18–29, 30–39, 40–49, 50–64, 65–74, and ≥ 75 years, accounting for Medicare eligibility beginning at age 65. The year of diagnosis was divided into 2004–2007, 2008–2011, 2012–2015, and 2016–2021. Comorbidities were assessed using the Charlson Comorbidity Index. Socioeconomic and geographic factors included median household

income, geographic location (reporting facility-level), self-reported primary insurance at diagnosis, race, and great-circle distance between the patient's residence and reported treatment facility ("Crowfly" distance).

Statistical Analysis

Baseline demographic, clinical, treatment, and facility-level socioeconomic characteristics were summarized according to four surgery-radiation approaches: BCS + RT, BCS – RT, Mx + RT, and Mx – RT. Chi-square tests were performed for categorical variables and Kruskal-Wallis tests for continuous variables.

To address confounding in treatment effect estimation, propensity score weighting was applied for each comparison. The propensity score, defined as the probability of receiving the treatment of interest, was estimated using a logistic regression, conditional on baseline clinical, demographic, and socioeconomic characteristics. Overlap propensity score weights were then calculated to estimate the average treatment effect in the overlap population, representing patients with clinical equipoise between the compared treatment strategies [23, 24]. Covariate balance after weighting was assessed using standardized mean differences (SMDs), with an absolute SMD < 0.1 indicating adequate balance (**Figure S1**). The distributions of propensity scores were examined to assess the positivity assumption (**Figure S2**).

Overall survival (OS) was defined from the date of diagnosis to all-cause death, last known follow-up, or administrative right-censoring on December 31, 2022. Unweighted Kaplan-Meier curves were examined descriptively, whereas overlap-weighted Kaplan-Meier curves were used to visualize survival patterns for all clinical comparisons. Overlap-weighted Cox proportional hazards models were used to estimate hazard ratios (HRs) for OS in the BCS + RT vs. BCS–RT and Mx + RT vs. Mx–RT groups. Age-stratified analyses were performed for both within-surgery radiotherapy comparisons, using age groups of < 40, 40–49, 50–64, 65–74, and ≥ 75 years. Within each age stratum, propensity scores and overlap weights were re-estimated to obtain age-specific ATO estimates. To mitigate potential propensity score model misspecification, the models additionally adjusted for the baseline covariates. To evaluate potential immortal-time bias, multivariable Cox models treated RT receipt as a time-varying exposure among patients undergoing BCS and among PMRT-indicated patients. The proportional hazards assumption was evaluated using Schoenfeld residuals.

Documented reasons for radiotherapy omission were summarized among patients undergoing BCS and among PMRT-indicated patients undergoing Mx to contextualize heterogeneity in radiotherapy omission, including patient refusal, clinical contraindications, and other documented reasons for omission. We also evaluated whether radiotherapy receipt decreased with age independently of measured baseline covariates by estimating covariate-adjusted marginal probabilities across age groups using multivariable logistic regression over the empirical covariate distribution, separately within the BCS and PMRT-indicated cohorts. All analyses were performed in R version 4.4.3 (R Foundation, Vienna) and statistical significance was defined as a two-sided $P < .05$.

RESULTS

1,457,243 female patients aged 18–90 years with stage I–III invasive breast cancer diagnosed between 2004–2021 were included in the analytic cohort (Table 1). Among them, 796,242 (54.6%) underwent BCS + RT, 339,816 (23.3%) underwent Mx–RT, 191,922 (13.2%) underwent Mx + RT, and 129,263 (8.9%) underwent BCS–RT. Median follow-up was longest among patients receiving Mx–RT (6.4 years [IQR: 3.5–10.0]), followed by BCS + RT (6.3 [3.7–9.9]), Mx + RT (5.7 [3.3–9.3]), and BCS–RT (4.7 [2.7–7.5]). The BCS–RT group had the oldest median age at diagnosis (74 years [66–81]), whereas patients undergoing Mx + RT had the youngest (53 [44–63]) and had the largest median size of tumor (3.5 cm [2.2–5.5]). Chemotherapy use was highest among Mx + RT patients (85.7%), followed by Mx–RT (44.1%), BCS + RT (37.1%), and BCS–RT (13.5%). Hormone therapy use was highest among BCS + RT patients (77.5%), followed by Mx + RT (72.7%), Mx–RT (65.2%), and BCS–RT (55.8%). Immunotherapy use was uncommon overall but highest among Mx + RT patients (14.4%). Patients undergoing Mx + RT had greater burden of disease, including increased nodal involvement and poorer tumor differentiation. Patient characteristics by radiotherapy receipt status are presented in **Table S1**.

