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Cost and Complications of Local Therapies for Early-Stage Breast Cancer

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Abstract

Background: Guideline-concordant local therapy options for early breast cancer include lumpectomy plus whole breast irradiation (Lump+WBI), lumpectomy plus brachytherapy, mastectomy alone, mastectomy plus reconstruction, and, in older women, lumpectomy alone. We performed a comparative examination of each treatment's complications and cost to assess their relative values.
Methods: Using the MarketScan database of younger women with private insurance and the SEER-Medicare database of older women with public insurance, we identified 105 211 women with early breast cancer diagnosed between 2000 and 2011. We used diagnosis and procedural codes to identify treatment complications within 24 months of diagnosis and compared complications by treatment using two-sided logistic regression. Mean total and complication-related cost, relative to Lump+WBI, were calculated from a payer's perspective and adjusted for differences in covariables using linear regression. All statistical tests were two-sided.
Results: Lump+WBI was the most commonly used treatment. Mastectomy plus reconstruction was associated with nearly twice the complication risk of Lump+WBI (Marketscan: 54.3% vs 29.6%, relative risk [RR] = 1.87, 95% confidence interval [CI] = 1.82 to 1.91, $P < .001$; SEER-Medicare: 66.1% vs 37.6%, RR = 1.75, 95% CI = 1.69 to 1.82, $P < .001$) and was also associated with higher adjusted total cost (Marketscan: $22 481 greater than Lump+WBI; SEER-Medicare: $1748 greater) and complication-related cost (Marketscan: $9017 greater; SEER-Medicare: $2092 greater). Brachytherapy had modestly higher total cost and complications than WBI. Lumpectomy alone entailed lower cost and complications in the SEER-Medicare cohort only.
Conclusions: Mastectomy plus reconstruction results in substantially higher complications and cost than other guideline-concordant treatment options for early breast cancer. These findings are relevant to patients evaluating their local therapy options and to value-based population health management.

Achieving value for patients, defined as the quality of outcomes per dollar spent, has captured the attention of health care policy makers as a way to improve care and reduce costs across whole populations (1,2). The case for value-based care is especially compelling in oncology, where both underuse of effective and inexpensive therapies and overuse of costly but equally effective or marginally better interventions are prevalent (1,3). Likewise, breast cancer is a cogent target within oncology as it

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now accounts for the highest number of new cancer cases in the United States and requires substantial societal resources for care of those diagnosed with the disease (4). Of the nearly 250 000 breast cancer patients diagnosed this year (4), over 60% will present with localized, early-stage disease (5) for which the National Comprehensive Cancer Network (NCCN) Guidelines identify several evidence-based local management options including mastectomy (Mast alone), mastectomy plus reconstruction (Mast+Recon), lumpectomy plus whole breast irradiation (Lump+WBI), and, in certain cases, lumpectomy plus brachytherapy (Lump+Brachy) or lumpectomy followed by endocrine therapy alone without radiation (Lump alone) (6).

Evidence suggests that real-world decision-making among these options is currently driven by patient and provider preferences, geography, and accessibility to certain treatments (7–10). Incorporating the risk of complications, cost, and considerations of value into the clinical decision may be a more rational approach to ensuring affordable, effective care for this broad and diverse patient population. Because the local treatment options above are associated with similar survival, their costs, complications, and quality of life implications underpin the value calculation (11,12). And yet, little research has sought to quantify and compare the expense and toxicities of these therapies in contemporary practice. To address this gap in knowledge, we compared the costs and complications associated with each local strategy using two complementary databases consisting of younger women with private insurance (MarketScan) and older women with public insurance (SEER-Medicare) diagnosed with breast cancer between 2000 and 2011.

Methods

Data Sources

The MarketScan Commercial Claims and Encounters database (Truven Health Analytics, Ann Arbor, MI) is a convenience sample of individual-level medical and drug insurance claims for patients under the age of 65 years. The claims are derived from 45 large employers and more than 100 health insurers that provide private insurance to employees, spouses, and dependents. Healthcare is provided under a variety of fee-for-service, capitated, and partially capitated health plans, including preferred provider organizations and health maintenance organizations. In 2002, the data set was expanded to include small- and medium-sized firms.

The Surveillance, Epidemiology, and End Results (SEER)–Medicare database captures clinical, pathological, and Medicare claims data for incident cancers diagnosed in Medicare beneficiaries who reside within one of 16 geographic areas accounting for 26% of the US population. The case ascertainment rate is approximately 98%, and 93% of patients in SEER are successfully linked to Medicare claims (13).

Study Subjects

A validated, claims-based algorithm was used to identify incident breast cancer cases in the MarketScan data from 2000 to 2011 (Supplementary Table 1, available online) (14). This algorithm has a published sensitivity of 82% to 87% and a specificity exceeding 99% for early-stage breast cancer (14,15). SEER data were used to identify incident breast cancer cases in the SEER-Medicare cohort during the same years. To enable determination of prediagnosis comorbidity and postdiagnosis treatments and outcomes, the cohorts were limited to patients with complete insurance coverage from 12 months prior through 24 months after diagnosis. In addition, as the intent was to assess the value of treatments appropriate for early breast cancer, we excluded patients treated with neoadjuvant chemotherapy or postmastectomy radiation, both of which are generally used for more advanced stage disease. Staging data are not available in MarketScan claims, so diagnosis codes were used to exclude patients with distant metastasis (Supplementary Table 2, available online). In contrast, staging data are present in the SEER-Medicare cohort and were used to limit this cohort to patients with early cancer, defined as stage T1-2 N0-1 M0 (16). The analytic cohorts were further limited to patients treated with either Lump+WBI, Lump+Brachy, Lump alone, Mast alone, and Mast+Recon. This approach yielded 44 344 patients from the MarketScan data (median age = 53 years) and 60 867 patients from the SEER-Medicare database (median age = 75 years) (Supplementary Table 1, available online).

