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Spending for Advanced Cancer Diagnoses: Comparing Recurrent Versus De Novo Stage IV Disease

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QUESTION ASKED: Does health care spending around the time of an advanced cancer diagnosis differ among patients with de novo stage IV versus recurrent advanced breast (BC), colorectal (CRC), or lung (LC) cancer?

SUMMARY ANSWER: Spending for patients with de novo advanced cancer is substantially greater than spending for patients with recurrent advanced cancer. This difference is largely attributable to higher spending for inpatient, outpatient (including chemotherapy), and physician services during the year after the advanced cancer diagnosis.

WHAT WE DID: Using SEER-Medicare data from 2008 to 2013, we identified patients with BC, CRC, and LC who had either de novo stage IV or recurrent advanced cancer. We estimated mean spending/patient/month (2012 US dollars) from 12 months before to 11 months after the advanced cancer diagnosis. We described the absolute difference in mean monthly spending for de novo versus recurrent advanced cancer during the year before and the year after the advanced cancer diagnosis for all medical services and by type of service provided (inpatient, outpatient, hospice, etc), and we estimated the relative difference in spending after controlling for type of advanced cancer, year of diagnosis, age, sex, comorbidity, and other factors.

WHAT WE FOUND: We identified 54,982 patients with advanced cancer. Before diagnosis, mean monthly spending was higher for recurrent patients (absolute difference: BC, $1,412; CRC, $3,002; LC, $2,805; all $P < .001$), whereas after the diagnosis, it was higher for de novo patients (absolute difference: BC, $2,443; CRC, $4,844; LC, $2,356; all $P < .001$). Spending differences were driven by inpatient, physician, and hospice services. Across the 2-year period around the advanced cancer diagnosis, adjusted mean monthly spending was higher for de novo versus recurrent

patients (spending ratio: BC, 2.39; 95% CI, 2.05 to 2.77; CRC, 2.64; 95% CI, 2.31 to 3.01; LC, 1.46; 95% CI, 1.30 to 1.65). The average increase in total monthly spending associated with chemotherapy and hospitalization was $7,301 and $15,817 for BC, $11,908 and $20,615 for CRC, and $5,995 and $10,762 for LC, respectively. Even when we controlled for hospitalizations, chemotherapy receipt, and other factors, mean monthly spending for an advanced cancer diagnosis was still 20% to 70% higher for patients with de novo versus recurrent disease.

BIAS, CONFOUNDING FACTORS, REAL-LIFE IMPLICATIONS: Implications of our study include that historical estimates of spending for advanced disease could overestimate actual spending because they do not account for recurrent disease and that historical estimates of spending for the continuing (ie, survivorship) phase of care could overestimate actual spending because they incorrectly include spending for recurrent disease. Findings from our study highlight the importance of clearly defining starting/stopping points and reimbursement amounts for episode-based payment models. Perhaps recurrence could be used to identify the end of an initial treatment episode or the beginning of a recurrent treatment episode. Alternatively, for payers who prefer total-cost-of-care reimbursement models, recurrence could also be used to develop fair reimbursement policies and help discriminate between high/low-value spending. The large spike in spending around the time of an advanced cancer diagnosis underscores the importance of assessing financial toxicity and providing social support to patients with advanced cancer. Last, our findings highlight the need for more research with regard to the goals, preferences, and values of patients with de novo and recurrent advanced cancer.

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original contribution

Spending for Advanced Cancer Diagnoses: Comparing Recurrent Versus De Novo Stage IV Disease

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abstract

PURPOSE Spending for patients with advanced cancer is substantial. Past efforts to characterize this spending usually have not included patients with recurrence (who may differ from those with de novo stage IV disease) or described which services drive spending.

METHODS Using SEER-Medicare data from 2008 to 2013, we identified patients with breast, colorectal, and lung cancer with either de novo stage IV or recurrent advanced cancer. Mean spending/patient/month (2012 US dollars) was estimated from 12 months before to 11 months after diagnosis for all services and by the type of service. We describe the absolute difference in mean monthly spending for de novo versus recurrent patients, and we estimate differences after controlling for type of advanced cancer, year of diagnosis, age, sex, comorbidity, and other factors.

RESULTS We identified 54,982 patients with advanced cancer. Before diagnosis, mean monthly spending was higher for recurrent patients (absolute difference: breast, $1,412; colorectal, $3,002; lung, $2,805; all $P <$ .001), whereas after the diagnosis, it was higher for de novo patients (absolute difference: breast, $2,443; colorectal, $4,844; lung, $2,356; all $P <$ .001). Spending differences were driven by inpatient, physician, and hospice services. Across the 2-year period around the advanced cancer diagnosis, adjusted mean monthly spending was higher for de novo versus recurrent patients (spending ratio: breast, 2.39 [95% CI, 2.05 to 2.77]; colorectal, 2.64 [95% CI, 2.31 to 3.01]; lung, 1.46 [95% CI, 1.30 to 1.65]).

CONCLUSION Spending for de novo cancer was greater than spending for recurrent advanced cancer. Understanding the patterns and drivers of spending is necessary to design alternative payment models and to improve value.

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INTRODUCTION

Much of the suffering and nearly all the mortality caused by cancer is attributable to advanced disease. Advanced disease develops in one of two ways: patients with de novo stage IV cancer have metastatic disease when their cancer is first diagnosed, and recurrent patients develop metastatic disease after treatment of a previously diagnosed localized (ie, stage I to III) cancer. For some cancer types, recurrence is more common than de novo metastatic disease (eg, breast cancer), whereas for others, de novo metastatic disease is more common (eg, lung cancer). Previously, we described differences in the treatments provided to and mortality experienced by patients with recurrent and de novo metastatic disease.[1] Recurrent patients were less likely to receive chemotherapy and radiation

compared with de novo patients. Patients with breast cancer with recurrence experienced inferior survival compared with de novo patients, whereas patients with lung and colorectal cancer with recurrence experienced similar survival compared with de novo patients.