Table 1
Tumor, Socioeconomic, and Demographic Characteristics by Surgery-Radiation Approach in National Cancer Database (2004–2021)

Total (N)	Overall ¹	Mx-RT ¹	Mx+RT ¹	BCS-RT ¹	BCS+RT ¹	pvalue ²
	1,457,243	339,816	191,922	129,263	796,242	
Age at diagnosis	61 (51, 70)	57 (47, 68)	53 (44, 63)	74 (66, 81)	61 (53, 69)	< 0.001
Median follow-up (years)	6.1 (3.5, 9.6)	6.4 (3.5, 10.0)	5.7 (3.3, 9.7)	4.7 (2.7, 7.5)	6.3 (3.7, 9.9)	
Race/ethnicity						< 0.001
NH White	1,125,976 (77.3%)	260,083 (76.5%)	137,529 (71.7%)	104,162 (80.6%)	624,202 (78.4%)	
NH Black	159,052 (10.9%)	35,606 (10.5%)	25,965 (13.5%)	13,032 (10.1%)	84,449 (10.6%)	
Hispanic	88,965 (6.1%)	22,006 (6.5%)	15,585 (8.1%)	6,636 (5.1%)	44,738 (5.6%)	
NH Asian	56,774 (3.9%)	15,811 (4.7%)	8,994 (4.7%)	3,213 (2.5%)	28,756 (3.6%)	
NH American Indian	4,545 (0.3%)	1,175 (0.3%)	699 (0.4%)	342 (0.3%)	2,329 (0.3%)	
NH Pacific Islander	1,504 (0.1%)	377 (0.1%)	266 (0.1%)	130 (0.1%)	731 (0.1%)	
Other/unknown	20,427 (1.4%)	4,758 (1.4%)	2,884 (1.5%)	1,748 (1.4%)	11,037 (1.4%)	
Tumor size (cm)	1.60 (1.00, 2.60)	1.90 (1.20, 3.00)	3.50 (2.20, 5.50)	1.30 (0.80, 2.10)	1.50 (0.90, 2.10)	< 0.001
Positive lymph nodes						< 0.001
0	982,840 (67.4%)	251,116 (73.9%)	37,827 (19.7%)	81,775 (63.3%)	612,122 (76.9%)	
1–3	291,424 (20.0%)	64,675 (19.0%)	83,074 (43.3%)	11,392 (8.8%)	132,283 (16.6%)	
4–9	74,253 (5.1%)	9,099 (2.7%)	43,945 (22.9%)	2,067 (1.6%)	19,142 (2.4%)	
≥ 10	32,565 (2.2%)	4,791 (1.4%)	20,771 (10.8%)	775 (0.6%)	6,228 (0.8%)	
Positive (unknown)	8,655 (0.6%)	1,400 (0.4%)	3,720 (1.9%)	329 (0.3%)	3,206 (0.4%)	

Total (N)	Overall¹	Mx-RT¹	Mx+RT¹	BCS-RT¹	BCS+RT¹	pvalue²
	1,457,243	339,816	191,922	129,263	796,242	
Unknown	67,506 (4.6%)	8,735 (2.6%)	2,585 (1.3%)	32,925 (25.5%)	23,261 (2.9%)	
Histology						< 0.001
Ductal	1,142,482 (78.4%)	260,027 (76.5%)	142,620 (74.3%)	98,302 (76.0%)	641,533 (80.6%)	
Lobular	245,130 (16.8%)	63,149 (18.6%)	41,434 (21.6%)	20,872 (16.1%)	119,675 (15.0%)	
Other	69,631 (4.8%)	16,640 (4.9%)	7,868 (4.1%)	10,089 (7.8%)	35,034 (4.4%)	
Tumor grade						< 0.001
Well diff.	318,769 (21.9%)	60,021 (17.7%)	14,728 (7.7%)	41,098 (31.8%)	202,922 (25.5%)	
Moderately diff.	603,958 (41.4%)	140,408 (41.3%)	69,113 (36.0%)	55,347 (42.8%)	339,090 (42.6%)	
Poorly diff.	385,673 (26.5%)	104,528 (30.8%)	68,431 (35.7%)	24,060 (18.6%)	188,654 (23.7%)	
Other/unknown	148,843 (10.2%)	34,859 (10.3%)	39,650 (20.7%)	8,758 (6.8%)	65,576 (8.2%)	
LVI						< 0.001
Not Present	849,510 (58.3%)	194,308 (57.2%)	68,765 (35.8%)	85,704 (66.3%)	500,733 (62.9%)	
Present/Identified	199,017 (13.7%)	42,348 (12.5%)	62,711 (32.7%)	9,987 (7.7%)	83,971 (10.5%)	
N/A or Unknown	408,716 (28.0%)	103,160 (30.4%)	60,446 (31.5%)	33,572 (26.0%)	211,538 (26.6%)	
Breast cancer subtype						< 0.001
HR+/HER2-	890,928 (61.1%)	185,241 (54.5%)	102,949 (53.6%)	88,885 (68.8%)	513,853 (64.5%)	
HR+/HER2+	116,467 (8.0%)	31,521 (9.3%)	21,603 (11.3%)	6,190 (4.8%)	57,153 (7.2%)	
HR-/HER2+	44,855 (3.1%)	14,119 (4.2%)	9,847 (5.1%)	2,133 (1.7%)	18,756 (2.4%)	
Triple Negative	139,998 (9.6%)	38,059 (11.2%)	23,956 (12.5%)	8,041 (6.2%)	69,942 (8.8%)	