Definitions of Study Variables

Breast surgery and radiation were classified using claims within one year of diagnosis as in prior studies (Supplementary Table 2, available online) (17). The most extensive breast surgery (lumpectomy vs mastectomy) within the first year after diagnosis was considered the definitive surgery. Oncologic breast surgeries in the second year of diagnosis were considered secondary surgeries not part of the initial treatment course. The Lump+WBI group was limited to those patients who received at least 15 unique external beam radiation treatments without concomitant brachytherapy. The Lump+Brachy group was limited to patients who received brachytherapy without concomitant external beam radiation. The Mast+Recon group included patients with mastectomy within one year of diagnosis and a code for breast reconstruction within two years of diagnosis (7).

Additional treatment variables derived from claims included receipt of chemotherapy, trastuzumab, axillary surgery, and/or contralateral mastectomy. For the SEER-Medicare cohort, tumor characteristics were extracted from SEER data. For the MarketScan cohort, adjuvant endocrine therapy within one year of diagnosis was determined using National Drug Codes (Supplementary Table 3, available online).

Statistical Analysis

Complications within two years of diagnosis were determined using claims and included wound complication, infection, hematoma/seroma, breast pain, fat necrosis, radiation pneumonitis, rib fracture, graft/implant complication, implant removal, and other postoperative complications (Supplementary Table 4, available online) (17–19). Risks of complications separately and in aggregate by treatment were compared using the chi-square test. The relative risk of complications was determined using multivariable logistic regression with candidate covariables selected based on a priori clinical significance and/or univariate statistical significance ($P < .25$). The model was iteratively refined to minimize collinearity. Goodness of fit was assessed using the Hosmer-Lemeshow method. Odds ratios were converted to relative risks (20).

Cumulative net payer cost within two years of diagnosis was calculated using all inpatient, outpatient, and carrier claims from within two years of diagnosis. All costs were adjusted to 2014 dollars using the Prospective Payment System for inpatient

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claims and the Medicare Economic Index for outpatient claims. Complication cost was determined by summing all costs occurring on days when a diagnosis or procedure code indicating a complication occurred. Noncomplication cost was the difference between total cost and complication cost and thus approximates the cost of treatment in the absence of complications. To account for highly skewed distribution of medical costs, generalized linear regression (log link function, gamma distribution) models were created for each cost outcome. Each cost model began with the candidate variables listed in Table 1 and was iteratively refined to optimize fit and minimize collinearity.

Exploratory analyses evaluated the impact of WBI fractionation (hypofractionation: 15–22 treatments; conventional fractionation: $\geq$23 treatments), unilateral vs bilateral mastectomy, and type of breast reconstruction on complications and cost.

All statistical tests were two-sided, with a *P* value of .05 or less indicating statistical significance. Analyses were conducted using SAS v. 9.3 (Cary, NC) and STATA/MP 13.1 (College Station, TX). Lump+WBI served as the referent category for all analyses. The SEER-Medicare data set and the MarketScan data set are assembled with different selection methodology. Therefore no direct statistical comparisons or inferences between these two groups were conducted. Our institutional review board granted this study exempt status.

Results

Patient Characteristics and Extent of Complications

We identified 105 211 patients (44 344 MarketScan, 60 867 SEER-Medicare) diagnosed with early-stage breast cancer between 2000 and 2011. Baseline features are enumerated in Table 1. Lump+WBI was the most common treatment in both cohorts.

Unadjusted and adjusted total complication rates are provided in Figure 1 and Table 2, respectively. Rates of individual complications for each treatment are enumerated in Supplementary Table 5 (available online). Mast+Recon was associated with the highest complication risk in all years studied for both cohorts (Figure 1). In adjusted models, Mast+Recon was associated with a statistically significantly higher complication risk than Lump+WBI (MarketScan: 54.3% vs 29.6%, relative risk [RR] = 1.87, 95% confidence interval [CI] = 1.82 to 1.91, $P < .001$; SEER-Medicare: 66.1% vs 37.6%, RR = 1.75, 95% CI = 1.69 to 1.82, $P < .001$). Common complications after Mast+Recon included infection (24.5% for MarketScan, 30.9% for SEER-Medicare), hematoma/seroma (16.3%, 20.3%), implant removal (15.0%, 19.9%), wound complication (12.8%, 11.7%, respectively), and graft/implant complications (9.5%, 13.6%) (Supplementary Table 5, available online). Unlike Mast+Recon, Mast alone was not associated with increased complication risk compared with Lump+WBI (MarketScan: RR = 0.88, 95% CI = 0.85 to 0.91; SEER-Medicare: RR = 0.98, 95% CI = 0.96 to 1.00).