Cost is another major burden associated with advanced disease.[2-4] Studies have suggested that spending during the initial phase of care is greater for patients with stage IV versus localized disease.[5-7] However, previous efforts to characterize spending for advanced cancer often have been limited because they focused predominantly on patients with de novo metastatic disease (largely because of the lack of recurrence status data in most tumor registries).[8-10] Although a few studies have generated spending estimates for breast cancer recurrence,[11-15] we still know

comparatively little about spending for recurrent metastatic disease. In addition, previous studies often have not analyzed spending across the entire episode of care. Patients with recurrent cancer may incur substantial costs for treatment/surveillance of the primary localized cancer.[16-20] Spending for these services, which occur before the advanced cancer diagnosis, affect lifetime cancer spending estimates and could affect advanced disease spending estimates.

To explore whether spending for recurrent and de novo advanced cancer differ meaningfully, we recently studied 7,112 adults with advanced breast, colorectal, and lung cancer treated in three Kaiser Permanente regions. We found higher spending for recurrent patients before the advanced cancer diagnosis and higher spending for de novo patients after the advanced cancer diagnosis.[21] Still, important questions remain with regard to advanced cancer spending, including spending patterns in the fee-for-service setting and the impact of various service types on spending differences. To evaluate spending across the entire initial care episode for advanced cancer, we compared mean monthly total and service-specific health care costs for a population-based sample of Medicare patients with breast, lung, or colorectal cancer who had either recurrent disease after prior treatment of a stage I to III cancer or de novo stage IV metastatic disease.

METHODS

Cohort Derivation

Using the linked SEER-Medicare claims database, we identified patients diagnosed with a primary breast, colorectal, or lung cancer.[22] All patients had to be continuously enrolled in Medicare Parts A and B, with no enrollment in a health maintenance organization, from the initial cancer diagnosis through the end of follow-up (the earlier of death, subsequent new primary cancer, or end of study [December 31, 2012]). Patients were excluded if the cancer diagnosis came from a death certificate, stage was 0/unknown, age at diagnosis was younger than 65 years, there was a previous history or cancer, Medicare eligibility was based on permanent disability/end-stage renal disease, or there were no Medicare claims from diagnosis through the end of follow-up. Part D enrollment was not required.

From this cohort, we identified two types of patients with advanced cancer: patients with de novo advanced cancer diagnosed with stage IV disease between 2008 and 2011 and patients with recurrent advanced cancer diagnosed with stage I to III disease (excluding stage IIIb lung cancer because of their high probability for having micrometastatic disease) between 1998 and 2011, treated with definitive local therapy (ie, surgery for all cancers except stage IIIa lung cancer where combined chemotherapy/radiation therapy was required) within 1 year of their initial cancer

diagnosis, and who subsequently developed recurrence between 2008 and 2011 (the same time range used for de novo diagnoses).[23] Recurrence status was determined using Medicare claims and our previously validated recurrence detection algorithms (area under the curve for recurrence detection, 0.924 to 0.953; median absolute error for recurrence timing, 2.1 to 5.5 months).[10,24] After the advanced cancer diagnosis date was determined, patients who were not continuously enrolled in Medicare for at least 12 months before that date were excluded. Patients who died less than 30 days after their advanced cancer diagnosis also were excluded.

Variable Derivations and Definitions

SEER files provided cancer features (eg, stage) and patient attributes (eg, sex). Claims during the 12 months preceding the advanced cancer diagnosis were used to derive a comorbidity score, excluding cancer diagnoses.[25-27] Claims also were used to identify receipt of chemotherapy (including cytotoxic, biologic, and oral agents) and radiation therapy.[28] For patients who developed recurrence, cancer-directed therapy for the initial stage I to III diagnosis would have occurred before recurrence. Thus, cancer-directed therapy was recorded both before and after the advanced cancer diagnosis and categorized on basis of time relative to the advanced cancer diagnosis. Among patients with de novo advanced disease, cancer therapy was only recorded after the initial cancer diagnoses. Hospitalizations and death were recorded during the 24-month period around the advanced cancer diagnosis.

The primary outcome was mean total monthly Medicare charges for all services provided. We calculated spending estimates for the 12-month period before (ie, from month -12 to month -1) and after (ie, from month 0 to month 11) the advanced cancer diagnosis. We also calculated monthly spending during the 24-month period surrounding (ie, from 12 months before to 11 months after) the advanced cancer diagnosis. Secondary outcomes included spending by Medicare file type, as follows: inpatient hospital and skilled nursing (Medicare Provider Analysis and Review), provider (National Claims History), outpatient (Outpatient Standard Analytical File), hospice, home health, durable medical equipment, and prescriptions (for patients enrolled in Part D). We included all spending that occurred before or within the month of death. Crude mean monthly spending estimates excluded patients who died in a previous month. Spending values were reported as 2012 US dollars.

Statistical Analyses

All analyses were performed separately for each cancer type. Mean monthly spending over time was plotted for all medical services as well as by type of service and by time from initial diagnosis to advanced disease (< 1, 1 to 2, > 2 to 4, or > 4 years). We analyzed differences in unadjusted

monthly spending between patients with recurrent and de novo advanced cancer during the year before and the year after the advanced cancer diagnosis using a permutation test. To estimate differences in total mean monthly spending across the 24-month observation period while controlling for other factors, we used multivariable linear regression to derive adjusted spending ratios (SRs). Model covariates were age, sex, race, ethnicity, income, marital status, comorbidity, year of advanced cancer diagnosis, type of advanced cancer (de novo or recurrent), month relative to the advanced cancer diagnosis, and month of death. To adjust for temporal differences in spending across the 24-month observation period, the model included an interaction term for advanced cancer type × month relative to advanced cancer diagnosis. There were multiple monthly spending estimates per patient, so general estimating equations were used to adjust for repeated measures. Log transformation of costs resulted in a reasonably approximate normal distribution, so log-transformed monthly cost was the dependent variable in these models. Some patients died during the 12-month period after the advanced cancer diagnosis, so monthly spending estimates during this period were adjusted on the basis of a patient's inverse probability of survival at the end of follow-up (using a logistic regression model that included selected variables listed in Appendix Table A1, online only).[29]

In a secondary analysis, we sought to describe the impact of hospitalization and chemotherapy on total monthly spending while controlling for other factors. To this end, we modified the primary model to indicate whether the patient was hospitalized or received chemotherapy during each month. After estimating monthly spending for the conditions of receiving and not receiving chemotherapy, we calculated the difference between these two values to derive the average increase in monthly spending associated with chemotherapy. The same method was applied to hospitalizations. All tests of statistical significance were two-sided. The institutional review board from the Dana-Farber/Harvard Cancer Center provided oversight for this project.