Total (N)	Overall ¹	Mx-RT ¹	Mx+RT ¹	BCS-RT ¹	BCS+RT ¹	pvalue ²
	1,457,243	339,816	191,922	129,263	796,242	
Unknown	264,995 (18.2%)	70,876 (20.9%)	33,567 (17.5%)	24,014 (18.6%)	136,538 (17.1%)	
CCI						< 0.001
0	1,215,913 (83.4%)	280,503 (82.5%)	164,285 (85.6%)	99,400 (76.9%)	671,725 (84.4%)	
1	181,629 (12.5%)	44,534 (13.1%)	21,570 (11.2%)	19,842 (15.4%)	95,683 (12.0%)	
2	39,906 (2.7%)	9,976 (2.9%)	4,137 (2.2%)	6,038 (4.7%)	19,755 (2.5%)	
≥ 3	19,795 (1.4%)	4,803 (1.4%)	1,930 (1.0%)	3,983 (3.1%)	9,079 (1.1%)	
Year of diagnosis						< 0.001
2004–2007	106,265 (7.3%)	26,855 (7.9%)	13,923 (7.3%)	10,367 (8.0%)	55,120 (6.9%)	
2008–2011	288,225 (19.8%)	77,502 (22.8%)	39,053 (20.3%)	20,411 (15.8%)	151,259 (19.0%)	
2012–2015	367,636 (25.2%)	92,424 (27.2%)	50,014 (26.1%)	28,799 (22.3%)	196,399 (24.7%)	
2016–2021	695,117 (47.7%)	143,035 (42.1%)	88,932 (46.3%)	69,686 (53.9%)	393,464 (49.4%)	
Urban rural status						< 0.001
Metro	1,197,750 (82.2%)	274,631 (80.8%)	156,453 (81.5%)	107,741 (83.4%)	658,925 (82.8%)	
Urban	184,155 (12.6%)	46,072 (13.6%)	24,968 (13.0%)	15,476 (12.0%)	97,639 (12.3%)	
Rural	27,653 (1.9%)	7,241 (2.1%)	3,966 (2.1%)	2,092 (1.6%)	14,354 (1.8%)	
Unknown	47,685 (3.3%)	11,872 (3.5%)	6,535 (3.4%)	3,954 (3.1%)	25,324 (3.2%)	
Geographic region						< 0.001
Northeast	278,903 (19.1%)	50,745 (14.9%)	28,768 (15.0%)	26,331 (20.4%)	173,059 (21.7%)	
South	511,171 (35.1%)	131,856 (38.8%)	63,861 (33.3%)	48,537 (37.5%)	266,917 (33.5%)	

Total (N)	Overall ¹	Mx-RT ¹	Mx+RT ¹	BCS-RT ¹	BCS+RT ¹	pvalue ²
	1,457,243	339,816	191,922	129,263	796,242	
Midwest	338,946 (23.3%)	74,965 (22.1%)	41,947 (21.9%)	29,529 (22.8%)	192,505 (24.2%)	
West	245,907 (16.9%)	52,861 (15.6%)	30,293 (15.8%)	22,700 (17.6%)	140,053 (17.6%)	
Unknown	82,316 (5.6%)	29,389 (8.6%)	27,053 (14.1%)	2,166 (1.7%)	23,708 (3.0%)	
Treatment facility size						< 0.001
100–499 cases/year	102,493 (7.0%)	22,244 (6.5%)	11,377 (5.9%)	10,859 (8.4%)	58,013 (7.3%)	
≥ 500 cases/year	577,457 (39.6%)	131,070 (38.6%)	67,538 (35.2%)	52,991 (41.0%)	325,858 (40.9%)	
Academic program ⁴	396,864 (27.2%)	89,484 (26.3%)	50,537 (26.3%)	34,918 (27.0%)	221,925 (27.9%)	
Others	380,429 (26.1%)	97,018 (28.6%)	62,470 (32.5%)	30,495 (23.6%)	190,446 (23.9%)	
Primary payer						< 0.001
Private/Managed	776,160 (53.3%)	192,180 (56.6%)	118,919 (62.0%)	30,656 (23.7%)	434,405 (54.6%)	
Medicaid	95,942 (6.6%)	23,896 (7.0%)	20,517 (10.7%)	5,228 (4.0%)	46,301 (5.8%)	
Medicare	527,650 (36.2%)	109,124 (32.1%)	41,787 (21.8%)	89,657 (69.4%)	287,082 (36.1%)	
Other/Unknown	57,491 (3.9%)	14,616 (4.3%)	10,699 (5.6%)	3,722 (2.9%)	28,454 (3.6%)	
Income⁴						< 0.001
Low Income (<\$46K)	179,486 (12.3%)	46,040 (13.5%)	26,035 (13.6%)	16,771 (13.0%)	90,640 (11.4%)	
Lower-Mid (\$46K-\$57K)	254,672 (17.5%)	61,451 (18.1%)	34,208 (17.8%)	23,780 (18.4%)	135,233 (17.0%)	
Upper-Mid (\$57K-\$74K)	301,707 (20.7%)	70,394 (20.7%)	39,531 (20.6%)	27,593 (21.3%)	164,189 (20.6%)	
High Income (\$74K+)	524,606 (36.0%)	117,870 (34.7%)	66,035 (34.4%)	44,085 (34.1%)	296,616 (37.3%)	

