RESEARCH

Medical Costs Associated with Use of Systemic Therapy in Adults with Colorectal Cancer

Brian S. Seal, RPh, MBA, PhD; Sean D. Sullivan, PhD; Scott Ramsey, MD, PhD; Kenneth M. Shermock, PharmD, PhD; Jinma Ren, PhD; Charlie Kreilick, Susan H. Foltz Boklage, MS; Satish Valluri, PhD, MPH, MS; Syam Sarma, PhD; and Carl V. Asche, PhD

ABSTRACT

BACKGROUND: New cytotoxic agents and regimens, as well as immunotherapeutics, have recently been introduced for treatment of colorectal cancer (CRC).

OBJECTIVE: To identify the patient-related and clinical and treatment-related factors associated with higher total health care expenditures in newly diagnosed patients with CRC who are receiving systemic therapy (biologic or chemotherapy) from a commercially insured population.

METHODS: A longitudinal, retrospective analysis was employed to estimate costs and determinants of CRC treatment in a U.S. claims database for health care services used by commercial patients aged 18 to 64 years, who were diagnosed with CRC between January 1, 2005, and June 30, 2009. Generalized linear regression modeling was used to estimate the influence of demographic, clinical, and treatment factors on medical expenditures.

RESULTS: Among the 5,160 patients newly diagnosed with CRC, 99.6% of patients had chemotherapy; 32.6% had biologics; and 85.6% had other pharmaceuticals (excluding the chemotherapy and biologics of interest). The average annualized per patient cost of CRC treatment was $97,400 and consisted of chemotherapy ($17,500), biologics ($30,400), other pharmaceuticals ($2,300), inpatient treatment ($26,300), and outpatient treatment ($42,900). From first line only, first and second lines only, and third+ lines, the cost per patient was $70,500, $100,100, and $152,900, respectively. After adjusting for health care inflation, the average treatment cost of CRC patients increased by 73% from 2005 to 2009. Adjusted analyses showed that the higher medical cost for CRC patients was associated with use of new regimens, metastasis, comorbidities, surgery, radiation, insurance plan, age, sex, and region.

CONCLUSION: The health care cost of CRC treatment is increasing significantly over time, which is most likely caused by the use of new regimens, higher chances of surgery and radiation, and occurrence of various comorbidities and metastatic diseases due to increasing survival time.

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What is already known about this subject

- Clinical studies indicate that bevacizumab in combination with 5-fluorouracil/leucovorin (FU/LV) and bevacizumab in combination with irinotecan plus FU/LV (Folfiri) are clinically more effective in comparison with standard chemotherapy options for the first-line treatment of metastatic colorectal cancer (CRC).
- An assessment of 8 commonly prescribed regimens reported that the largest cost differential for 6 cycles of planned treatment was $35,971, between Folfiri ($36,999) and FU/LV ($1,028).
- A study in Greece illustrated that the mean 20-week total cost varied between €18,242 and €19,701 per patent for using cetuximab.