RESULTS

We identified 54,982 patients 65 years of age or older who developed advanced breast, colorectal, or lung cancer between 2008 and 2011. The proportion having recurrent disease varied by cancer type (80% breast, 62% colorectal, 12% lung, 38% overall; $P < .01$; Appendix Table A1). The mean age was 76 years. Blacks represented a significantly greater proportion of patients with de novo versus recurrent advanced cancer (9.3% v 7.6%; $P < .01$), as did those who had an annual income of less than \$40,000 (41.3% v 37.8%; $P < .01$). Among those for whom grade was known, having grade 3/4 disease was more common among de novo versus recurrent patients (57% v 35%; $P < .01$). Hospitalization, chemotherapy, radiation therapy, and

death were all more common after a de novo versus recurrent advanced cancer diagnosis.

Plots and estimates of unadjusted total mean monthly spending (Figs 1-3; Table 1) demonstrate several consistent patterns across all three cancer types. Before the advanced cancer diagnosis, spending was significantly higher among patients with recurrent versus de novo advanced disease ($P < .001$). These differences persisted whether we analyzed recurrences that occurred less than or more than 1 year after the initial cancer diagnosis (data not shown). At the time of the advanced cancer diagnosis, spending for de novo patients peaked at a higher amount than for recurrent patients. This peridiagnosis spending peak predominantly was due to inpatient spending and was largest for patients with colorectal cancer. After the advanced cancer diagnosis, spending for de novo patients was significantly higher than for recurrent patients ($P < .001$). Finally, comparison of patients with de novo and recurrent cancer showed that monthly spending estimates for most categories of medical service before and after the advanced cancer diagnosis were statistically significantly different.

We stratified spending by Medicare file type to describe how patterns of spending differed for patients with de novo versus recurrent cancer and to explore which types of services were responsible for spending throughout the 24-month observation period (Figs 1, 2 and 3; Table 1). Inpatient services accounted for the largest share of spending before and after the advanced cancer diagnosis, except for patients with recurrent breast cancer. Provider and outpatient spending was significantly higher for recurrent patients before the advanced cancer diagnosis and for de novo patients after the advanced cancer diagnosis ($P < .001$). Although inpatient services accounted for the largest absolute increase in spending after versus before an advanced cancer diagnosis, hospice services were responsible for the largest relative increase in spending over time.

Multivariable analysis showed that comorbidity was associated with the largest increase in spending across all cancer types (Table 2). Compared with patients with recurrent advanced disease, those with de novo metastatic cancer had significantly higher monthly spending for breast (SR, 2.4; 95% CI, 2.05 to 2.77; $P < .001$), colorectal (SR, 2.6; 95% CI, 2.31 to 3.01; $P < .001$), and lung (SR, 1.5; 95% CI, 1.30 to 1.65; $P < .001$) cancer. Other factors associated with significantly greater monthly spending among patients with colorectal and lung cancer included being married (v not) and being in the highest (v lowest) income group. In contrast, patients with breast cancer who were married had significantly lower spending. Spending during the last month of life was significantly greater than spending during the preceding months, with the largest impact occurring for breast (SR, 2.7; 95% CI, 2.46 to 2.85; $P < .001$) followed by colorectal (SR, 1.6; 95% CI, 1.49 to
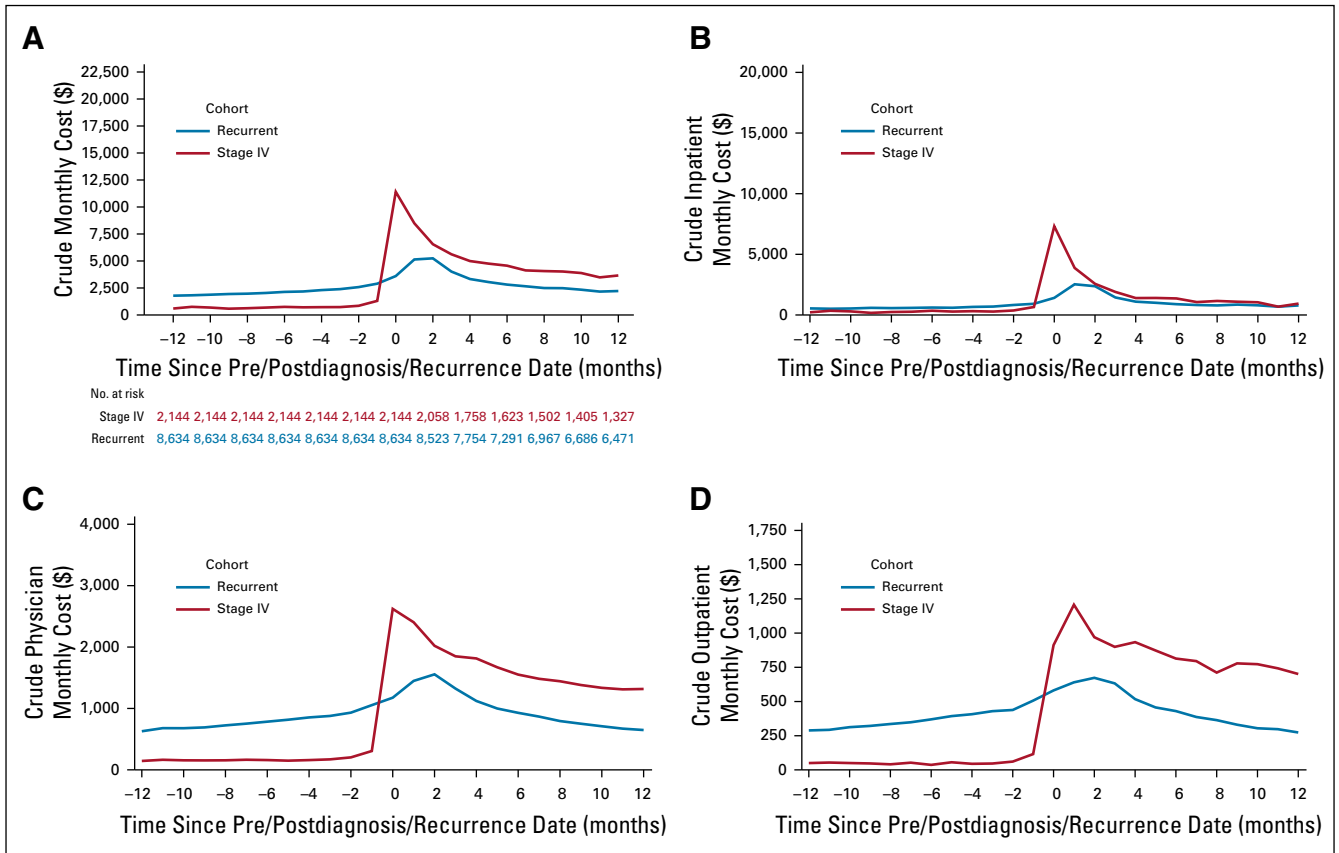
FIG 1. Unadjusted mean per-patient per-month spending for all Medicare fee-for-service files from 1 year before to 1 year after an advanced breast cancer diagnosis for patients with de novo stage IV (red) versus recurrent (blue) advanced disease. (A) Total spending. (B) Inpatient (Medicare provider analysis and review) spending. (C) Physician (national claims history) spending. (D) Outpatient (Outpatient standard analytic file) spending. Spending estimates reflect constant 2012 US dollars. Statistical comparisons of spending for de novo versus recurrent patients are presented in Table 2.