Alternative breast conserving strategies were also compared with Lump+WBI. In both cohorts, Lump+Brachy was associated with higher complication risk than Lump+WBI (Marketscan: 44.5% vs 29.6%, RR = 1.47, 95% CI = 1.40 to 1.53; SEER-Medicare: 50.6% vs 37.6%, RR = 1.36, 95% CI = 1.31 to 1.41). In the SEER-Medicare population, where Lump alone is a guideline-concordant treatment option for selected patients (6), Lump alone was associated with lower complication risk than Lump+WBI (30.5% vs 37.6%, RR = 0.87, 95% CI = 0.83 to 0.90).

Counterintuitively, Lump alone had modestly higher complications than Lump+WBI among the younger women in the MarketScan cohort (31.0% vs 29.6%, RR = 1.10, 95% CI = 1.04 to 1.16). This result is likely because of the finding that 13.3% (335/2513) of patients who underwent Lump alone (defined as within the first year of diagnosis) subsequently underwent mastectomy and reconstruction in the second year after diagnosis. Furthermore, use of mastectomy and reconstruction in year 2, after initial management with Lump alone in year 1, increased substantially over time, rising to 36.2% (47/130) of patients initially managed with Lump alone in 2011 in the MarketScan cohort.

We next performed exploratory analyses on treatment subgroups including hypofractionated WBI, bilateral mastectomy, and subtypes of reconstruction (Supplementary Table 6, available online). Hypofractionated WBI was associated with a similar rate of complications as conventional WBI (Marketscan: RR = 0.99, 95% CI = 0.91 to 1.07; SEER-Medicare: RR = 1.01, 95% CI = 0.96 to 1.07; referent hypofractionated WBI). In comparison with Lump+WBI, bilateral Mast alone was associated with higher complication risk in the Marketscan cohort (RR = 1.21, 95% CI = 1.10 to 1.33) but not in the SEER-Medicare cohort (RR = 1.07, 95% CI = 0.96 to 1.18). In contrast, unilateral Mast alone was associated with lower complication risk than Lump+WBI in the MarketScan cohort (RR = 0.86, 95% CI = 0.82 to 0.89) but not in the SEER-Medicare cohort (RR = 0.98, 95% CI = 0.95 to 1.00).

For patients undergoing Mast+Recon, both bilateral Mast+Recon (MarketScan: RR = 1.80, 95% CI = 1.75 to 1.86; SEER-Medicare: RR = 1.83, 95% CI = 1.68 to 1.96) and unilateral Mast+Recon (MarketScan: RR = 1.80, 95% CI = 1.75 to 1.84; SEER-Medicare: RR = 1.73, 95% CI = 1.67 to 1.80) resulted in similar complication risk relative to Lump+WBI. All reconstruction techniques (implant, autologous tissue transfer, tissue expanders, or a combination) were associated with statistically significantly higher complication risk than Lump+WBI (RR range = 1.47–2.20).

Cost

Trends in adjusted cost for each treatment are provided in Supplementary Figure 1 (available online). All interventions experienced cost growth exceeding inflation among both patient cohorts. For comparing costs, we included only patients diagnosed in the final two years of the study period so that costs accrued during the subsequent 24 months would reflect contemporary expenditures. Table 3 stratifies the findings by treatment strategy and highlights the portion attributable to complications. Cost differentials relative to Lump+WBI are graphically summarized in Figure 2.

In the MarketScan cohort, Lump+WBI was associated with the lowest adjusted mean cumulative cost ($65 608) among options that provided a breast mound (ie, all treatments except for Mast alone). Mast+Recon was associated with a 34% higher adjusted cost per patient ($88 089) because of both cost of intervention ($77 316 vs $63 834) and cost of complications ($10 402 vs $1385). In the SEER-Medicare cohort, Mast+Recon was also associated with higher adjusted mean cost than lumpectomy plus WBI ($35 835 vs $34 087), which was attributable solely to cost of complications ($2641 vs $549). Subgroup analysis showed that bilateral Mast+Recon and Mast+Recon involving a combination of autologous transfer and implant were associated with higher cost for both cohorts (Supplementary Table 7, available online). Mast alone was associated with lower cost than

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Table 1 Baseline characteristics by local treatment strategy for each cohort*