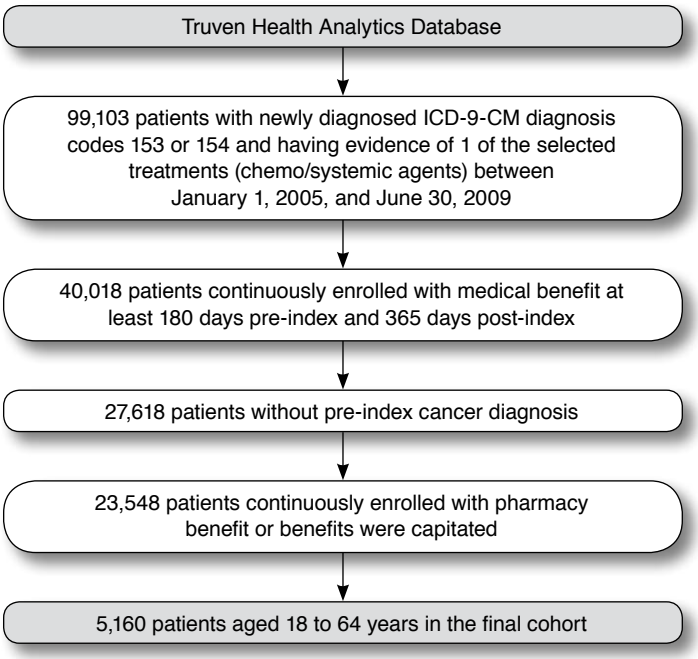
What this study adds

- Previous studies have demonstrated that new CRC regimens could have higher costs; however, little is known about the trend of medical costs over time and the impact due to health care inflation and other confounding factors. Our study adds an economic assessment of comparative costs and cost-effectiveness, as they are important for assessing the value of treatment regimens for CRC.
- Our findings have demonstrated that health care costs of CRC treatment is increasing significantly over time.

Colorectal cancer (CRC) is among the most common malignancies in developed countries.[1] In 2008, it was estimated that there were 1,233,000 incident cases of CRC diagnosed worldwide: 663,000 new cases diagnosed in men and 570,000 new cases in women, and almost 60% of the cases occurred in developed regions.[2] Additionally, the medical costs associated with the diagnosis and treatment of CRC patients are substantial,[1,3-7] which undoubtedly has become a significant economic burden on the countries and the families with CRC patients. Compared with matched patients with no cancer, total monthly costs were $14,585 higher for metastatic CRC patients, which was driven by higher inpatient ($7,546) and outpatient ($6,749) care.[5] Furthermore, with the development of pharmaceuticals and medical technology, infusing new chemotherapies and biologics, CRC therapies could further increase the cost burden on the health system.

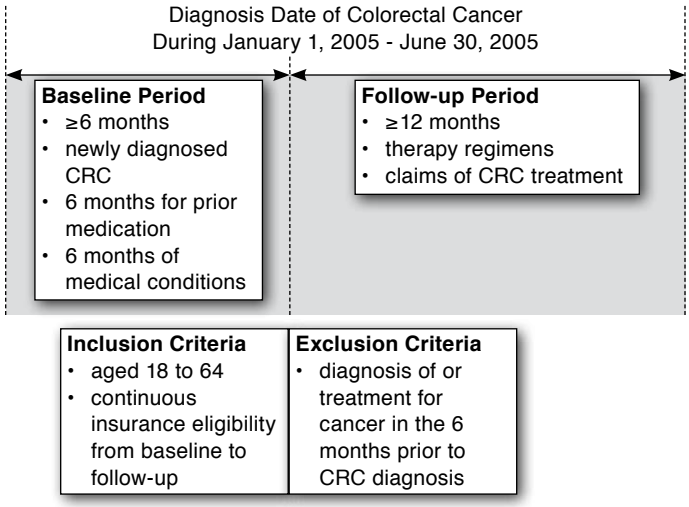
New cytotoxic agents and regimens, as well as immunotherapeutics, have been introduced during the past 8 years.[8] Clinical studies indicate that bevacizumab in combination with 5-fluorouracil/leucovorin (FU/LV) and bevacizumab in combination with irinotecan plus FU/LV (Folfiri) are clinically more effective in comparison with standard chemotherapy options for the first-line treatment of metastatic CRC.[9] However, these expanded options have increased treatment costs and, in some cases, toxicity. As an example, an assessment of 8 commonly prescribed regimens reported that the largest cost differential for 6 cycles of planned treatment was $35,971, between Folfiri ($36,999) and FU/LV ($1,028).[6] A study in Greece illustrated that the mean 20-week total cost varied between €18,242 and €19,701 per patent for using cetuximab.[4] Although previous studies have demonstrated that new CRC regimens could have

FIGURE 1 Population Identification: Patients in the Database



ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

FIGURE 2 Cohort Selection



CRC = colorectal cancer.

higher costs, little is known about the trend of medical costs over time and the impact due to health care inflation and other confounding factors. Therefore, economic assessment of comparative costs and cost-effectiveness are important for assessing the value of treatment regimens for CRC. The aim of this study was to identify the patient-related and clinical and treatment-related factors associated with higher total health care expenditures in newly diagnosed patients with CRC who are receiving systemic therapy (biologic or chemotherapy) from a commercially insured population.