1.70; $P < .001$) and lung (SR, 1.3; 95% CI, 1.24 to 1.34; $P < .001$) cancer.

Chemotherapy receipt was associated with significantly higher total monthly spending for patients with breast (SR, 8.3; 95% CI, 8.01 to 8.70; $P < .001$), colorectal (SR, 9.1; 95% CI, 8.67 to 9.52; $P < .001$), and lung (SR, 4.8; 95% CI, 4.62 to 4.93; $P < .001$) cancer. Hospitalization also was associated with significantly higher monthly spending for patients with breast (SR, 21.7; 95% CI, 20.92 to 22.50; $P < .001$), colorectal (SR, 23.3; 95% CI, 22.49 to 24.05; $P < .001$), and lung (SR, 12.4; 95% CI, 12.11 to 12.66; $P < .001$) cancer. The average increases in total monthly spending associated with chemotherapy and hospitalization were $7,301 and $15,817 for breast, $11,908 and $20,615 for colorectal, and $5,995 and $10,762 for lung, respectively. Even after adding chemotherapy and hospitalization to the model, the spending differential between patients with de novo and recurrent cancer remained significant: breast SR, 1.7 (95% CI, 1.46 to 1.90; $P < .001$); colorectal SR, 1.5 (95% CI, 1.34 to 1.68; $P < .001$); and lung SR, 1.2 (95% CI, 1.09 to 1.35; $P < .001$).

DISCUSSION

Using Medicare fee-for-service claims for a population-based sample of patients with breast, colorectal, and lung cancer, we found substantially greater spending for patients with de novo versus recurrent advanced disease. This difference was largely attributable to higher spending for inpatient, outpatient (including chemotherapy), and physician services during the year after the advanced cancer diagnosis. That said, even when we controlled for hospitalizations, chemotherapy receipt, and other factors, mean monthly spending during the 2-year period surrounding the advanced cancer diagnosis was still 20% to 70% higher for patients with de novo versus recurrent advanced disease.

There could be several reasons for why spending around a de novo advanced cancer diagnosis was greater than spending around a recurrent advanced cancer diagnosis. Many patients with recurrent disease received surgery and/or adjuvant treatment of their initial cancer diagnosis, so they may not have been eligible to receive treatment

TABLE 1. Mean Monthly Spending (Unadjusted) for Patients With De Novo and Recurrent Advanced Cancer During the Year Before and the Year After the Advanced Cancer Diagnosis by Medicare File Type in 2012 US Dollars

	Year Before Advanced Cancer Diagnosis					Year After Advanced Cancer Diagnosis				
	De Novo		Recurrent		Absolute Difference*	De Novo		Recurrent		Absolute Difference*
Cancer Type	$	%	$	%	$	$	%	$	%	$
Breast										
Inpatient	316	43.4	637	29.7	−321†	2,296	39.7	1,274	38.1	1,022†
Physician	174	23.8	789	36.9	−615†	1,802	31.1	1,055	31.5	747†
Outpatient	55	7.5	370	17.3	−315†	885	15.3	480	14.3	405†
Hospice	6	0.8	11	0.5	−5	299	5.2	137	4.1	162†
Home health	52	7.1	91	4.3	−39†	217	3.8	125	3.7	92†
DME	20	2.7	40	1.8	−20†	75	1.3	62	1.8	13‡
Prescriptions	106	14.6	204	9.5	−98†	217	3.7	215	6.4	2
Monthly total	729	100	2,141	100	−1,412†	5,791	100	3,348	100	2,443†
Annualized total§	8,748		25,692		−16,944	69,492		40,176		29,316
Colorectal										
Inpatient	436	49.7	2,094	54.0	−1,658†	4,520	47.1	2,104	44.4	2,416†
Physician	193	22.0	1,003	25.9	−810†	2,816	29.4	1,303	27.5	1,513†
Outpatient	75	8.5	366	9.4	−291†	1,189	12.4	554	11.7	635†
Hospice	4	0.4	31	0.8	−27†	428	4.5	308	6.5	120†
Home health	44	5.0	154	4.0	−110†	244	2.5	184	3.9	60†
DME	17	2.0	88	2.3	−71†	239	2.5	126	2.7	113†
Prescriptions	107	12.2	142	3.7	−35†	153	1.6	164	3.5	−11
Monthly total	877	100	3,879	100	−3,002†	9,587	100	4,743	100	4,844†
Annualized total§	10,524		46,548		−36,024	115,044		56,916		58,128
Lung										
Inpatient	445	44.8	1,723	45.4	−1,278†	3,725	46.0	2,553	44.4	1,172†
Physician	237	23.9	1,142	30.1	−905†	2,228	27.5	1,541	26.8	687†
Outpatient	90	9.1	566	14.9	−476†	1,116	13.8	722	12.6	394†
Hospice	3	0.3	9	0.2	−6‡	463	5.7	371	6.5	92†
Home health	47	4.7	115	3.0	−68†	196	2.4	190	3.3	6
DME	33	3.3	54	1.4	−21†	75	0.9	78	1.4	−3
Prescriptions	138	13.9	189	5.0	−51†	296	3.7	288	5.0	8
Monthly total	993	100	3,798	100	−2,805†	8,099	100	5,743	100	2,356†
Annualized total§	11,916		45,576		−33,660	97,188		68,916		28,272