	MarketScan cohort*					SEER-Medicare cohort*				
Variable	Lump+WBI (n = 16 700) No. (%)	Lump+ Brachy (n = 2313) No. (%)	Lump alone (n = 2513) No. (%)	Mast alone (n = 11 432) No. (%)	Mast+Recon (n = 11 386) No. (%)	Lump+WBI (n = 29 764) No. (%)	Lump+ Brachy (n = 2733) No. (%)	Lump alone (n = 7502) No. (%)	Mast alone (n = 19 096) No. (%)	Mast+Recon (n = 1772) No. (%)
Age, y										
<40	592 (3.5)	5 (0.2)	259 (10.3)	697 (6.1)	1221 (10.7)					
40–49	4480 (26.8)	381 (16.5)	911 (36.3)	2519 (22.0)	4320 (37.9)					
50–59	8657 (51.8)	1354 (58.5)	1135 (45.2)	5861 (51.3)	4753 (41.7)					
60–64	2971 (17.8)	573 (24.8)	208 (8.3)	2355 (20.6)	1092 (9.6)					
66–69						7368 (24.8)	661 (24.2)	644 (8.6)	3051 (16.0)	758 (42.8)
70–74						8981 (30.2)	823 (30.1)	963 (12.8)	4692 (24.6)	614 (34.7)
75–79						7376 (24.8)	661 (24.2)	1379 (18.4)	4746 (24.9)	293 (16.5)
80–84						4431 (14.9)	429 (15.7)	1892 (25.2)	3968 (20.8)	81 (4.6)
85+						1608 (5.4)	159 (5.8)	2624 (35.0)	2639 (13.8)	26 (1.5)
Race										
White						26 508 (89.1)	2467 (90.3)	6643 (88.6)	16 363 (85.7)	1642 (92.7)
Black						1678 (5.6)	151 (5.5)	498 (6.6)	1475 (7.7)	82 (4.6)
Other						1578 (5.3)	115 (4.2)	361 (4.8)	1258 (6.6)	48 (2.7)
Type of coverage										
non-HMO	13 713 (82.1)	1989 (86.0)	2035 (81.0)	9304 (81.4)	9200 (80.8)					
HMO	2987 (17.9)	324 (14.0)	478 (19.0)	2128 (18.6)	2186 (19.2)					
Covered individual										
Employ	10 304 (61.7)	1461 (63.2)	1439 (57.3)	6651 (58.2)	6641 (58.3)					
Depen	6396 (38.3)	852 (36.8)	1074 (42.7)	4781 (41.8)	4745 (41.7)					
Comorbidity										
0	15 145 (90.7)	2065 (89.3)	2289 (91.1)	9676 (84.6)	10 564 (92.8)	19 971 (67.1)	1810 (66.2)	4216 (56.2)	11 098 (58.1)	1270 (71.7)
1	1355 (8.1)	212 (9.2)	183 (7.3)	1396 (12.2)	721 (6.3)	6723 (22.6)	627 (22.9)	1948 (26.0)	5038 (26.4)	378 (21.3)
≥2	200 (1.2)	36 (1.6)	41 (1.6)	360 (3.2)	101 (0.9)	3070 (10.3)	296 (10.8)	1338 (17.8)	2960 (15.5)	124 (7.0)
Year										
2000	270 (1.6)	4 (0.2)	126 (5.0)	275 (2.4)	221 (1.9)	2015 (6.77)	30 (1.1)	481 (6.4)	1755 (9.2)	96 (5.4)
2001	300 (1.8)	1 (0.0)	116 (4.6)	282 (2.5)	238 (2.1)	2288 (7.69)	14 (0.5)	524 (7.0)	1938 (10.2)	114 (6.4)
2002	336 (2.0)	9 (0.4)	182 (7.2)	462 (4.0)	326 (2.9)	2528 (8.49)	63 (2.3)	597 (8.0)	1977 (10.4)	117 (6.6)
2003	635 (3.8)	51 (2.2)	240 (9.6)	658 (5.8)	529 (4.7)	2581 (8.67)	110 (4.0)	519 (6.9)	1781 (9.3)	122 (6.9)
2004	824 (4.9)	65 (2.8)	230 (9.2)	649 (5.7)	594 (5.2)	2550 (8.57)	142 (5.2)	616 (8.2)	1708 (8.9)	122 (6.9)
2005	1125 (6.7)	92 (4.0)	272 (10.8)	903 (7.9)	750 (6.6)	2406 (8.08)	191 (7.0)	649 (8.7)	1574 (8.2)	119 (6.7)
2006	1212 (7.3)	176 (7.6)	239 (9.5)	885 (7.7)	804 (7.1)	2479 (8.33)	256 (9.4)	680 (9.1)	1483 (7.8)	113 (6.4)
2007	1921 (11.5)	321 (13.9)	267 (10.6)	1172 (10.3)	1252 (11.0)	2502 (8.41)	333 (12.2)	616 (8.2)	1505 (7.9)	162 (9.1)
2008	1870 (11.2)	382 (16.5)	214 (8.5)	1288 (11.3)	1307 (11.5)	2476 (8.32)	371 (13.6)	626 (8.3)	1469 (7.7)	170 (9.6)
2009	2748 (16.5)	419 (18.1)	288 (11.5)	1721 (15.1)	1795 (15.8)	2618 (8.8)	390 (14.3)	641 (8.5)	1389 (7.3)	219 (12.4)
2010	2915 (17.5)	424 (18.3)	209 (8.3)	1727 (15.1)	1848 (16.2)	2619 (8.8)	418 (15.3)	745 (9.9)	1294 (6.8)	213 (12.0)
2011	2544 (15.2)	369 (16.0)	130 (5.2)	1410 (12.3)	1722 (15.1)	2702 (9.08)	415 (15.2)	808 (10.8)	1223 (6.4)	205 (11.6)
Chemotherapy										
No	10 263 (61.5)	1876 (81.1)	2200 (87.5)	8554 (74.8)	7248 (63.7	24 658 (82.9)	2484 (90.9)	7124 (95.0)	15 710 (82.3)	1263 (71.28)
Yes	6437 (38.5)	437 (18.9)	313 (12.5)	2878 (25.2)	4138 (36.3)	5106 (17.2)	249 (9.1)	378 (5.0)	3386 (17.7)	509 (28.72)

(continued)