Total (N)	Overall ¹	Mx-RT ¹	Mx+RT ¹	BCS-RT ¹	BCS+RT ¹	pvalue ²
	1,457,243	339,816	191,922	129,263	796,242	
Unknown	196,772 (13.5%)	44,061 (13.0%)	26,113 (13.6%)	17,034 (13.2%)	109,564 (13.8%)	
Crowfly distance (miles)⁵						< 0.001
≤ 5	365,516 (25.1%)	78,607 (23.1%)	44,723 (23.3%)	36,255 (28.0%)	205,931 (25.9%)	
5–10	307,551 (21.1%)	68,229 (20.1%)	39,424 (20.5%)	27,716 (21.4%)	172,182 (21.6%)	
11–25	367,001 (25.2%)	87,117 (25.6%)	49,698 (25.9%)	29,969 (23.2%)	200,217 (25.1%)	
26–50	141,161 (9.7%)	37,534 (11.0%)	19,998 (10.4%)	11,754 (9.1%)	71,875 (9.0%)	
> 50	93,812 (6.4%)	27,759 (8.2%)	13,869 (7.2%)	7,843 (6.1%)	44,341 (5.6%)	
Unknown	182,202 (12.5%)	40,570 (11.9%)	24,210 (12.6%)	15,726 (12.2%)	101,696 (12.8%)	
Chemotherapy use						< 0.001
No/unknown	829,990 (57.0%)	190,039 (55.9%)	27,391 (14.3%)	111,766 (86.5%)	500,794 (62.9%)	
Yes	627,253 (43.0%)	149,777 (44.1%)	164,531 (85.7%)	17,497 (13.5%)	295,448 (37.1%)	
Hormone therapy use						< 0.001
No/unknown	407,228 (27.9%)	118,126 (34.8%)	52,388 (27.3%)	57,183 (44.2%)	179,531 (22.5%)	
Yes	1,050,015 (72.1%)	221,690 (65.2%)	139,534 (72.7%)	72,080 (55.8%)	616,711 (77.5%)	
Immunotherapy use						< 0.001
No/unknown	1,334,730 (91.6%)	308,066 (90.7%)	164,195 (85.6%)	125,373 (97.0%)	737,096 (92.6%)	
Yes	122,513 (8.4%)	31,750 (9.3%)	27,727 (14.4%)	3,890 (3.0%)	59,146 (7.4%)	
Abbreviations: Mx, Mastectomy; BCS, Breast-conserving surgery; RT, radiotherapy; NH, Non-Hispanic; LVI, lymphovascular invasion; CCI, Charlson comorbidity index.						

Total (N)	Overall ¹	Mx-RT ¹	Mx+RT ¹	BCS-RT ¹	BCS+RT ¹	pvalue ²
	1,457,243	339,816	191,922	129,263	796,242	
¹ Median (Q1, Q3); n (%).						
² Kruskal-Wallis rank sum test; Pearson's Chi-squared test.						
³ Academic/research programs treating ≥ 500 cases/year.						
⁴ Median household income for each patient's area of residence, estimated using 2020 American Community Survey data and adjusted for 2020 inflation.						
⁵ The great circle distance between the patient's residence and the case-reporting hospital.						

During follow-up, 236,994 deaths occurred. The overall 5-year and 10-year OS estimates were 89.9% (95% CI: 89.9%–90.0%) and 78.1% (95% CI: 78.0%–78.2%), respectively. In unweighted analyses, patients receiving BCS + RT demonstrated better survival than those undergoing Mx – RT, with 5-year OS of 94.0% (95% CI: 94.0%–94.1%) vs. 88.1% (88.0%–88.2%) and 10-year OS of 84.4% (84.2%–84.5%) vs. 76.0% (75.8%–76.2%) (**Figure S3**). Within the BCS cohort, the unweighted survival gap between radiotherapy and no radiotherapy was substantial, with 5-year OS of 94.0% (94.0%–94.1%) vs. 78.2% (78.0%–78.5%) and 10-year OS of 84.4% (84.2%–84.5%) vs. 55.1% (54.7%–55.5%) (**Figure S4**). For PMRT-indicated Mx patients, survival difference was less pronounced between PMRT and no PMRT, with corresponding 5-year OS of 83.2% (83.0%–83.4%) vs. 79.0% (78.7%–79.2%) and 10-year OS of 69.1% (68.8%–69.4%) vs. 65.0% (64.7%–65.4%) (**Figure S5**).

After overlap weighting, survival differences were attenuated but remained clinically meaningful. Patients receiving BCS + RT continued to demonstrate better survival than those undergoing Mx – RT, with 5-year OS of 93.2% (95% CI: 93.1%–93.3%) vs. 89.3% (89.2%–89.4%) and 10-year OS of 83.7% (83.5%–83.8%) vs. 77.2% (77.0%–77.3%) (Fig. 1). Within the BCS cohort, the weighted survival differences remained markedly pronounced in favor of adjuvant radiotherapy, with 5-year OS of 89.5% (95% CI: 89.3%–89.6%) vs. 82.6% (82.4%–82.9%) and 10-year OS of 71.8% (71.5%–72.1%) vs. 62.8% (62.3%–63.2%) (Fig. 2a). Among PMRT-indicated Mx patients, weighted survival estimates were smaller but persisted after weighting, with 5-year OS of 82.9% (82.6%–83.1%) vs. 80.5% (80.3%–80.8%) and 10-year OS of 69.1% (68.8%–69.5%) vs. 68.1% (67.7%–68.4%) for PMRT and no PMRT, respectively (Fig. 2b).