Methods

Data Source

A retrospective analysis was performed using enrollment, medical, and pharmacy claims data from the MarketScan Commercial and Claims Encounter database (Truven Health Analytics). The MarketScan database provides anonymous paid claims data for individual patients covered by commercial health plans that represent several different kinds of employers in the United States and approximately 18 to 20 million commercial lives annually. The database records annual prevalence, cost, demographic, clinical, and utilization statistics for health conditions by type of insurance coverage. Health care services utilized by newly diagnosed patients between January 1, 2005, and June 30, 2009, were included in this analysis. Eligible patients satisfied the following requirements: (a) aged 18 to 64 years when newly diagnosed with CRC and (b) at least 6 months of patient history prior to CRC diagnosis and at least 1-year post-index continuous enrollment.

Inclusion and Exclusion Criteria

Patients newly diagnosed between January 1, 2005, and June 30, 2009, with malignant neoplasm of colon (*International Classicafication of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] diagnosis code 153) or malignant neoplasm of rectum, rectosigmoid junction, and anus (ICD-9-CM diagnosis code 154) and having evidence of 1 of the selected treatments (oxaliplatin, irinotecan, fluorouracil [FU], leucovorin [LV], capecitabine, bevacizumab [Avastin] cetuximab, and panitumumab) were identified. As depicted in Figure 1 and Figure 2, our study utilized a look-back period of 180 days to establish whether patients had prior evidence of CRC. Diagnosis of CRC is termed the "index event" for this analysis. Patients with at least 6 months of patient history prior to and at least 1 year of continuous enrollment post-index event were included in the analysis. Patients who had a diagnosis of or treatment for cancer in the 6 months prior to CRC diagnosis and patients who were not continuously enrolled with pharmacy benefits were excluded. Also, we removed patients aged either over 64 or less than 18 years at diagnosis and deleted information when the exact age at the end of the study was more than aged 65 years.

Patients were followed from initial CRC diagnosis (index date) to disenrollment or June 30, 2010 (Figure 2). Chemotherapy and biologic treatments over time were analyzed to identify lines of therapy. Total health care costs, including costs associated with CRC and other comorbidities, were calculated.

TABLE 1 Patient Demographics and Comorbidities at Diagnosis

Item	N	%
Age		
18-50 years	1,618	31.4
51-60 years	2,698	52.3
61-64 years	844	16.4
Gender		
Male	2,822	54.7
Female	2,338	45.3
Metastasis		
No	2,102	40.7
Yes	3,058	59.3
Comorbidities		
All[a]	1,113	21.6
Diabetes	654	12.7
Chronic obstructive pulmonary disease	238	4.6
Cerebrovascular disease	76	1.5
Congestive heart failure	68	1.3
Peripheral vascular disease	46	0.9
Chronic renal failure	31	0.6

[a]*All comorbidities included myocardial infarction, dementia, paralysis, various cirrhodites , moderate-severe liver disease, ulcers, rheum (including rheumatoid arthritis, systemic lupus, mixed connective tissue disorder, polymyositis, rheumatic polymyositis), malignant cancer, metastatic cancer, autoimmunodeficiency syndrome, and the 6 listed in this table.*

Lines of Therapy

The daily chemotherapy and/or biologic use profile was examined to define each treatment regimen and lines of therapy by temporal relationship and sequencing of treatment regimens. First-line therapy was defined as all chemotherapy and/or biologic drugs given to a patient during the first 36 days after initiation of treatment and administered for 1 or more cycles. Discontinuation of a single drug from a combination regimen was not considered a change in line of therapy. The addition or substitution of chemotherapy or a biologic agent was considered a new line of therapy.

Systemic chemotherapy and biologic treatments were analyzed over time to identify lines of therapy. This included the following products: oxaliplatin, irinotecan, FU, LV, capecitabine, bevacizumab [Avastin], cetuximab, and panitumumab.