Table 1 Continued

Variable	MarketScan cohort*					SEER-Medicare cohort*				
	Lump+WBI (n = 16 700) No. (%)	Lump+ Brachy (n = 2313) No. (%)	Lump alone (n = 2513) No. (%)	Mast alone (n = 11 432) No. (%)	Mast+Recon (n = 11 386) No. (%)	Lump+WBI (n = 29 764) No. (%)	Lump+ Brachy (n = 2733) No. (%)	Lump alone (n = 7502) No. (%)	Mast alone (n = 19 096) No. (%)	Mast+Recon (n = 1772) No. (%)
Trastuzumab										
No	15 672 (93.8)	2233 (96.5)	2482 (98.77)	11 005 (96.26)	10 643 (93.5)	28 998 (97.4)	2688 (98.4)	7439 (99.2)	18 591 (97.4)	1665 (94.0)
Yes	1028 (6.2)	80 (3.5)	31 (1.23)	427 (3.74)	743 (6.5)	766 (2.57)	45 (1.7)	63 (0.8)	505 (2.6)	107 (6.0)
Axillary surgery										
No	3456 (20.7)	514 (22.2)	1788 (71.2)	5830 (51.0)	2009 (17.6)	2042 (6.86)	106 (3.9)	3347 (44.6)	943 (4.9)	32 (1.8)
Yes	13 244 (79.3)	1799 (77.8)	725 (28.9)	5602 (49.0)	9377 (82.4)	27 722 (93.1)	2627 (96.1)	4155 (55.4)	18 153 (95.1)	1740 (98.19)
Bilateral mastectomy										
No	16 700 (100)	2313 (100)	2513 (100)	10 801 (94.5)	8015 (70.4)	29 764 (100)	2733 (100)	7502 (100)	18 542 (97.1)	1485 (83.8)
Yes	0 (0)	0 (0)	0 (0)	631 (5.5)	3371 (29.6)	0 (0)	0 (0)	0 (0)	554 (2.9)	287 (16.2)
Node positive										
No	14 520 (87.0)	2259 (97.7)	2381 (94.8)	10 239 (89.6)	9986 (87.7)	25 307 (85.0)	2604 (95.3)	7038 (93.8)	15 462 (81.0)	1464 (82.62)
Yes	2180 (13.1)	54 (2.3)	132 (5.3)	1193 (10.4)	1400 (12.3)	4457 (15.0)	129 (4.7)	464 (6.2)	3634 (19.0)	308 (17.38)
Endocrine therapy										
Yes	9930 (59.5)	1436 (62.1)	585 (23.3)	3574 (31.3)	5107 (44.9)					
No	6770 (40.5)	877 (37.9)	1928 (76.7)	7858 (68.7)	6279 (55.2)					
ER positive										
Yes						24 414 (82.0)	2387 (87.3)	6102 (81.3)	14060 (73.6)	1389 (78.39)
No						3441 (11.6)	208 (7.6)	553 (7.4)	2684 (14.1)	247 (13.94)
Unknown						1909 (6.41)	138 (5.1)	847 (11.3)	2352 (12.3)	136 (7.67)

*P value < .001 (chi-square) for all comparisons of treatment strategy by patient and treatment characteristics for each cohort. Brachy = brachytherapy; Depen = dependent; Employ = employee; HMO = Health Maintenance Organization; Lump = lumpectomy; Mast = mastectomy; SEER = Surveillance, Epidemiology, and End Results; WBI = whole breast irradiation.

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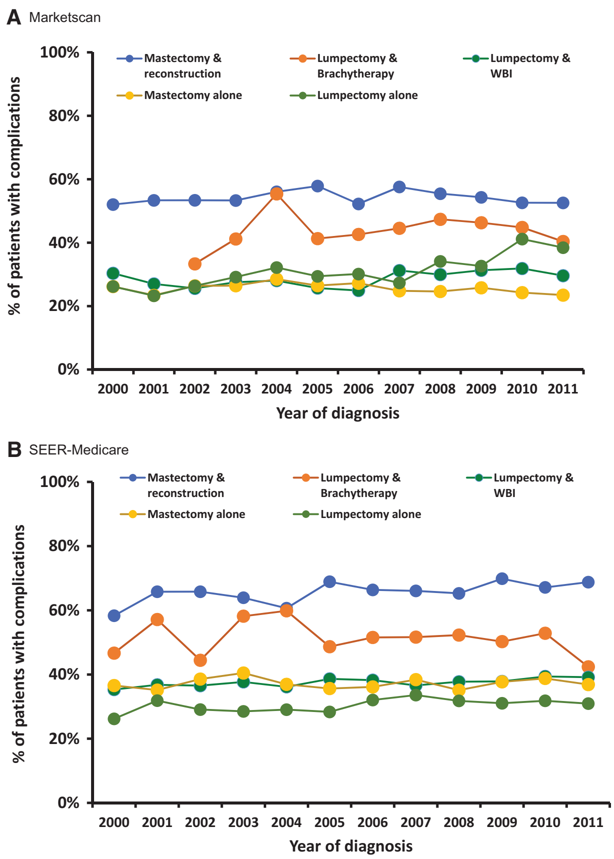

Figure 1. Complications by year of diagnosis and local therapy (unadjusted). Unadjusted time trends in risk of any complication by type of local therapy. Data for lumpectomy plus brachytherapy in 2000 and 2001 are not shown for the MarketScan cohort because of small numbers (n = 5). SEER = Surveillance, Epidemiology, and End Results; WBI = whole breast irradiation.