NOTE. Mean monthly spending represents the average of every month before an advanced cancer diagnosis (ie, months −12 to −1) or every month after an advanced cancer diagnosis (ie, months 0 to 11).

Abbreviation: DME, durable medical equipment.

*De novo versus recurrent.

†$P < .001$ using a permutation test for the comparison between de novo and recurrent spending.

‡$P < .05$ using a permutation test for the comparison between de novo and recurrent spending.

§Annualized total spending estimates simply reflect the monthly total spending estimates × 12.

again when advanced disease developed. In addition, they may have been less inclined to receive aggressive care because they had different treatment goals.[30] Among those who did receive therapy, early treatment discontinuation and early cancer-related symptoms may have been more likely because their disease was less responsive to therapy.

Alternatively, patients with de novo disease may have had more spending around their advanced cancer diagnosis because they tended to present with symptomatic disease, whereas patients with recurrent disease may have been more likely to present with abnormal surveillance scans and a lower burden of disease.
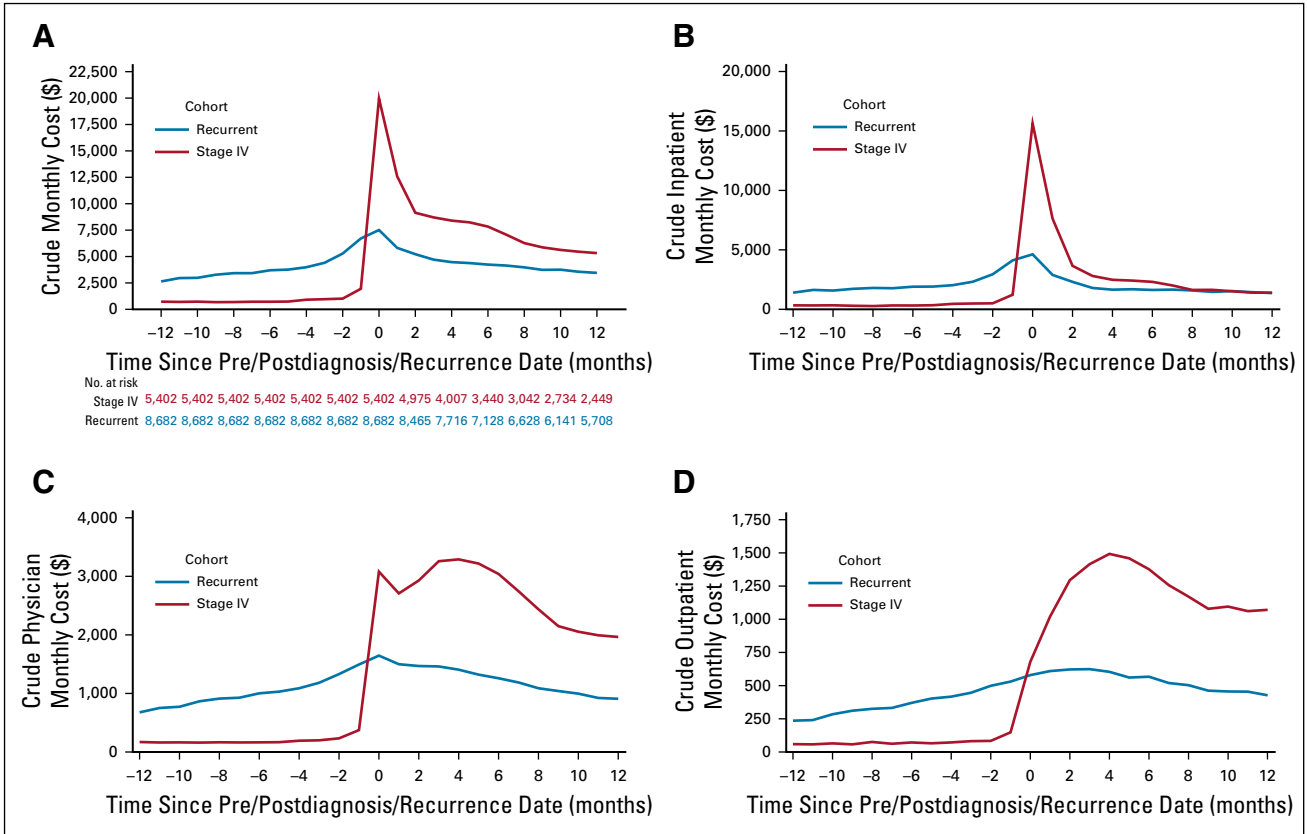
FIG 2. Unadjusted mean per-patient per-month spending for all Medicare fee-for-service files from 1 year before to 1 year after an advanced colorectal cancer diagnosis for patients with de novo stage IV (red) versus recurrent (blue) advanced disease. (A) Total spending. (B) Inpatient (Medicare provider analysis and review) spending. (C) Physician (national claims history) spending. (D) Outpatient (outpatient standard analytic file) spending. Spending estimates reflect constant 2012 US dollars. Statistical comparisons of spending for de novo versus recurrent patients are presented in Table 2.