Overall, radiotherapy receipt was associated with 37% (HR, 0.63; 95% CI: 0.62–0.63) and 14% (HR, 0.86; 95% CI: 0.84–0.87) lower hazards of all-cause mortality after BCS and PMRT-indicated Mx, respectively. After age-stratification, weighted within-surgery comparisons demonstrated a consistent association between radiotherapy receipt and improved OS across age groups (Fig. 3). Among patients undergoing BCS, adjuvant radiotherapy receipt was associated with higher 5-year OS and a lower hazard of mortality compared with no radiotherapy in every age group, with HRs ranging from 0.494 (95% CI: 0.475–0.515) among patients aged 50–64 years to 0.713 (95% CI: 0.699–0.727) among patients aged ≥ 75 years

(Fig. 3a). Similarly, among PMRT-indicated mastectomy patients, OS was higher for PMRT across age groups compared to no PMRT, although the magnitude was more modest, with HRs ranging from 0.773 (95% CI: 0.745–0.801) among patients aged ≥ 75 years to 0.937 (95% CI: 0.893–0.982) among patients aged 40–49 years (Fig. 3b). Associations with OS remained directionally consistent when radiotherapy receipt was modeled as a time-varying exposure in sensitivity analyses (**Table S2**).

We observed substantial heterogeneity in documented reasons for radiotherapy omission. Among PMRT-indicated Mx patients, radiotherapy receipt declined progressively with age, with a sharper decline among those aged 75 years or older (from 59.2% in the 65–74 years group to 41.6%) (Table 2a). Similarly, radiotherapy receipt after BCS remained high among patients aged < 40 , 40–49, and 50–64 years ($> 90\%$) but decreased beginning at age 65, with a pronounced decline among those aged ≥ 75 years (58.6%) (Table 2b). Across both cohorts, reduced radiotherapy utilization among older patients was driven largely by radiotherapy not being selected as part of the treatment plan or by patient refusal despite physician recommendation. Documented patient risk factors such as frailty or comorbidities, death before planned radiotherapy, and unspecified reasons for radiotherapy omission were uncommon ($< 4\%$) across all age groups in both cohorts. Age-related declines in radiotherapy receipt persisted after adjusting for baseline covariates, including comorbidities. Among PMRT-indicated patients, the adjusted marginal probability of radiotherapy receipt progressively declined from 66.9% among patients aged < 40 years to 57.1% for patients aged ≥ 75 years (**Figure S6**). After BCS, the adjusted probability peaked at 92.5% among patients aged 50–64 years and subsequently decreased to 86.4% among those aged 65–74 years and 72.1% among those aged ≥ 75 years.

Table 2
a. Reasons of RT Non-Receipt by Age, among Mx Patients Indicated for PMRT

Reason for no RT	< 40	40–49	50–64	65–74	75+
Radiation received	25131 (72.8%)	46633 (69.2%)	67803 (66.0%)	26257 (59.2%)	12676 (41.6%)
Not administered: RT not selected among treatment options ¹	7915 (22.9%)	17794 (26.4%)	29187 (28.4%)	14509 (32.7%)	13035 (42.8%)
Not administered: patient risk factors ²	215 (0.6%)	430 (0.6%)	907 (0.9%)	583 (1.3%)	1118 (3.7%)
Not administered: recommended, documented patient refusal	1019 (3.0%)	2106 (3.1%)	4064 (4.0%)	2501 (5.6%)	3241 (10.6%)
Not administered: recommended, reason not documented	205 (0.6%)	411 (0.6%)	699 (0.7%)	335 (0.8%)	259 (0.9%)
Not administered: recommended, death prior to RT	24 (0.1%)	44 (0.1%)	137 (0.1%)	141 (0.3%)	124 (0.4%)

Abbreviations: Mx, Mastectomy; RT, radiotherapy; PMRT, Post-mastectomy radiotherapy.

¹Treatment plan offered multiple alternative treatment options and the patient did not select RT.

²Examples include advanced frailty, comorbid conditions, etc.

Table 2
b. Reasons of RT Non-Receipt by Age, among BCS Patients

Reason for no RT	< 40	40–49	50–64	65–74	75+
Radiation received	23708 (91.6%)	114806 (94.3%)	345692 (94.5%)	222970 (85.8%)	89066 (58.6%)
Not administered: RT not selected among treatment options ¹	1308 (5.1%)	4043 (3.3%)	10102 (2.8%)	20664 (7.9%)	39518 (26.0%)
Not administered: patient risk factors ²	107 (0.4%)	247 (0.2%)	1087 (0.3%)	2043 (0.8%)	4579 (3.0%)
Not administered: recommended, documented patient refusal	635 (2.5%)	2351 (1.9%)	8024 (2.2%)	13177 (5.1%)	17583 (11.6%)
Not administered: recommended, reason not documented	108 (0.4%)	296 (0.2%)	813 (0.2%)	785 (0.3%)	932 (0.6%)
Not administered: recommended, death prior to RT	8 (0.0%)	48 (0.0%)	267 (0.1%)	340 (0.1%)	198 (0.1%)

Abbreviations: BCS, Breast-conserving surgery; RT, radiotherapy; PMRT, Post-mastectomy radiotherapy.

¹Treatment plan offered multiple alternative treatment options and the patient did not select RT.

²Examples include frailty, comorbid conditions, etc.

DISCUSSION

In this large NCDB cohort of patients with stage I–III breast cancer, BCS + RT was associated with higher OS compared with Mx – RT after overlap weighting on clinical, socioeconomic, and demographic characteristics. Radiotherapy receipt corresponded to a 37% reduction in hazard of all-cause mortality observed among patients undergoing BCS and a 14% reduction among PMRT-indicated patients undergoing Mx. The association between radiotherapy receipt and improved OS persisted across age groups. Despite these findings, radiotherapy omission increased with age and was driven largely by radiotherapy not being selected as part of treatment and by patient refusal, rather than documented patient risk factors or contraindications. Age-related declines in radiotherapy receipt persisted after

adjusting for baseline covariates such as comorbidities. These findings raise concern for potential age-related underutilization of radiotherapy among patients who may remain eligible for postoperative treatment.