Statistical Analyses

The medical costs of CRC treatment consisted of chemotherapy, biologics, other pharmaceuticals, inpatient, and outpatient. Other pharmaceuticals excluded the chemotherapy and biologics of interest. Inpatient expenditure included other related costs except chemotherapy, biologics, and surgery. Outpatient expenditure included surgery, office visit, hospital, emergency room, and other related costs.

TABLE 2 Lines of Systemic Treatment for Colorectal Cancer Patients

Agent	First Line Only (N = 2,306)	First and Second Lines Only (N = 1,825)	Third + Lines (N = 1,029)	Chi-square	*P*
Chemotherapy					
Yes	2,292	1,817	1,028	4.2	0.124
No	14	8	1		
Biologics					
Yes	281	539	864	1,679.8	< 0.001
No	2,025	1,286	165		

All statistics were computed using SAS 9.2 (SAS Institute Inc., Cary, NC). Descriptive statistics included mean, frequency, and percentage. The chi-square test was employed to examine the distribution of chemotherapy and biologics across patients who received first line only, first and second lines only, and third + lines of treatment (the two-sided *P* value was set at 0.05). The excess expenditures associated with additional lines of therapy were estimated as the difference between the total medical expenditures for those with first line of therapy versus second and third + lines of therapy. Generalized linear regression modeling (with gamma distribution and log link function) was used to estimate the influence of demographic, clinical, and treatment factors on medical expenditures (the variables with $P < 0.05$ were considered as statistically significant factors). We also used nonlinear regression modeling to fit the trend of treatment costs for CRC patients from 2005 to 2009 in order to examine whether the costs increased over time after adjusting for health care inflation.

Results

A total of 5,160 subjects diagnosed with CRC were included in the analysis. The profiles of patients in this study are shown in Table 1.

Treatments

Among the patients newly diagnosed with CRC, all patients received either chemotherapy or biologics: 32.6% (1,684 of 5,160) received biologics, and 85.6% (4,417 of 5,160) had other pharmaceuticals (excluding the chemotherapy and biologics of interest). Of these patients, 44.7% (2,306 of 5,160) received first line only; 35.4% (1,825 of 5,160) received first and second lines only, and 19.9% (1,029 of 5,160) received third + lines of treatment for CRC. Table 2 shows that regardless of what therapy line was selected, chemotherapy was most likely used to treat CRC patients. However, biologics were more commonly added into regimens in the third + lines (84.0%) compared with the first line only (12.2%) and the first and second lines only (29.5%).

TABLE 3 Comparison of Treatment Cost Components for Patients with Systemic Colorectal Cancer Therapy (×1000 Dollars, Average Annualized Cost Per Patient)

	Total Costs		Chemotherapy		Biologics		Other Pharmaceuticals[a]		Inpatient[b]		Outpatient[c]	
	N	Mean and SD	N	Mean and SD	N	Mean and SD	N	Mean and SD	N	Mean and SD	N	Mean and SD
All patients	5,160	97.4 ± 85.0	5,137	17.5 ± 18.6	1,684	30.4 ± 32.0	4,417	2.3 ± 4.6	4,953	26.3 ± 38.5	5,160	42.9 ± 44.1
First line only	2,306	70.5 ± 71.6	2,292	12.2 ± 15.8	281	19.4 ± 22.7	1,960	1.9 ± 3.7	2,175	22.2 ± 41.0	2,306	33.4 ± 39.6
First and second lines only	1,825	100.1 ± 76.9	1,817	18.5 ± 17.9	539	26.8 ± 30.4	1,549	2.2 ± 4.6	1,786	28.4 ± 35.6	1,825	44.1 ± 38.0
Third+ lines	1,029	152.9 ± 97.6	1,028	27.5 ± 21.0	864	36.1 ± 34.3	908	3.4 ± 6.0	992	31.6 ± 36.9	1,029	61.8 ± 55.7

[a]*Other pharmaceuticals excluded the chemo and biologics of interest.*

[b]*Inpatient expenditure included other related costs of inpatient treatment except chemotherapy, biologics, and surgery.*

[c]*Outpatient expenditure included surgery, office visit, hospital, emergency room, and other related costs of outpatient treatment.*

SD = standard deviation.

