Regional Medicare Expenditures and Survival Among Older Women With Localized Breast Cancer

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Background: Despite evidence on large variation in breast cancer expenditures across geographic regions, there is little understanding about the association between expenditures and patient outcomes.

Objectives: To examine whether Medicare beneficiaries with nonmetastatic breast cancer living in regions with higher cancer-related expenditures had better survival.

Research Design: A retrospective cohort study of women with localized breast cancer from the Surveillance, Epidemiology, and End Results-Medicare linked database. Hospital referral regions (HRR) were categorized into quintiles based on risk-standardized per patient Medicare expenditures on initial phase of breast cancer care. Hierarchical generalized linear models were estimated to examine the association between patients' HRR quintile and survival.

Subjects: In total, 12,610 Medicare beneficiaries diagnosed with stage II–III breast cancer during 2005–2008 who underwent surgery.

Measures: Outcome measures for our analysis were 3- and 5-year overall survival.

Results: Risk-standardized per patient Medicare expenditures on initial phase of breast cancer care ranged from $13,338 to $26,831 across the HRRs. Unadjusted 3- and 5-year survival varied from 66.7% to 92.2% and 50.0% to 84.0%, respectively, across the HRRs, but there was no significant association between HRR quintile and survival in bivariate analysis ($P=0.08$ and 0.28, respectively). After adjustment for sociodemographic and clinical characteristics, quintiles of regional cancer expenditures remained unassociated with patients' 3-year ($P=0.35$) and 5-year survival ($P=0.20$). Further analysis adjusting for treatment factors (surgery type and receipt of radiation and systemic therapy) and stratifying by cancer stage showed similar results.

Conclusions: For Medicare beneficiaries with nonmetastatic breast cancer, residence in regions with higher breast cancer–related expenditures was not associated with better survival. More attention to value in breast cancer care is warranted.

Key Words: breast cancer, expenditure, survival, regional variation

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Breast cancer is the most common malignancy in women, with almost 250,000 women diagnosed annually in the United States.[1] It is also the most costly cancer in the United States, with total breast cancer expenditures reaching $16.5 billion in 2010 and projected to grow to $20.5 billion by 2020.[2] Increase in costs of breast cancer care over the last few decades has been linked to improved life expectancy.[3,4] However, comparison with European countries shows mixed evidence regarding whether the additional

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spending on breast cancer care in the United States provides good "value" in terms of quality adjusted life years gained or people's willingness to pay for the additional life years.[4,5]

Costs of breast cancer care vary widely by geographic region.[6–9] For example, among 80 hospital referral regions (HRRs) across the United States, mean 6-month Medicare spending varied from $28,854 in the lowest spending quintile to $37,971 in the highest spending quintile for women newly diagnosed with stage IV breast cancer during 2002–2007.[8] Similarly, mean Medicare expenditures for initial breast cancer care (2 mo before through 12 mo after diagnosis) ranged from $15,053 to $23,480 across HRR quintiles for women with stage I–III disease during 2005–2008.[6] Moreover, there is evidence for substantial differences in use of breast conserving treatment and radiation therapy across regions, which may also result in variability in expenditures.[10,11]

It has been shown that HRRs with higher overall expenditures on breast cancer care tended to utilize more resources in virtually all components of care (eg, surgery, radiation therapy, systemic therapy), especially newer and expensive technologies such as intensity-modulated radiation therapy.[6] Given such large variation in resource utilization across geographic regions, an important question that remains largely unaddressed is whether women residing in HRRs with higher expenditures experience better outcomes. Answer to this question can inform geographic variation within the United States in value of care (ie, patient outcomes relative to cost) and help identify opportunities for delivering high-value care.

To shed light on this issue, we examined whether patients with nonmetastatic breast cancer living in regions with higher breast cancer–related Medicare expenditures had increased rates of survival. We examined 3- as well as 5-year survival while controlling for patient sociodemographic and clinical characteristics. Findings from this study can inform future discussions on value of cancer care. Ultimately, by identifying exemplary care patterns in regions with low expenditure and good outcomes, and improving care in regions with high expenditure but poor outcomes, we can enhance overall value in care.

METHODS

Study Design

We conducted a retrospective cohort study of women with localized breast cancer identified from the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database. A previous study estimated risk-standardized per patient Medicare expenditure on breast cancer care for HRRs in SEER registry areas.[6] By linking these estimates to patient-level data from the SEER-Medicare dataset, we analyzed the association between risk-standardized breast cancer care expenditure of a patient's HRR and her survival.