Table 2. Logistic regression models for any local treatment complication*

Variable	MarketScan cohort* RR (95% CI)	MarketScan cohort* P†	SEER-Medicare cohort RR (95% CI)	SEER-Medicare cohort P†
Local therapy				
Lump+WBI	1 (Ref)		1 (Ref)	
Lump+Brachy	1.47 (1.40 to 1.53)	<.001	1.36 (1.31 to 1.41)	<.001
Lump alone	1.10 (1.04 to 1.16)	.001	0.87 (0.83 to 0.90)	<.001
Mast alone	0.88 (0.85 to 0.91)	<.001	0.98 (0.96 to 1.00	.08
Mast+Recon	1.87 (1.82 to 1.91)	<.001	1.75 (1.69 to 1.82)	<.001
Age, y				
<40	1 (Ref)			
40–49	1.04 (0.99 to 1.10)	.14		
50–59	1.05 (1.00 to 1.11)	.06		
60–64	1.08 (1.01 to 1.14)	.01		
66–69			1 (Ref)	
70–74			1.00 (0.97 to 1.03)	1.00
75–79			0.97 (0.94 to 1.00)	.05
80–84			0.94 (0.91 to 0.97)	<.001
85+			0.94 (0.90 to 0.98)	.003
Race				
White			1 (Ref)	
Black			0.95 (0.90 to 0.99)	.02
Other/Unknown			0.88 (0.84 to 0.93)	<.001
Comorbidity				
0	1 (Ref)		1 (Ref)	
1	1.24 (1.19 to 1.29)	<.001	1.10 (1.08 to 1.13)	<.001
2 or higher	1.37 (1.26 to 1.48)	<.001	1.26 (1.22 to 1.29)	<.001
Chemotherapy				
None	1 (Ref)		1 (Ref)	
Without trastuzumab	1.14 (1.11 to 1.18)	<.001	1.05 (1.01 to 1.08)	.01
With trastuzumab	1.20 (1.14 to 1.27)	<.001	1.03 (0.97 to 1.10)	.32
Axillary surgery				
No			1 (Ref)	
Yes			1.14 (1.09 to 1.19)	<.001
Node positive				
No			1 (Ref)	
Yes			1.11 (1.08 to 1.15)	<.001

*No patients were excluded from either model. Brachy = brachytherapy; Lump = lumpectomy; Mast = mastectomy; Recon = reconstruction; SEER = Surveillance, Epidemiology, and End Results; WBI = whole breast irradiation.
†All P values were two-sided and calculated in the logistic regression models.

Lump+WBI among both MarketScan ($48 258) and SEER-Medicare ($22 182) patients.

With regard to lumpectomy-based strategies, Lump+Brachy was associated with $11 522 excess cost over Lump+WBI among MarketScan patients and $3530 excess cost among SEER-Medicare patients. In contrast, hypofractionated WBI was associated with $2467 and $4462 in savings per patient in Marketscan and SEER-Medicare, respectively, compared with conventional WBI (Supplementary Table 7, available online). Among MarketScan patients, Lump alone ($70 520) was more costly than Lump+WBI because of the cost associated with frequent secondary surgeries performed in the second year after diagnosis (Table 3). Among SEER-Medicare patients, Lump alone was associated with the lowest cumulative costs ($21 005) of all interventions.

Discussion

Utilizing two large databases comprised of younger women with private insurance and older women with public insurance, we characterized costs and complications during the first 24 months after diagnosis of early breast cancer treated with one of five common local therapy strategies. Despite the considerable clinical and sociodemographic differences between the two cohorts, we observed a striking concordance in the results of our analysis. In both populations, Mast+Recon was associated with nearly two-fold increased complication risk compared with Lump+WBI, a finding that persisted throughout the study interval of 2000 to 2011. Additionally, compared with Lump+WBI, Mast+Recon yielded $22 481 higher total cost and $9017 higher complication-related cost in the MarketScan cohort, and $1748 higher total cost and $2092 higher complication-related cost in the SEER-Medicare cohort.

The direct comparison of complication risk and cost outcomes between Mast+Recon and Lump+WBI, in addition to the three other treatment strategies included in this analysis, is a novel addition to the literature, which informs ongoing public health discussions aimed at identifying high-value treatment options for common cancers. Prior literature has typically focused on comparing complications and cost within only one or two treatment options (17,19,21–26) and thus lacks a comprehensive comparative assessment of all the common treatment options typically presented to a patient with early breast cancer. For example, in 2001, a seminal paper by Barlow et al. concluded

Table 3. Unadjusted and Adjusted 2-year Costs by Local Therapy Strategy, Diagnosis years 2010–2011*