We analyzed spending during the 24-month period that spanned the advanced cancer diagnosis (ie, 12 months before to 11 months after) for several reasons. First, the monetary impact of an advanced cancer diagnosis extends over many months and may include evaluative services provided before and treatments provided after the advanced cancer diagnosis. Second, the date of the recurrent cancer diagnosis was estimated using claims, so the true advanced cancer diagnosis date may have been a few months before or after the estimated date. Third, studying the 12-month period before the advanced cancer diagnosis allowed us to compare the survivorship phase of care among patients previously treated for stage I to III cancer to the prediagnosis phase of care among patients who developed de novo stage IV advanced cancer.

Not surprisingly, spending patterns differed during the 12 months before versus 12 months after the advanced cancer diagnosis. Before, spending in the recurrent cohort exceeded spending in the de novo cohort. This was due to multiple factors. Among patients who developed recurrence less than 1 year after their initial cancer diagnosis, prerecurrence spending was driven by treatment of the initial localized cancer. Among patients who developed recurrence more than 1 year after their initial cancer diagnosis,

prerecurrence spending reflected survivorship care and evaluative services used to help to diagnosis recurrence. Our findings not only confirm previous research that demonstrated higher net costs for cancer survivors[31] but also extend the existing knowledge base by describing the impact of cancer recurrence on the survivorship phase of care. (Most previous studies were not able to discriminate between patients diagnosed with stage I to III cancer who did v did not develop recurrent disease.)

After the advanced cancer diagnosis, spending in the de novo cohort exceeded spending in the recurrent cohort. This also was due to multiple factors, particularly hospitalizations, outpatient services (including chemotherapy), and physician services. Of note, lower total spending after the advanced cancer diagnosis in the recurrent cohort did not translate into greater spending for hospice services. In fact, hospice spending was greater for patients with de novo versus recurrent cancer ($P < .05$). Hospice was responsible for the largest relative increase in spending after versus before the advanced cancer diagnosis, but it still only accounted for a small proportion of total monthly spending in the postdiagnosis period (4.1% to 6.5%; Table 2).
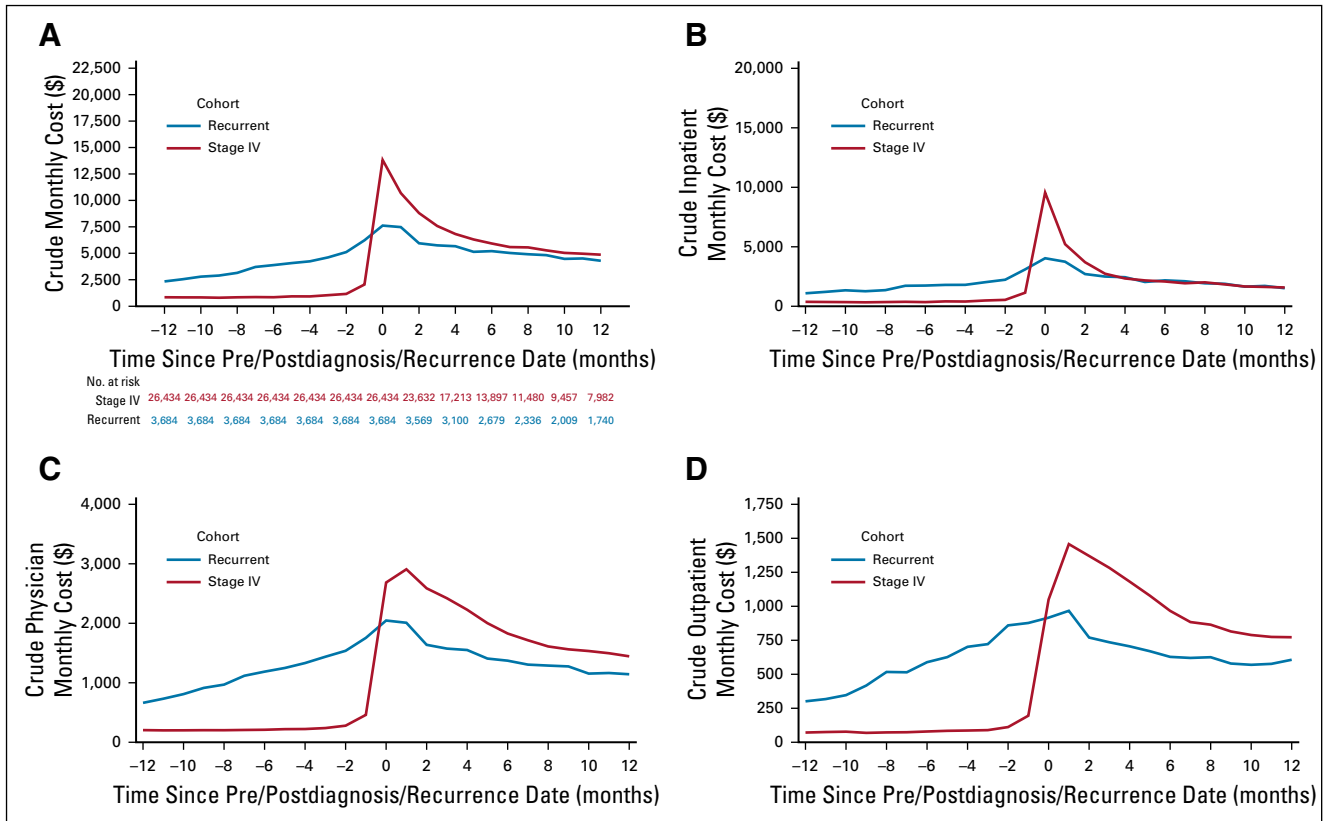
FIG 3. Unadjusted mean per-patient per-month spending for all Medicare fee-for-service files from 1 year before to 1 year after an advanced lung cancer diagnosis for patients with de novo stage IV (red) versus recurrent (blue) advanced disease. (A) Total spending. (B) Inpatient (Medicare provider analysis and review) spending. (C) Physician (national claims history) spending. (D) Outpatient (outpatient standard analytic file) spending. Spending estimates reflect constant 2012 US dollars. Statistical comparisons of spending for de novo versus recurrent patients are presented in Table 2.