Data Sources and Study Sample

The SEER-Medicare dataset includes patient-level information from SEER registries, including demographic and cancer characteristics, which has been linked with Medicare claims. The geographic regions covered by SEER registries represent 28% of the US population, and the SEER-Medicare linked database included data from States of California, Connecticut, Georgia, Hawaii, Iowa, Kentucky, Louisiana, New Jersey, New Mexico, and Utah, as well as Detroit metropolitan area and multicounty Seattle-Puget Sound area.[12–14] Our cohort included female Medicare beneficiaries who were diagnosed with stage II–III breast cancer during 2005–2008 and underwent surgery (either lumpectomy or mastectomy) within 9 months of diagnosis. We excluded patients with stage 0, I, or IV breast cancer because their survival was less amenable to differences in care given their generally good or poor prognosis.[1,15] Patients who were previously diagnosed with any cancer (regardless of cancer site) or had a second cancer (not of the breast) any time between diagnosis through 1 year after surgery were also excluded. For patients who had multiple diagnoses of breast cancer during 2005–2008, only their first breast cancer diagnosis was included in analysis.

The diagnosis years selected were the most recent ones that would allow for at least 5-year follow-up, as vital status was recorded through the end of 2013. We excluded women under 67 years of age at time of diagnosis and those without continuous Medicare Parts A and B fee-for-service coverage during the 2 years before breast cancer diagnosis, so that patients in our sample had a 2-year look back period to adequately assess comorbidity status.[16] Therefore, overall our sample selection and construction of measures used information from 2003 to 2013 SEER-Medicare data. Patients covered by Medicare advantage plans at any time during the 2-year look back period or the 12 months after diagnosis were excluded to ensure a complete record of their claims. Patients who were dually eligible for Medicaid were retained in sample.

We used beneficiary mailing zip code to assign each woman to her HRR of residence as defined by the Dartmouth Atlas,[17] and then linked patient-level data to previous estimates of risk-standardized per beneficiary Medicare expenditure on initial breast cancer care by HRR.[6] HRRs reflect regional markets for tertiary-level medical care.[18] Because risk-standardized expenditures were only calculated for HRRs with at least 25 patients with breast cancer (stage I–III) to ensure adequate sample size for the estimate,[6] patients in smaller HRRs (ie, <25 patients with stage I–III breast cancer) were excluded from our cohort. The broader patient population involved in the Medicare expenditure measure (ie, stage I–III patients) provided a more exogenous assessment of spending and allowed for a larger sample size in estimating expenditures. It served as a marker for intensity of breast cancer care in the HRR.

Measures

We obtained measures of HRR-specific, risk-standardized per patient breast cancer–related Medicare expenditures from a previous study.[6] Detailed methods for this measure were published previously.[6] Briefly, for each HRR, risk-standardized per patient Medicare expenditure on initial phase of breast cancer care was calculated by adjusting for patient sociodemographic characteristics and health conditions and taking the difference in risk-adjusted expenditures between patients with breast cancer and matched controls while accounting for clustering in data by HRR. Health conditions adjusted for in the model included comorbidity status and tumor characteristics for patients with breast cancer and comorbidity status alone for matched controls. Medicare expenditures across all care settings (including inpatient, physician, hospital-based outpatient, home health, durable medical equipment, and hospice care, but except Part D claims) during the initial phase of care, that is, 2 months before through 12 months after diagnosis date (for cancer patients) or index date (for matched controls), were included. Expenditures were adjusted for differences in input prices across geographic regions and were inflation adjusted to 2009 US dollars. HRRs were categorized into quintiles based on their risk-standardized per patient Medicare expenditures on initial phase of breast cancer care (quintile 1 = lowest expenditure and quintile 5 = highest expenditure). These HRR quintiles were our primary independent variable.

Outcome measures for our analysis were 3- and 5-year overall survival. For each patient in our cohort, we measured survival status at 3 and 5 years after diagnosis. These timeframes allowed us to reasonably capture the health impact of potentially different treatment patterns in regions with varying levels of resource utilization.

Patient-level characteristics included age at diagnosis, race (white, black, or other), marital status, income quintile (based on median household income of patients' census tract or zip code), residence in a metropolitan area (yes/no), year of diagnosis, Elixhauser comorbidity score,[19] disability status,[20] access to care (receipt of an influenza vaccine and any primary care provider visit in the year before surgery), and tumor characteristics. We assessed comorbidity for each patient using a modified Elixhauser index based on her International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes from 24 through 3 months before the diagnosis of breast cancer.[19] Consistent with prior work,[3,6] our determination of comorbidities used claims that were billed on an inpatient claim or on ≥2 outpatient/physician claims that were billed at least 30 days apart. Patients were classified as either "disabled" or "not disabled" according to a validated, claims-based disability index using information on type of medical services received over the year before diagnosis.[20] Tumor characteristics included stage, size, laterality, presence of a positive lymph node, hormone receptor status, and grade.