Treatment	Unadjusted costs, $ Total Mean (95% CI)	Unadjusted costs, $ Total Median (IQR)	Unadjusted costs, $ Complication Mean (95% CI)	Unadjusted costs, $ Noncomplication Mean (95% CI)	Unadjusted costs, $ Noncomplication Median (IQR)	Adjusted costs, $ Total Mean (95% CI)	Adjusted costs, $ Complication Mean (95% CI)	Adjusted costs, $ Noncomplication Mean (95% CI)
MarketScan								
Lump+WBI	77 309 (75 768 to 78 850)	60 258 (41 228–93 905)	1431 (1270 to 1592)	75 878 (74 361 to 77 395)	59 209 (40 374–91 950)	65 608 (64 067 to 67 149)	1385 (1210 to 1560)	63 834 (62 348 to 65 320)
Lump+Brachy	72 184 (68 637 to 75 732)	60 339 (39 424–89 279)	1718 (1308 to 2128)	70 467 (66 970 to 73 963)	58 805 (38 340–87 453)	77 130 (72 423 to 81 837)	1802 (1206 to 2399)	75 058 (70 536 to 79 581)
Lump alone	60 741 (53 872 to 67 611)	45 714 (16 972–79 532)	3331 (2294 to 4367)	57 411 (50 636 to 64 185)	38 684 (15 763–75 064)	70 520 (63 964 to 77 077)	3620 (1789 to 5452)	67 169 (61 018 to 73 321)
Mast alone	49 214 (46 608 to 51 821)	26 244 (11584–59 058)	2134 (1551 to 2717)	47 080 (44 675 to 49 486)	25 231 (11 254–56 834)	48 258 (46 707 to 49 811)	1897 (1575 to 2219)	46 798 (45 305 to 48 292)
Mast+Recon	95 922 (93 527 to 98 316)	75 848 (49 229–117 680)	10 065 (9250 to 10 881)	85 857 (83 630 to 88 083)	66 620 (43 008–105 407)	88 089 (85 509 to 90 670)	10 402 (8772 to 12 032)	77 316 (75 076 to 79 556)
SEER-Medicare								
Lump+WBI	36 816 (36 251 to 37382)	30 790 (23 842–42 198)	584 (529 to 640)	36 231 (35 672 to 36 791)	30 195 (23 463–41 252)	34 087 (33 633 to 34 541)	549 (497 to 602)	33 539 (33 087 to 33 992)
Lump+Brachy	36 128 (34 983 to 37 272)	31 545 (26 503–40 967)	701 (560 to 841)	35 427 (34 283 to 36 570)	30 881 (25 739–40 251)	37 617 (36 356 to 38 877)	708 (536 to 879)	36 904 (35 651 to 38 157)
Lump alone	19 461 (18 662 to 20 260)	14 645 (9919–23 432)	490 (390 to 590)	18 971 (18 179 to 19 762)	14 251 (9655–22 740)	21 005 (20 452 to 21 557)	530 (434 to 626)	20 442 (19 897 to 20 987)
Mast alone	25 367 (24 551 to 26 183)	19 191 (13 208–29 228)	677 (569 to 785)	24 690 (23 884 to 25 496)	18 558 (12 723–28 623)	22 182 (21 751 to 22 612)	656 (564 to 748)	21 517 (21 094 to 21 941)
Mast+Recon	43 154 (40 813 to 45 496)	37 288 (26 861–53 043)	2962 (2463 to 3462)	40 192 (37 882 to 42 502)	33 562 (24 549–49 157)	35 835 (34 140 to 37 531)	2641 (1734 to 3548)	33 035 (31 452 to 34 619)

*Adjusted costs are adjusted for the variables listed in Table 1. Each cost model was iteratively refined to remove covariables that did not statistically significantly contribute to the model. No patients were excluded from any calculation. All figures are reported in 2014 dollars. Brachy = brachytherapy; CI = confidence interval; Lump = lumpectomy; Mast = mastectomy; Recon = reconstruction; SEER = Surveillance, Epidemiology, and End Results; WBI = whole breast irradiation.

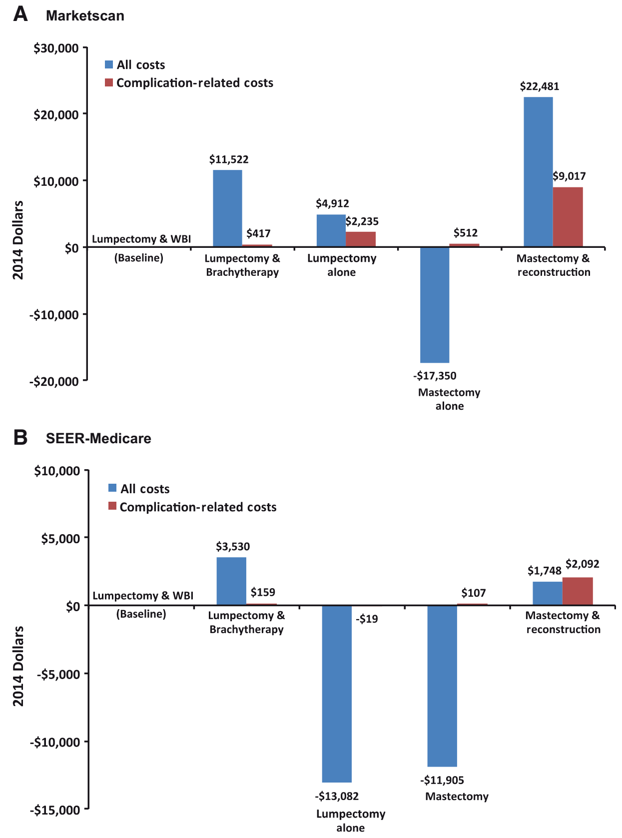

Figure 2. Adjusted total and complication-related cost relative to lumpectomy and whole breast irradiation for patients diagnosed in 2010 and 2011. Adjusted difference in total cost and complication-related cost of local therapy options, relative to lumpectomy plus whole breast irradiation, for patients diagnosed in 2010 and 2011. SEER = Surveillance, Epidemiology, and End Results; WBI = whole breast irradiation.