Our findings validate results from previous studies of patients with metastatic disease,[11-15,31-33] and our spending estimates were similar to those derived from our previous analysis of data from three capitation-based Kaiser Permanente regions.[21] Our results extend the current knowledge base because they were based on a population-based sample of patients with multiple different cancer types, evaluated fee-for-service spending before and after the advanced cancer diagnosis, and described advanced cancer spending by type of service (including hospitalizations and chemotherapy). Our analysis was uniquely able to account for recurrence because it made use of a novel, claims-based recurrence detection tool. Analyses have demonstrated that this tool is highly accurate, but misclassification risk remains.[10,24] For example, the algorithm cannot exclude all patients with locoregional recurrence; this could have introduced a downward bias for the recurrence spending estimates among patients with breast cancer. Patients who developed recurrence but did not receive any treatment could have been inappropriately excluded from the recurrence sample. If so, then we may have overestimated total spending for recurrence. Finally, we estimated spending from the payer/health system perspective, so we did not include patients' potentially substantial out-of-pocket financial liabilities.[34]

Implications of our study include that historical estimates of spending for advanced disease could overestimate actual spending because they do not account for recurrent disease and historical estimates of spending for the continuing (ie, survivorship) phase of care could overestimate actual spending because they incorrectly include spending for recurrent disease.[4,31,35] Our findings highlight the importance of clearly defining starting/stopping points and reimbursement amounts for episode-based payment models. Perhaps recurrence status should be used to identify the end of an initial treatment and the beginning of a recurrent treatment episode and to help to develop fair reimbursement policies for these episodes. For payers who prefer reimbursement models that are based on total cost of care, recurrence could be used to adjust payment amounts and to help to discriminate between high- and low-value spending areas or institutions. The large spike in spending around the time of an advanced cancer diagnosis underscores the importance of assessing financial toxicity and providing social support to patients with advanced cancer. Finally, our findings highlight the need for more research with regard to the goals, preferences, and values of patients with de novo and recurrent advanced cancer.

TABLE 2. Ratio of Mean Monthly Spending for Selected Characteristics While Controlling for Other Factors

	Breast Cancer			Colorectal Cancer			Lung Cancer		
Variable	SR	95% CI	P	SR	95% CI	P	SR	95% CI	P
Type of advanced cancer									
Recurrent	Ref	—	—	Ref	—	—	Ref	—	—
De novo	2.39	2.05 to 2.77	< .001	2.64	2.31 to 3.01	< .001	1.46	1.30 to 1.65	< .001
Age group, years									
65-74	Ref	—	—	Ref	—	—	Ref	—	—
75-84	0.88	0.83 to 0.94	< .001	0.84	0.80 to 0.89	< .001	0.98	0.94 to 1.01	.189
≥ 85	0.80	0.73 to 0.88	< .001	0.68	0.63 to 0.74	< .001	0.74	0.69 to 0.79	< .001
Sex									
Male	—	—	—	Ref	—	—	Ref	—	—
Female	—	—	—	1.31	1.24 to 1.38	< .001	1.44	1.38 to 1.49	< .001
Race									
White	Ref	—	—	Ref	—	—	Ref	—	—
Black	0.95	0.80 to 1.05	.292	1.05	1.01 to 1.27	.330	0.99	1.00 to 1.19	.818
API or other	0.91	0.86 to 1.05	.191	1.13	0.95 to 1.16	.030	1.09	0.93 to 1.06	.041
Ethnicity									
Hispanic	Ref	—	—	Ref	—	—	Ref	—	—
Non-Hispanic	0.76	0.69 to 0.85	< .001	0.86	0.78 to 0.95	.003	0.94	0.86 to 1.02	.146
Marital status									
Married	Ref	—	—	Ref	—	—	Ref	—	—
Not married	1.08	1.02 to 1.14	.006	0.92	0.87 to 0.97	.004	0.93	0.89 to 0.97	< .001
Median annual household income, $*									
< 40,000	Ref	—	—	Ref	—	—	Ref	—	—
40,000-60,000	0.90	0.84 to 0.96	.001	1.02	0.96 to 1.09	.467	1.05	1.00 to 1.09	.032
> 60,000	0.99	0.92 to 1.06	.749	1.13	1.06 to 1.2	< .001	1.19	1.13 to 1.25	< .001
No. of comorbidities†									
0	Ref	—	—	Ref	—	—	Ref	—	—
1	1.95	1.83 to 2.08	< .001	2.12	1.99 to 2.26	< .001	2.38	2.28 to 2.49	< .001
≥ 2	3.35	3.14 to 3.57	< .001	3.44	3.24 to 3.66	< .001	3.51	3.35 to 3.67	< .001
Year of advanced cancer diagnosis									
2008	Ref	—	—	Ref	—	—	Ref	—	—
2009	0.99	0.91 to 1.07	.751	1.00	0.93 to 1.07	.972	1.00	0.95 to 1.05	.988
2010	0.99	0.92 to 1.07	.760	1.01	0.94 to 1.09	.719	1.01	0.96 to 1.06	.626
2011	1.00	0.93 to 1.07	.922	1.07	1.00 to 1.15	.062	1.02	0.97 to 1.07	.534
Month relative to death									
Previous months	Ref	—	—	Ref	—	—	Ref	—	—
Last month of life	2.65	2.46 to 2.85	< .001	1.59	1.49 to 1.70	< .001	1.29	1.24 to 1.34	< .001

NOTE. The ratio compares mean monthly spending for one subgroup relative to the reference subgroup for that variable (eg, spending for patients with de novo v recurrent advanced cancer). The multivariable model analyzes spending for the 25-month period from 12 months before to 12 months after the metastatic cancer diagnosis. Covariates in the multivariable model included all variables listed in the table plus month and an interaction between month and de novo/recurrent status. Deaths could only have occurred after the advanced cancer diagnosis (ie, in the second half of the observation period).