In addition, we measured indicators of cancer treatments received, including surgery type (lumpectomy vs. mastectomy), receipt of radiation therapy (yes/no), and receipt of systemic therapy (yes/no). These 3 treatment factors, that is, surgery, radiation therapy, and systemic therapy, were shown to contribute the most to Medicare expenditures on initial breast cancer care.[6] ICD-9-CM diagnosis and procedure codes, Current Procedural Terminology codes, and Healthcare Common Procedure Coding System codes were used to identify these treatments.

Statistical Analysis

We first summarized patient characteristics using descriptive statistics and assessed bivariate associations of HRR expenditure quintile and other patient characteristics with 3- and 5-year survival using χ^2 tests. We then plotted Kaplan-Meier curves to illustrate patterns of survival over time in each HRR quintile. To assess differences in outcomes, we compared survival rates at 3 and 5 years, respectively, across HRR quintiles. We used dichotomous rather than time-to-event outcomes to improve interpretation of results. Specifically, for each endpoint (3- and 5-year survival), we applied a separate multivariable hierarchical generalized linear model (HGLM) with a logit link and binomial distribution to examine the adjusted association between a patient's HRR quintile (in terms of risk-standardized per patient Medicare expenditure on initial phase of breast cancer care) and survival. This patient-level HGLM model adjusted for patient sociodemographic and clinical characteristics and accounted for clustering of patients by HRR. HRR quintile was the key explanatory variable and was included in each model. Other patient characteristics were considered as candidate explanatory variables and only those that were significant at the $P < 0.10$ level in multivariable analysis were retained in final model.

To assess the potential role of treatment factors in mediating the relationship of HRR expenditure quintile and patients' tumor characteristics with survival, we estimated an incremental regression model for 3- and 5-year survival, respectively, by further adjusting for patients' use of surgery, radiation therapy, and systemic therapy. In addition, we conducted separate analysis for women with stage II and stage III breast cancer to examine potential differences in the relationship between HRR quintile and survival by cancer stage. We also evaluated possible effect of treatment modalities in moderating the association between tumor characteristics and survival by estimating interaction terms between treatment indicators and tumor characteristics. As no meaningful interaction effects were identified, we only presented results related to main effects.

To help illustrate our findings, we also calculated risk-standardized 5-year survival rates for each HRR and constructed a scatter plot for the relationship between risk-standardized expenditures and survival rates across the HRRs. Risk-standardized 5-year survival rates were calculated based on risk-adjustment models similar to the HGLM model described above but after removing variables measuring the HRR quintiles. We divided the predicted number of patients who survived in a given HRR (accounting for the HRR's random effect) by the expected number of patients who survived (without the HRR's random effect) and then multiplied this ratio by the sample overall survival rate.[21] Pearson correlation coefficient was estimated to assess HRR-level association between risk-standardized expenditure and survival.

All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC). All statistical tests were 2-sided and $P < 0.05$ were considered statistically significant.

RESULTS

Sample Characteristics

Our sample included 12,610 women with stage II–III breast cancer residing in 85 HRRs with a mean age of 76.8 years (SD = 6.7). In this cohort, 76.2% of patients had stage II disease and 23.8% were diagnosed with stage III disease (Table 1). Most patients had hormone receptor positive breast cancer (76.0%) and tumors > 2 cm (78.6%).

TABLE 1. Sample Characteristics and Bivariate Association With 3- and 5-Year Survival