that Lump+WBI was more expensive than mastectomy within the first six months of diagnosis, but that mastectomy was more expensive when including costs within five years. This study was limited, though, as less than 5% of the sample underwent breast reconstruction (23). As another example, our group has previously reported excess complications with Lump+Brachy compared with Lump+WBI (17,19,21), but these studies did not contextualize complications of brachytherapy relative to mastectomy with or without reconstruction, which is frequently the alternative to Lump+Brachy, the treatment contemplated by patients seeking to avoid a protracted course of WBI.

In recent years, there has been a marked increase in the use of bilateral mastectomy and reconstruction to treat early breast cancer (27–32). While some of these procedures are clearly medically indicated, the choice for mastectomy is often driven by nonmedical factors such as patient preferences for more "complete" cancer treatment by extirpating the entirety of the affected organ, patient fears of in-breast recurrence following Lump+WBI, or patient anxiety regarding the need for ongoing mammographic surveillance of the conserved breast (8). Our finding of substantially higher cost of Mast+Recon compared with Lump+WBI highlights an important conflict that will be increasingly confronted in an era focused on "value" in health care. Specifically, patients may prefer a more expensive treatment such as Mast+Recon for nonmedical reasons when a less expensive treatment such as Lump+WBI may be equally effective from a purely medical perspective. If such a patient is receiving care from a health care entity with a financial stake in promoting "high-value" care, the entity may profit financially if the patient receives the lower-cost intervention and, conversely, may experience a financial loss if the patient receives the higher-cost intervention. Developing a framework to guide health care entities, physicians, and patients through such conflicted decisions will become increasingly important as innovative reimbursement models employing episodic payments or value-based insurance designs begin to permeate the marketplace (3).

Aside from the marked differences between Mast+Recon and Lump+WBI, our study findings also reveal important differences in cost and complications across the different lumpectomy-based options. Specifically, Lump+Brachy yielded an approximately 40% higher relative risk of complications and higher costs than Lump+WBI. The differences in cost were mainly attributable to the procedure itself, as differences in cost because of complications were small: $417 greater for brachytherapy in the MarketScan cohort and $159 greater in the SEER-Medicare cohort. Notably, the shorter course of brachytherapy may decrease indirect patient costs because of travel and lost work and thereby offset a portion of its excess cost. Regarding Lump+WBI, our findings confirm other randomized and population-based studies, which have shown that hypofractionated treatment reduces cost without increasing complications (33–35). The opportunity to encourage this form of WBI should be examined closely in light of recent evidence concluding that only one-third of eligible American women receive hypofractionated WBI (36).

Another key result is that Lump alone was a high-value intervention in older patients, in whom it is considered guideline-concordant (6). However, in the younger cohort, Lump alone was associated with higher costs and complications because of the high prevalence of mastectomy occurring in the second year after diagnosis. The underlying cause of mastectomy—for example, because of true local relapse vs fear of recurrence vs initial pathological findings requiring mastectomy—cannot be determined. However, these procedures and underlying causes were not considered "complications" in our study design and thus do not influence our finding of excess complications and complication-related cost in this group. Finally, our study illustrates that mastectomy alone is a high-value intervention for women who do not prioritize retaining a native or reconstructed breast mound.

In interpreting results of this study, we note that not all individual patients would have been eligible for every treatment strategy. For example, a patient with early breast cancer may have extensive premalignant changes in the breast or a hereditary breast cancer syndrome, thus prompting treatment with Mast alone or Mast+Recon. Nevertheless, our population findings remain broadly representative of actual aggregate outcomes for American patients, the majority of whom are candidates for multiple therapeutic approaches. Another limitation is that analyses relied on the perspective of the payer and were unable to evaluate outcomes such as patient satisfaction or quality of life following one treatment compared with another. Complementary patient-level data are needed to inform physician-patient discussions on the entirety of the risks and benefits of their treatment options. Thirdly, this study is limited by the nature of claims data, which rely on the accuracy of coders and are not comprehensive of all provider and patient characteristics or all potential complications. Future studies should also explore long-term costs, for example, the costs of surveillance mammography and treating second cancers, which are also likely to differ by chosen initial treatment. Finally, although we adjusted for important clinical variables in all analyses, residual confounding may exist in this retrospective study design.

In conclusion, there are major differences in cost and complication profile within two years of diagnosis among guideline-concordant local treatment strategies for breast cancer. Mast alone is a high-value treatment for patients who do not wish to retain a breast mound. Mast+Recon is associated with considerably higher cost and complications. Lump alone can be a high-value intervention for older patients but is not high value for younger patients. Lumpectomy plus hypofractionated WBI combines high oncologic effectiveness, breast preservation, and a favorable complication profile. These findings should be helpful to patients contemplating their treatment options for early breast cancer and will inform ongoing public health discussions aimed at identifying high-value treatment options for common cancers.

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Notes

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