Abbreviations: API, Asian/Pacific Islander; Ref, referent group; SR, spending ratio.

*On the basis of the census tract of residence.

†On the basis of the scoring system developed by Charlson et al,[25] Klabunde et al,[26] and Deyo et al.[27]

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Spending for Advanced Cancer Diagnoses: Comparing Recurrent Versus De Novo Stage IV Disease

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APPENDIX

TABLE A1. Characteristics of Patients With Advanced Breast, Colorectal, or Lung Cancer, 2008 to 2011

Characteristic	De Novo, No. (%)	Recurrent, No. (%)
No. of patients	33,980	21,002
Mean age, years (SD)	76.5 (7.0)	76.3 (7.1)
Age group, years		
65-74	15,817 (46.6)	9,806 (46.7)
75-84	13,644 (40.2)	8,492 (40.4)
≥ 85	4,519 (13.3)	2,704 (12.9)
Sex*		
Male	16,140 (47.5)	5,711 (27.2)
Female	17,840 (52.5)	15,291 (72.8)
Region*		
Northeast	6,762 (19.9)	4,832 (23.0)
South	9,838 (29.0)	5,337 (25.4)
Midwest	4,551 (13.4)	2,900 (13.8)
West	12,829 (37.8)	7,933 (37.8)
Race*		
White	28,983 (85.3)	18,422 (87.7)
Black	3,167 (9.3)	1,589 (7.6)
API/other	1,830 (5.4)	991 (4.7)
Ethnicity*		
Hispanic	1,649 (4.9)	1,145 (5.5)
Non-Hispanic	32,331 (95.2)	19,857 (94.6)
Marital status		
Married	16,077 (47.3)	9,935 (47.3)
Unmarried/unknown	17,903 (52.7)	11,067 (52.7)
Median annual household income, $*		
< 40,000	14,045 (41.3)	7,938 (37.8)
40,000-60,000	12,031 (35.4)	7,469 (35.6)
> 60,000	7,904 (23.3)	5,595 (26.6)
Comorbidity score*†		
0	16,606 (48.9)	8,532 (40.6)
1	8,919 (26.3)	5,861 (27.9)
≥ 2	8,455 (24.9)	6,609 (31.5)
Year of metastatic diagnosis*		
2008	8,744 (25.7)	5,638 (26.9)
2009	8,698 (25.6)	5,413 (25.8)
2010	8,575 (25.2)	5,064 (24.1)
2011	7,963 (23.4)	4,887 (23.3)
Cancer type*		
Breast	2,144 (6.3)	8,636 (41.1)
Colorectal	5,402 (15.9)	8,682 (41.3)
Lung	26,434 (77.8)	3,684 (17.5)
Cancer grade*		
1/2	6,809 (20.0)	12,539 (59.7)
3/4	8,969 (26.4)	6,811 (32.4)
Unknown	18,202 (53.6)	1,652 (7.9)

(continued in next column)

TABLE A1. Characteristics of Patients With Advanced Breast, Colorectal, or Lung Cancer, 2008 to 2011 (continued)

Characteristic	De Novo, No. (%)	Recurrent, No. (%)
Hormone receptor status (only patients with breast cancer)*		
Positive	1,447 (67.5)	6,341 (73.4)
Negative	386 (18.0)	1,699 (19.7)
Unknown	311 (14.5)	596 (6.9)
Cancer stage‡		
I	—	5,940 (28.3)
II	—	6,795 (32.4)
III	—	8,267 (39.4)
IV	33,980 (100.0)	—
Time from primary cancer to recurrence, years§		
< 1	—	7,803 (37.2)
1-2	—	4,550 (21.7)
2-4	—	4,580 (21.8)
≥ 4	—	4,069 (19.4)
Chemotherapy receipt‖ (relative to advanced cancer diagnosis)		
−13 months or before	—	6,036 (28.7)
−12 to −7 months	—	4,678 (22.3)
−6 to −1 months	—	7,185 (34.2)
0 to 5 months*	19,185 (56.5)	9,332 (44.4)
6 to 11 months	10,279 (30.3)	6,255 (29.8)
Radiation therapy‖ (relative to advanced cancer diagnosis)		
−13 months or earlier	—	4,420 (21.1)
−12 to −7 months	—	1,778 (8.5)
−6 to −1 months	—	2,900 (13.8)
0 to 5 months*	13,373 (39.4)	4,217 (20.1)
6 to 11 months*	4,294 (12.6)	1,777 (8.5)
Inpatient hospitalization within 12 months after advanced cancer diagnosis*	27,985 (82.4)	11,933 (56.8)
Death within 12 months after advanced cancer diagnosis*	22,624 (66.6)	7,282 (34.7)

Abbreviations: API, Asian/Pacific Islander; SD, standard deviation.

*Indicates statistically significantly difference for de novo versus recurrent patients on the basis of the χ^2 test ($P < .01$).

†Determined using claims from 13 months before to 1 month before being diagnosed with metastatic (either de novo or recurrent) cancer.

‡By definition, patients with recurrent cancer could only have had stage I to III disease, and patients with de novo metastatic disease could only have had stage IV disease.

§Recurrence was only evaluated for patients diagnosed with stage I to III cancer; patients with de novo stage IV cancer had advanced disease at diagnosis.

‖Patients with recurrence could have received chemotherapy or radiation therapy for their initial stage I to III cancer diagnosis (ie, before recurrence), whereas patients with de novo stage IV disease had no evidence of cancer before their stage IV diagnosis. Therefore, among patients with de novo advanced cancer, chemotherapy and radiation therapy use were only ascertained after the initial cancer diagnosis.