Patient Characteristics	N (%)	% Surviving (3 y)	P^*	% Surviving (5 y)	P^*
HRR quintile of risk-standardized per patient Medicare expenditure on initial breast cancer care					
1 (lowest)	1604 (12.7)	79.6	0.08	67.4	0.28
2	2488 (19.7)	80.2		68.8	
3	3324 (26.4)	82.0		70.3	
4	3499 (27.8)	82.3		69.2	
5 (highest)	1695 (13.4)	81.2		68.2	
Age at diagnosis (y)					
67–69	2109 (16.7)	90.1	< 0.001	82.7	< 0.001
70–74	3136 (24.9)	89.3		80.1	
75–79	3048 (24.2)	83.5		71.6	
80–84	2447 (19.4)	75.4		60.5	
85–94	1870 (14.8)	62.4		42.2	
Race					
White	11,088 (87.9)	81.5	< 0.001	69.3	< 0.001
Black	1030 (8.2)	77.4		62.4	
Other	492 (3.9)	86.0		77.2	
Marital status					
Married	5046 (40.0)	87.2	< 0.001	77.7	< 0.001
Not married	7096 (56.3)	77.1		63.1	
Unknown	468 (3.7)	82.5		66.5	
Median household income					
< \$33,000	2778 (22.0)	78.9	< 0.001	65.4	< 0.001
\$33,000–\$39,999	1881 (14.9)	79.5		67.0	
\$40,000–\$49,999	2684 (21.3)	80.6		66.9	
\$50,000–\$62,999	2392 (19.0)	82.8		70.5	
≥ \$63,000	2875 (22.8)	84.3		74.6	
Metropolitan area residence					
Yes	10,470 (83.0)	81.9	< 0.001	69.7	< 0.001
No	2140 (17.0)	78.7		65.9	
Year of diagnosis					
2005	3276 (26.0)	80.2	0.006	67.8	0.10
2006	3181 (25.2)	80.3		68.5	
2007	3167 (25.1)	81.8		69.5	
2008	2986 (23.7)	83.2		70.5	
Comorbidity score					
0	5478 (43.4)	88.1	< 0.001	78.7	< 0.001
1–2	4838 (38.4)	81.4		68.5	
≥ 3	2294 (18.2)	65.0		47.1	
Disability status					
Not disabled	11,177 (88.6)	84.4	< 0.001	72.9	< 0.001
Disabled	1433 (11.4)	57.0		38.9	
Prior receipt of flu shot					
No	5273 (41.8)	80.8	0.22	67.8	0.008
Yes	7337 (58.2)	81.7		70.0	
Prior PCP visit					
No	804 (6.4)	77.4	0.003	64.3	0.003
Yes	11,806 (93.6)	81.6		69.4	
Cancer stage					
II	9612 (76.2)	84.9	< 0.001	73.9	< 0.001
III	2998 (23.8)	69.9		53.5	
Tumor size (cm)					
< 2	2488 (19.7)	91.0	< 0.001	82.5	< 0.001
2–5	8470 (67.2)	81.4		68.6	
> 5	1436 (11.4)	66.2		50.7	
Unknown	216 (1.7)	68.1		54.6	
Laterality					
Right-sided	6204 (49.2)	81.8	0.21	69.3	0.57
Left-sided	6406 (50.8)	80.9		68.8	
Positive node(s)					
No	5425 (43.0)	81.6	0.43	69.8	0.11
Yes	7185 (57.0)	81.1		68.5	
Hormone receptor status					
Negative	2291 (18.2)	69.8	< 0.001	57.4	< 0.001
Positive	9580 (76.0)	84.6		72.4	
Unknown	739 (5.9)	74.4		61.6	
Tumor grade					
1	1876 (14.9)	88.5	< 0.001	78.9	< 0.001
2	5388 (42.7)	84.9		72.5	
3	4571 (36.3)	74.7		61.7	
4	146 (1.2)	71.2		57.5	
Unknown	629 (5.0)	79.7		65.5	
Type of surgery					
Lumpectomy	5234 (41.5)	86.6	< 0.001	76.3	< 0.001
Mastectomy	7376 (58.5)	77.6		63.9	
Receipt of radiation therapy					
No	6454 (51.2)	74.7	< 0.001	60.3	< 0.001
Yes	6156 (48.8)	88.3		78.2	
Receipt of chemotherapy					
No	7960 (63.1)	78.6	< 0.001	65.0	< 0.001
Yes	4650 (36.9)	85.9		76.0	

*P-value based on χ^2 test of the association between each covariate and survival. HRR indicates hospital referral region; PCP, primary care physician.

Association of Regional Risk-standardized Expenditures With Survival

The average risk-standardized Medicare expenditure on initial breast cancer care was \$19,597 per patient across the 85 HRRs, but varied from \$13,338 to \$26,831 suggesting a 2-fold difference in resource utilization across the HRRs (Fig. 1A). Use of major treatment modalities also varied across HRR expenditure quintiles (Table 2). In general, HRRs in higher expenditure quintiles had a greater proportion of patients undergoing lumpectomy (rather than mastectomy) or receiving radiation and systemic therapy.

Unadjusted 3- and 5-year survival in our overall sample was 81.3% and 69.0%, respectively. Across the HRRs, 3-year survival ranged from 66.7% to 92.2% and 5-year survival varied from 50.0% to 84.0%. However, survival did not differ significantly by the HRR expenditure quintiles. Survival at 3 years was 79.6%, 80.2%, 82.0%, 82.3%, and 81.2% among patients in HRR quintiles 1–5, respectively ($P = 0.08$; Table 1), whereas survival at 5 years was 67.4%, 68.8%, 70.3%, 69.2%, and 68.2% in quintiles 1–5, respectively ($P = 0.28$; Table 1). Kaplan-Meier curves also suggested similar survival patterns across the HRR quintiles (Fig. 1B).