TABLE 4 Comparison of Treatment Cost Components for Patients With and Without Metastasis (×1000 Dollars, Average Annualized Cost Per Patient)

	Total Costs		Chemotherapy		Biologics		Other Pharmaceuticals		Inpatient		Outpatient	
	N	Mean and SD	N	Mean and SD	N	Mean and SD	N	Mean and SD	N	Mean and SD	N	Mean and SD
No metastasis	2,102[a]	61.8 ± 50.4	2,092	11.2 ± 13.2	137	16.1 ± 23.6	1,848	1.8 ± 3.4	1,968	19.4 ± 27.8	2,102	30.0 ± 26.0
With metastasis	3,058[a]	121.8 ± 94.7	3,045	21.8 ± 20.5	1,547	31.6 ± 32.4	2,569	2.7 ± 5.3	2,985	30.9 ± 43.6	3,058	51.7 ± 51.2

[a]*Unequal variance t-test, t = 29.5, P < 0.01.*

SD = standard deviation.

Also, 59.3% (3,058 of 5,160) of patients were found with metastatic diseases when they were diagnosed with CRC. Patients with metastatic diseases were more likely to have chemotherapy combined with biologics (50.6% vs. 6.5%) compared with those without metastasis ($x^2 = 1{,}100$; $P < 0.01$). In addition, all patients received some form of outpatient care, and more than 95% were admitted as inpatients.

Medical Costs

The average annualized cost of CRC treatment per patient was $97,400, including chemotherapy ($17,500), biologics ($30,400), other pharmacy ($2,300), inpatient treatment ($26,300), and outpatient treatment ($42,900). The total costs were significantly increased from first line only ($70,500), first and second lines only ($100,100), to third+ lines ($152,900). Outpatient expenditure (including surgery, office visit, hospital, and emergency room) was the leading cost for CRC treatment at each treatment line (see Table 3).

We also compared the treatment cost of CRC patients with and without metastasis. The results indicated that the average annualized cost for patients with metastasis was nearly twice that of those without metastasis ($121,800 vs. $61,800, t = 29.5, $P < 0.01$), and the distribution of cost components was similar to those mentioned above (Table 4).

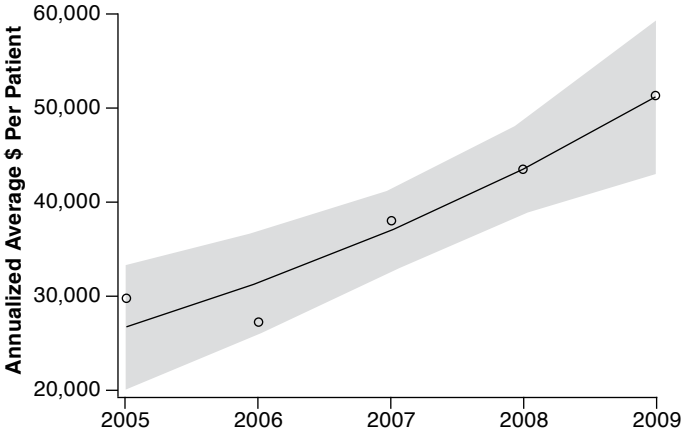
Cost Trend Over Time. From 2005 to 2009, the annualized health care inflation rate in the United States varied between 3.17% and 4.42%.[10] In order to examine whether the medical cost of CRC treatment increased over time after adjusting for health care inflation, we conducted the following analysis and found that after adjusting for health care inflation, the average treatment cost of a CRC patient increased significantly from $29,701 to $51,397. Figure 3 depicts the trend of medical costs over time as demonstrated by an exponent distribution ($F = 415.58$; $P < 0.01$) as follows:

$$Cost = e^{(10.0312+0.1622\times[year-2004])}$$

Cost is the inflation adjusted cost for CRC treatment, and *year* is from 2005 to 2009. As seen in Figure 3, medical costs trended upwards over time (increased by 17.6% annually) even when health care inflation had been adjusted. The question remains: What were the reasons behind the macro level of costs increasing? To address this question, our study analyzed the determinants of cost.