An Early Breast Cancer Trialists' Cooperative Group (EBCTCG) meta-analysis of randomized trials demonstrated that radiotherapy following BCS reduced 10-year recurrence by approximately half and 15-year breast cancer mortality by approximately one-sixth [11], while a separate PMRT meta-analysis showed that radiotherapy significantly reduced recurrence and breast cancer mortality after Mx among women with 1–3 and ≥ 4 positive nodes [12]. Observational studies have reported improved OS among patients receiving postoperative radiotherapy after BCS compared with BCS alone [25, 26]. Our results extend these studies by demonstrating that, among PMRT-indicated Mx patients, PMRT was associated with a modest absolute survival gain but a meaningful relative reduction in mortality hazard in a real-world population.

Several clinical trials have supported omission of radiotherapy after BCS among selected older women with low-risk, hormone receptor-positive, node-negative breast cancer receiving endocrine therapy [17, 18, 27]. However, these studies should not be generalized to older patients with broader stage I–III disease or to older PMRT-indicated Mx patients. In our analyses, the association between radiotherapy receipt and higher OS remained evident across age groups among both patients undergoing BCS as well as PMRT-indicated Mx patients, suggesting that among the general patient population, patients still experience survival advantages associated with radiotherapy across age groups.

We observed a decline in radiotherapy utilization with increasing age after adjusting for measured covariates. This finding is consistent with prior studies reporting that radiotherapy use decreases substantially with age [28] and that chronological age may influence radiotherapy recommendation independent of clinical risk [14, 19, 20]. Our findings suggest that this pattern may reflect treatment non-selection and patient refusal rather than documented contraindications and patient risk factors such as frailty or comorbidities. Factors like fear of side effects [29], logistical burden [26], socioeconomic factors [29], as well as physician recommendation [14, 30] remain major determinants of treatment acceptance. Many of these factors are incompletely captured in NCDB and could correlate with age. Given the observed association between radiotherapy receipt and improved survival across age groups, physicians should discuss the potential survival benefits of adjuvant radiotherapy while incorporating functional status, comorbidity, and patient preferences to support informed, individualized treatment decisions.

To our knowledge, this paper is the first to jointly investigate age-stratified survival associations of postoperative radiotherapy within clinically indicated surgical strata encompassing both patients undergoing BCS and PMRT-indicated Mx patients. We disaggregated reasons for radiotherapy omission and estimated adjusted marginal probabilities of radiotherapy receipt across age strata, providing insight into whether omission reflected patient preference, risk factors, or other documented baseline covariates in a large, real-world population. By characterizing both age-specific survival patterns, reasons for

radiotherapy omission, and adjusted utilization, our analyses may inform more individualized decision-making surrounding adjuvant radiotherapy utilization in the U.S.

Despite these strengths, several limitations should be considered. As with all observational studies, residual confounding from unmeasured prognosticators remains possible despite propensity-score weighting and covariate adjustment. Variables such as genetic risk, functional status, and comorbidity burden are incompletely captured within NCDB and may influence both treatment selection and survival. Misclassification of the reasons for radiotherapy omission is also possible. In addition, our follow-up time may be insufficient to capture late mortality differences due to recent advances in long-term breast cancer survival [31]. The NCDB lacks information on adherence to indicated systemic therapies, particularly adjuvant endocrine therapy [32, 33], which may have influenced survival estimates. Furthermore, the NCDB does not capture recurrence and cause-specific mortality, limiting the comprehensive analysis of survival differences. Finally, because the NCDB is derived from Commission on Cancer–accredited hospitals, our findings may not be fully generalizable to non-CoC–accredited settings or international populations.

CONCLUSION

In a large cohort of locoregional stage I–III breast cancer patients, radiotherapy receipt was associated with improved overall survival across surgical approaches and age groups. In contrast, radiotherapy omission increased substantially with age after covariate adjustment and was driven primarily by treatment nonselection and patient refusal. These findings suggest that chronological age alone should not determine omission of postoperative radiotherapy and underscore the need for individualized counseling that weighs expected survival benefit, treatment burden, and patient preferences.

DECLARATIONS

Clinical Trial Number

Not applicable.

Author Contributions

Concept and design: LS, MLP, XKZ, SCF, RT.

Data curation, formal analysis, and interpretation: LS, YC, MS.

Drafting of the manuscript: LS.

Critical review of the manuscript for important intellectual content: LS, MLP, AY, SCF, XKZ, RT.

Statistical analysis: LS.

Administrative support: LS, AY, YC, MS.

Supervision: MLP, SCF, XKZ, RT.

Conflict of Interest Disclosures

The authors declare no conflicts of interest.

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Data Sharing Statement

The data used in this analysis were provided by the National Cancer Database under a data use agreement. Investigators interested in the NCDB data may apply for access to the National Cancer Database Participant User Files at <https://www.facs.org/quality-programs/cancer-programs/national-cancer-database/puf/>.

Ethics Approval

This is an observational study. No ethical approval is required.