After adjusting for patient sociodemographic and clinical characteristics, there was no significant difference in the odds of survival between patients in the lowest expenditure

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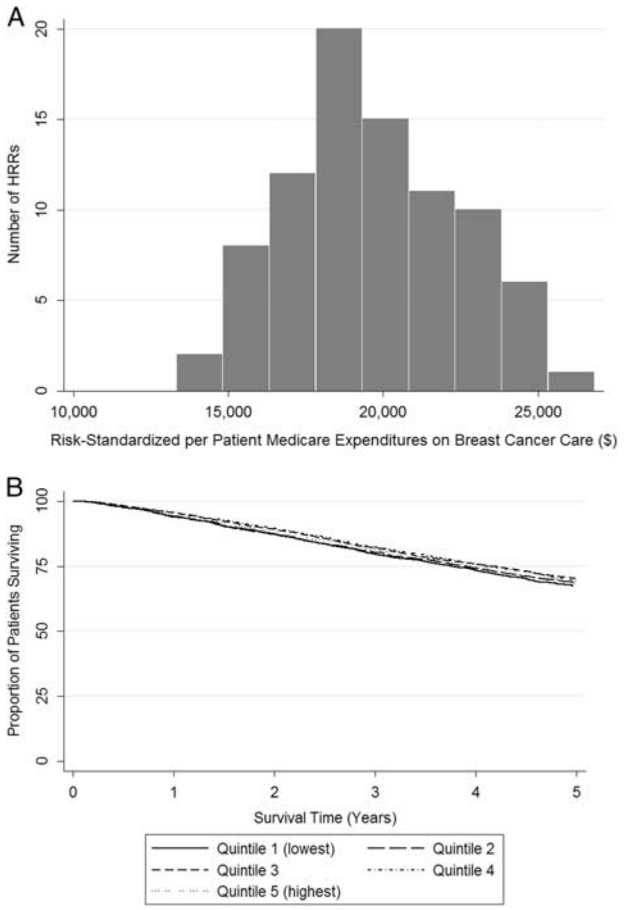

FIGURE 1. A, Distribution of risk-standardized per patient Medicare expenditure on initial phase of breast cancer care across HRRs. B, Kaplan-Meier curve of survival over time across expenditure quintiles. Quintiles 1–5 reflect the lowest to highest quintiles of risk-standardized per patient Medicare expenditure on initial breast cancer care among HRRs. HRR indicates hospital referral region.

quintile regions and those in any of the higher expenditure quintiles. Specifically, the odds ratios of 3-year survival were 1.05 [95% confidence interval (CI), 0.86–1.28], 1.18 (95% CI, 0.97–1.44), 1.18 (95% CI, 0.97–1.43), and 1.09 (95% CI, 0.88–1.34), respectively, for quintiles 2–5 relative to quintile 1 (overall $P=0.35$) (Table 3). Further adjusting for treatment factors generated similar results where the adjusted odds ratios ranged from 1.07 to 1.18 for quintiles 2–5 compared with quintile 1 (overall $P=0.44$). The association between other patient characteristics (eg, tumor characteristics) and survival remained largely unchanged as well.

Likewise, we did not observe a statistically significant association between regional expenditure quintile and 5-year survival (Table 3). Adjusted odds ratios were 1.15 (95% CI, 0.97–1.36), 1.19 (95% CI, 1.01–1.41), 1.10 (95% CI, 0.93–1.30), and 1.03 (95% CI, 0.86–1.24), respectively, for 5-year survival at the 4 higher expenditure quintiles relative to quintile 1 (overall $P=0.20$). Further adjustment for treatment factors did not change these results or the association between other patient characteristics and survival. Separate analyses of patients with stage II and stage III breast cancer produced similar results (Supplemental Digital Content 1, http://links.lww.com/MLR/B480).

When data were analyzed at the regional level, the results were consistent in that there was no statistically significant association between regional-level breast cancer expenditures and regional-level survival outcomes. Figure 2 illustrates the distribution of risk-standardized 5-year survival rates according to risk-standardized expenditures on breast cancer care across the 85 HRRs. Pearson correlation coefficient between risk-standardized expenditures and risk-standardized 5-year survival rate was −0.006 ($P=0.95$). There was substantial variation in the expenditure-survival profile across the HRRs. In total, 21 HRRs (24.7%) attained "high-value" care (upper left quadrant of Fig. 2; lower than median expenditure and higher than median survival), whereas 22 HRRs (25.9%) provided "low-value" care (lower right quadrant of Fig. 2; higher than median expenditure and lower than median survival).

TABLE 2. Use of Breast Cancer Treatment Across Quintiles of HRRs

	HRR Quintile of Risk-standardized Per Patient Medicare Expenditure on Initial Breast Cancer Care				
Treatment	**1 (Lowest)**	**2**	**3**	**4**	**5 (Highest)**
Surgery (%)					
Lumpectomy	38.2	35.7	45.5	43.6	41.1
Mastectomy	61.9	64.3	54.5	56.4	58.9
Radiation therapy (%)	46.6	44.5	50.9	51.1	48.6
Systemic therapy (%)	34.5	36.7	35.8	38.2	39.7

HRR indicates hospital referral region.

DISCUSSION

We found that women who resided in areas with higher breast cancer expenditures were no more likely to survive than their counterparts in lower-spending regions. Similarly, our regional-level analysis showed that risk-standardized expenditure was not correlated with HRR risk-standardized survival rate. Notably, there was substantial variation in value of care (ie, survival outcomes relative to medical expenditures) provided in different HRRs.

Methodologically, our study improves upon previous research assessing the relationship between intensity of resource utilization and outcomes of care in patients with breast cancer. Two studies on breast cancer care have documented no significant association between medical spending and survival.[8,9] However, both studies relied on total per patient expenditure (rather than isolating cancer-specific expenditure), and analyzed samples of patients whose outcomes were less amenable to differences in intensity of care (ie, women with stage IV breast cancer or a high proportion of women with stage 0–I breast cancer).[8,9] Therefore, their results could be confounded by regional variation in noncancer

TABLE 3. Adjusted Association of Patient Characteristics With 3- and 5-Year Survival

	3-Year Survival*				5-Year Survival*			
	Without Adjustment for Treatment Factors		With Adjustment for Treatment Factors		Without Adjustment for Treatment Factors		With Adjustment for Treatment Factors	
Patient Characteristics	**Adjusted OR (95% CI)**	***P***	**Adjusted OR (95% CI)**	***P***	**Adjusted OR (95% CI)**	***P***	**Adjusted OR (95% CI)**	***P***
HRR quintile of risk-standardized per patient Medicare expenditure on initial breast cancer care								
1 (lowest)	Reference	0.35	Reference	0.44	Reference	0.20	Reference	0.15
2	1.05 (0.86–1.28)		1.07 (0.88–1.30)		1.15 (0.97–1.36)		1.16 (0.98–1.38)	
3	1.18 (0.97–1.44)		1.18 (0.97–1.42)		1.19 (1.01–1.41)		1.18 (0.998–1.39)	
4	1.18 (0.97–1.43)		1.16 (0.96–1.40)		1.10 (0.93–1.30)		1.08 (0.91–1.27)	
5 (highest)	1.09 (0.88–1.34)		1.07 (0.87–1.32)		1.03 (0.86–1.24)		1.01 (0.84–1.21)	
Age at diagnosis (y)								
67–69	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001
70–74	0.95 (0.78–1.15)		0.99 (0.82–1.20)		0.87 (0.74–1.01)		0.90 (0.77–1.05)	
75–79	0.61 (0.51–0.74)		0.69 (0.57–0.83)		0.57 (0.49–0.66)		0.63 (0.54–0.74)	
80–84	0.39 (0.33–0.47)		0.48 (0.40–0.58)		0.36 (0.31–0.42)		0.44 (0.38–0.52)	
85–94	0.22 (0.18–0.27)		0.30 (0.24–0.37)		0.18 (0.15–0.21)		0.23 (0.20–0.28)	
Race								
White	NA†		NA†		Reference	0.07	Reference	0.04
Black	NA†		NA†		1.02 (0.87–1.20)		1.00 (0.85–1.18)	
Other	NA†		NA†		1.33 (1.05–1.69)		1.37 (1.08–1.75)	
Marital status								
Married	Reference	< 0.001	Reference	0.004	Reference	< 0.001	Reference	0.001
Not married	0.81 (0.72–0.91)		0.84 (0.75–0.95)		0.81 (0.73–0.89)		0.83 (0.76–0.92)	
Unknown	1.04 (0.79–1.37)		1.11 (0.84–1.48)		0.82 (0.65–1.03)		0.86 (0.68–1.09)	
Median household income								
< $33,000	NA†		NA†		Reference	0.004	Reference	0.01
$33,000–$39,999	NA†		NA†		0.95 (0.83–1.10)		0.95 (0.82–1.10)	
$40,000–$49,999	NA†		NA†		0.89 (0.78–1.02)		0.88 (0.76–1.01)	
$50,000–$62,999	NA†		NA†		1.00 (0.86–1.16)		0.97 (0.83–1.12)	
≥ $63,000	NA†		NA†		1.16 (1.00–1.34)		1.12 (0.96–1.30)	
Metropolitan area residence								
Yes	Reference	0.02	Reference	0.09	Reference	0.04	Reference	0.11
No	0.85 (0.74–0.98)		0.89 (0.77–1.02)		0.87 (0.76–0.99)		0.90 (0.79–1.03)	
Comorbidity score								
0	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001
1–2	0.64 (0.57–0.73)		0.67 (0.59–0.76)		0.62 (0.56–0.69)		0.65 (0.58–0.71)	
≥ 3	0.32 (0.28–0.36)		0.34 (0.30–0.39)		0.29 (0.26–0.33)		0.31 (0.27–0.35)	
Disability status								
Not disabled	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001
Disabled	0.46 (0.40–0.52)		0.52 (0.45–0.60)		0.45 (0.39–0.51)		0.50 (0.44–0.57)	
Prior receipt of flu shot								
No	NA†		NA†		Reference	0.008	Reference	0.06
Yes	NA†		NA†		1.13 (1.03–1.24)		1.09 (1.00–1.20)	
Prior PCP visit								
No	Reference	0.10	Reference	0.43	Reference	0.03	Reference	0.18
Yes	1.19 (0.97–1.47)		1.09 (0.88–1.34)		1.23 (1.02–1.48)		1.14 (0.94–1.37)	