Author Contribution

LS-wrote the main manuscript text and prepared figures , contributed to analysisYC-wrote the main manuscript and prepared figures, contributed to analysisAY-wrote the main manuscript and prepared figures, contributed to analysisMS-contributed to analysis, prepared figuresSF-contributed to designKZ-contributed to statistics and designRT-contributed to statistics and designMP-contributed to statistics, design, All authors reviewed the manuscript

Acknowledgement

n/a

Data Availability

All data supporting the findings of this study are available within the paper and its Supplementary Information

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Figures

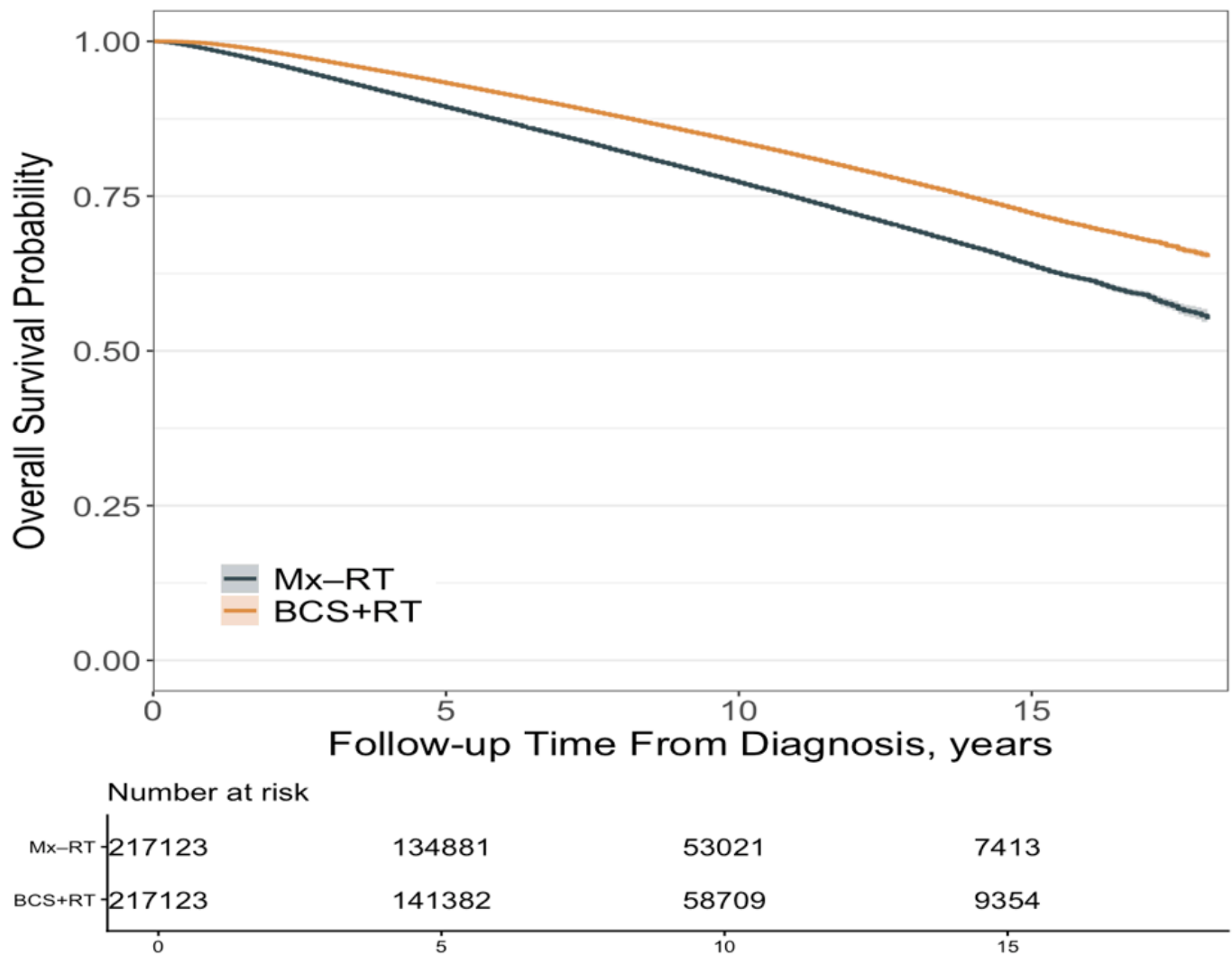


Figure 1

Overlap-weighted Kaplan–Meier Curves of Overall Survival Comparing Mastectomy without adjuvant RT vs BCS with adjuvant RT.

*Kaplan-Meier curves are overlap propensity score–weighted and balanced across age, race/ethnicity, tumor size, number of positive lymph nodes, histology, tumor grade, lymphovascular invasion, breast cancer receptor, Charlson-Deyo score, year of diagnosis group, urban/rural status, region, facility level, insurance, income, distance from home to treatment facility, chemotherapy use, hormone therapy use, and immunotherapy use.