(*Continued*)

TABLE 3. Adjusted Association of Patient Characteristics With 3- and 5-Year Survival (*continued*)

	3-Year Survival*				5-Year Survival*			
	Without Adjustment for Treatment Factors		With Adjustment for Treatment Factors		Without Adjustment for Treatment Factors		With Adjustment for Treatment Factors	
Patient Characteristics	**Adjusted OR (95% CI)**	***P***	**Adjusted OR (95% CI)**	***P***	**Adjusted OR (95% CI)**	***P***	**Adjusted OR (95% CI)**	***P***
Cancer stage								
II	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001
III	0.50 (0.44–0.56)		0.42 (0.37–0.47)		0.45 (0.40–0.50)		0.37 (0.33–0.42)	
Tumor size (cm)								
< 2	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001
2–5	0.61 (0.52–0.72)		0.65 (0.55–0.76)		0.63 (0.56–0.72)		0.66 (0.59–0.75)	
> 5	0.39 (0.32–0.47)		0.40 (0.33–0.50)		0.44 (0.37–0.52)		0.45 (0.38–0.54)	
Unknown	0.38 (0.27–0.54)		0.38 (0.26–0.54)		0.47 (0.34–0.65)		0.47 (0.34–0.65)	
Hormone receptor status								
Negative	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001
Positive	2.04 (1.80–2.32)		2.20 (1.93–2.51)		1.72 (1.53–1.93)		1.84 (1.64–2.08)	
Unknown	1.38 (1.12–1.72)		1.59 (1.28–1.98)		1.34 (1.10–1.64)		1.53 (1.26–1.87)	
Tumor grade								
1	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001	Reference	< 0.001
2	0.83 (0.70–0.99)		0.82 (0.69–0.98)		0.77 (0.67–0.88)		0.76 (0.66–0.87)	
3	0.58 (0.49–0.69)		0.56 (0.47–0.67)		0.59 (0.51–0.68)		0.56 (0.48–0.65)	
4	0.50 (0.33–0.78)		0.51 (0.33–0.79)		0.49 (0.33–0.72)		0.48 (0.32–0.72)	
Unknown	0.75 (0.58–0.98)		0.74 (0.57–0.97)		0.68 (0.54–0.85)		0.67 (0.53–0.84)	
Type of surgery								
Lumpectomy	—		Reference	0.37	—		Reference	0.45
Mastectomy	—		1.06 (0.94–1.20)		—		1.04 (0.94–1.16)	
Receipt of radiation therapy								
No	—		Reference	< 0.001	—		Reference	< 0.001
Yes	—		2.00 (1.77–2.25)		—		1.86 (1.67–2.06)	
Receipt of systemic therapy								
No	—		Reference	< 0.001	—		Reference	< 0.001
Yes	—		1.32 (1.15–1.51)		—		1.33 (1.19–1.49)	

*Model also adjusted for year of diagnosis.
†NA (covariate not included in final regression model because it was not statistically significant at $P < 0.10$ level).
CI indicates confidence interval; HRR, hospital referral region; NA, not applicable; OR, odds ratio; PCP, primary care physician.

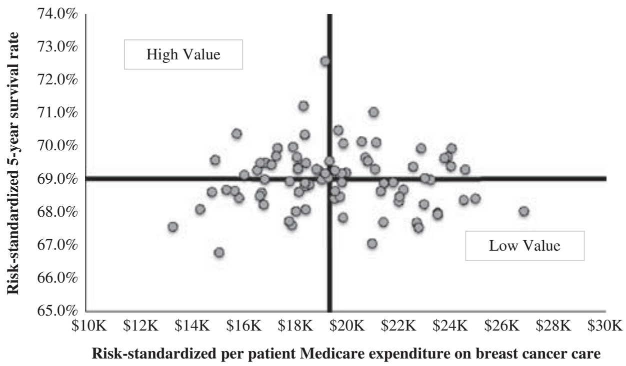

FIGURE 2. Distribution of risk-standardized per patient Medicare expenditure on initial phase of breast cancer care and risk-standardized 5-year survival rate among 85 HRRs. Each dot in the figure reflects a HRR. The bold lines indicate median risk-standardized per patient Medicare expenditure on initial breast cancer care and median risk-standardized 5-year survival rate among the 85 HRRs. HRR indicates hospital referral region.

care expenses and might underestimate the association between expenditure and survival given the particularly low and high survival rates in these patients (ie, 5-year relative survival = 22% for stage IV and 100% for stage I).[1,15] In contrast, we analyzed expenditures specifically on breast cancer care and studied women with stage II–III disease, the group in which treatment intensity would most likely impact survival.