**Numbers at risk are based on effective sample sizes and do not reflect raw patient counts.

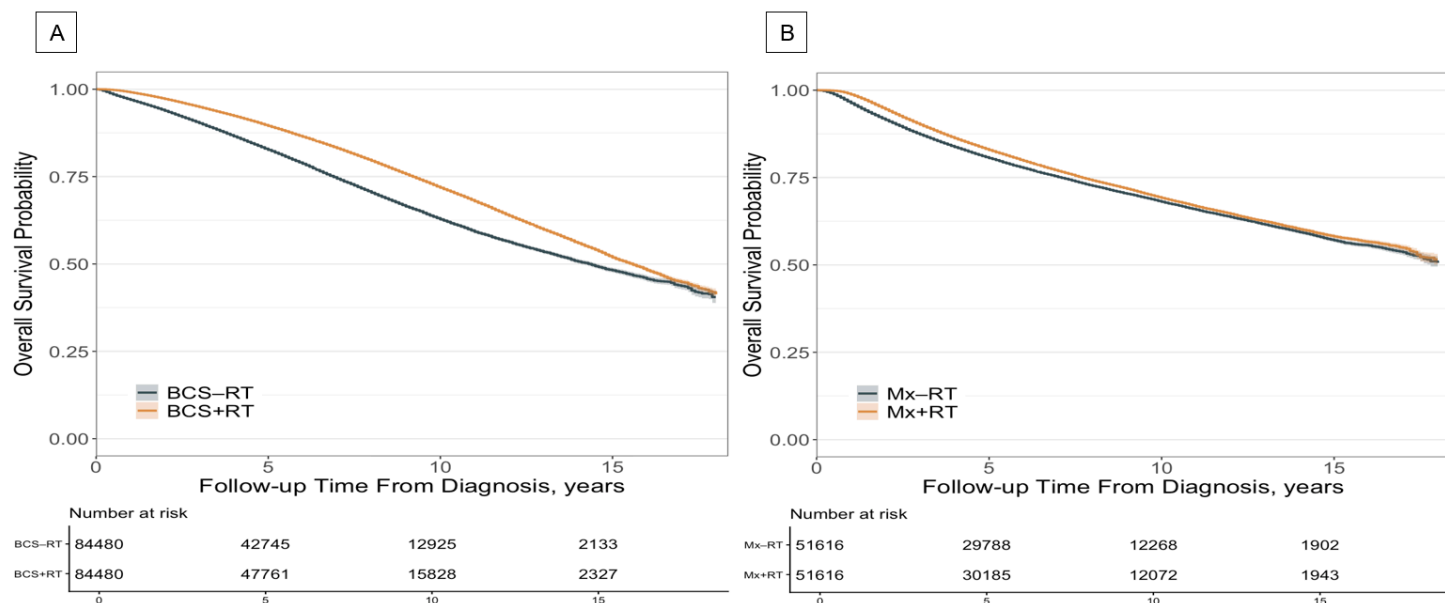


Figure 2

Overlap-weighted Kaplan-Meier Curves of Overall Survival and Adjuvant Radiotherapy among (A) BCS Patients and (B) PMRT-indicated Mastectomy Patients.

*Kaplan-Meier curves are overlap propensity score-weighted and balanced across age, race/ethnicity, tumor size, number of positive lymph nodes, histology, tumor grade, lymphovascular invasion, breast cancer receptor, Charlson-Deyo score, year of diagnosis group, urban/rural status, region, facility level, insurance, income, distance from home to treatment facility, chemotherapy use, hormone therapy use, and immunotherapy use.

**Numbers at risk are based on effective sample sizes and do not reflect raw patient counts.

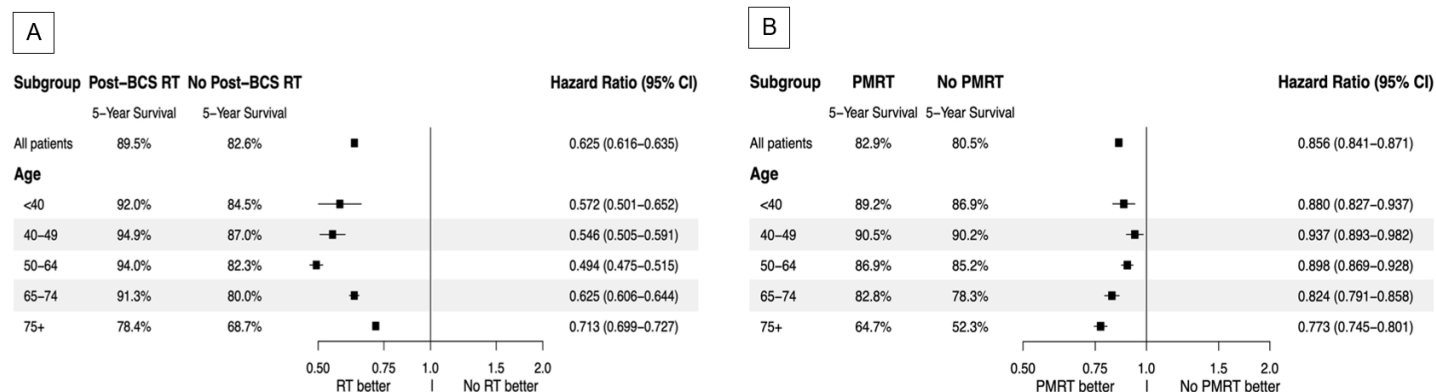


Figure 3

Overlap-weighted Age-stratified Association Between Overall Survival and Adjuvant Radiotherapy among (A) BCS patients and (B) PMRT-indicated Mastectomy Patients.

*Hazard ratios estimated using overlap propensity score–weighted Cox proportional hazards models; adjusted for age, race/ethnicity, tumor size, number of positive lymph nodes, histology, tumor grade, lymphovascular invasion, breast cancer receptor, Charlson-Deyo score, year of diagnosis group, urban/rural status, region, facility level, insurance, income, distance from home to treatment facility, chemotherapy use, hormone therapy use, and immunotherapy use.

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