Nevertheless, our study also showed no significant difference in patient survival across the HRR quintiles, despite their large difference in expenditures. Risk-standardized per patient Medicare expenditure on the initial phase of breast cancer care differed by $13,493 between the lowest-spending and highest-spending HRRs ($13,338 vs. $26,831). This magnitude of difference is equivalent to a substantial proportion of annual cost of initial care for many common cancer types (eg, $21,412 per elderly female patient with bladder cancer and $33,167 per elderly female patient with leukemia).[2] The lack of association between Medicare spending and patient survival observed in our study is consistent with the growing literature documenting marked variation in costs of care, including cancer care, where high-cost regions did not attain health benefits.[22–25] These findings suggest opportunities for reducing resource use in high-expenditure regions without compromising patient outcomes.

Efforts to reduce costs in high-spending areas can benefit from more research on causes of geographic variation in costs. Previous research showed that conventional measures of patient and treatment factors (eg, receipt of chemotherapy, type of radiation therapy) only explained a small proportion of the variation in Medicare expenditure on breast cancer care across HRRs,[6] calling for additional research on other factors that may contribute to the large differences in costs of breast cancer care. Moreover, not all additional utilization of services in high-spending regions is necessarily wasted.[26] Research on other cancer types suggests that utilization of both recommended and nonrecommended services were higher at high-spending areas.[24] Similar studies in breast cancer care with in-depth comparison of practice patterns between high-spending and low-spending regions are warranted to inform cost-containment strategies that can better target sources of inefficiency (eg, use of ineffective or nonrecommended services), rather than across-the-board restriction on resource use which may have unintended consequences on quality of care.

Moreover, we found substantial variation in the expenditure-survival profile across HRRs. Some HRRs demonstrated low expenditure and high survival, indicating high-value care, whereas others had poor survival rates even though they also had low expenditures. These results underscore the importance of considering costs in conjunction with patient outcomes, rather than focusing on cost reduction alone. Heterogeneity in these expenditure-survival patterns also offers a unique opportunity to identify exemplary practices at high-value regions. Learning from "positive deviants" in health care, that is, institutions that exhibit high performance, has been a demonstrated approach to improve care for a variety of health problems.[27,28] A similar approach can be used in future breast cancer care research to help understand geographic variation in value of care and discern successful practices that may lead to low expenditure and high survival.

Our findings should be interpreted with several limitations in mind. First, as an observational study, we cannot infer any causal relationship between medical expenditures and patient outcomes. However, the results still provide meaningful insight to inform "value" in breast cancer care. Second, as our sample was limited to elderly Medicare patients living in SEER regions which are not nationally representative, our results may not be generalizable to younger patients or to other areas of the country. Third, the Medicare expenditure measure used in our analysis did not include payments from other insurers, patient out-of-pocket expenses, or expenditures from Part D claims such as hormone therapy.[6] Future research capturing these expenditure components will provide additional insights and may be better able to detect potential differences in survival across geographic regions with different spending. Nevertheless, for most elderly Medicare beneficiaries, Medicare is the primary payer[29] and hence incurs most of the expenditures. Moreover, HRRs with higher overall expenditures have been shown to have higher expenditures on components of care as well (eg, radiation therapy, systemic therapy).[6] Therefore, variation in Medicare expenditure on breast cancer care captured in our study should reasonably reflect major differences in resource utilization across HRRs. Fourth, we used diagnosis and procedure codes in claims data to identify comorbidities and treatment types which may not accurately capture all detailed clinical information. However, use of claims data allowed us to evaluate the expenditure-survival relationship in a broad population of elderly cancer patients. Finally, our analysis focused on survival and did not examine patient-centered outcomes such as quality of life and other psychosocial outcomes that may be important to cancer patients.[30] Likewise, we measured 3- and 5-year survival, which cannot fully capture the impact of recurrent disease or metastases that may arise years later. Further studies assessing these additional aspects of patient outcomes in relationship to resource utilization will provide additional insights.

CONCLUSIONS

Our study found that among patients with stage II–III breast cancer, survival was not different between those in high-expenditure versus low-expenditure HRRs. This finding suggests potential opportunities to reduce costs in regions with high spending on breast cancer care without jeopardizing patient outcomes. It also calls for additional research to identify sources of inefficiency in high-spending regions to best inform strategies for containing costs while preserving quality of care.

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