Determinants of Cost. Generalized linear regression modeling (GLM) was employed to estimate the influence of therapy lines and demographic/clinical covariates on medical expenditures for CRC treatment (Table 5). We found that patients receiving

FIGURE 3 Colorectal Cancer Treatment Cost (Health Care Inflation Adjusted) Increase from 2005 to 2009



Note: Nonlinear regression showed that the medical cost trended upwards over time (increased by 17.6% annually) even when health care inflation had been adjusted ($F = 415.58$, $P < 0.01$).

Folfiri did not have higher costs; in fact, they had lower costs than those receiving FOLFOX (FU/LV + oxaliplatin) or FU. However, patients receiving FolfoxA (FOLFOX + bevacizumab) or FolfiriA (Folfiri + bevacizumab) or bevacizumab alone had higher costs for CRC treatment. CRC patients with post-index metastasis had higher total costs. CRC patients aged 61 to 64 years had lower medical expenditures than those patients aged 18 to 50 years, but the cost difference was not significant between patients aged 51 to 60 years and those aged 18 to 50 years. Patients from the Northeast, North central, and West regions had higher costs than those from other areas of the United States. As compared with 2005, the average costs in 2006 were higher but not in 2007, 2008, and 2009. Male patients cost more than female patients. Patients having comprehensive insurance plans (health maintenance organizations and indemnity insurance plans) had lower costs than those having preferred provider organization insurance plans. The patients who waited less than 30 days between diagnosis and treatment had higher costs than those within 30-59 days. Other factors associated with higher cost included post-index surgery, post-index radiation and comorbidities (Charlson Comorbidity Index). In addition, we found that a number of factors were not associated with higher costs of CRC treatment, such as pre-index metastatic diseases and index colon cancer (vs. rectal cancer).

Discussion

This study comprehensively analyzed medical costs associated with the use of chemotherapy and biologics among adults with CRC using a nationwide database. Our study found that the health care costs of CRC treatment have increased significantly over time, which is most likely attributable to the use of a new drug regimen, increased use of surgery and radiation, and the occurrence of various comorbidities and metastatic diseases.

Undoubtedly, the development of new CRC treatments has brought significant benefits to patients. From the late 1980s to the early twenty-first century, the 5-year survival rate of CRC in Europe increased by approximately 20%; for example, in Switzerland, it increased from 49.5% to 65.3%.[11] Furthermore, the 5-year survival rate of CRC was higher in the United States than in Europe.[12] Until recently, 3 regimens dominated first-line treatment of CRC: FU, available since the 1960s, which has been routinely administered with FU/LV since the early 1990s or with irinotecan (IFL or Folfiri) since 2000.[8,13,14] In the past decade, the U.S. Food and Drug Administration approved several new drugs, such as capecitabine, oxaliplatin, bevacuzimab, cetuximab, and panitumumab, which have been widely used in the treatment of CRC patients.[8] This study found that biologics, including bevacuzimab, cetuximab, and panitumumab, were more likely added into regimens in the third + lines as compared with earlier lines.

The heath care costs of CRC patients, however, increased with the use of these new treatments. This study found the average annualized cost of CRC treatment per patient was $97,400, and it increased significantly from the first line only to the third + lines. Furthermore, we must also consider the effect of immortal time bias (immortal time refers to a span of time in the observation or follow-up period of a cohort during which the outcome under study could not have occurred).[15] Our study findings were based on an assumption that all CRC patients could survive from first line to third + lines. We did not factor in those patients who died before entering the late-stage treatment cohorts who may have had a worse prognosis requiring that they pay more for treatment. Hence, the cost of CRC treatment at late lines may very well have been more expensive.

This study also found that patients with post-index metastasis had higher costs than those with no metastasis due to higher expenditure on outpatient costs, biologics, inpatient, and chemotherapy. The increase in biologic and chemotherapy treatment costs could mainly be attributed to the high price of "new drugs." Patients receiving FolfoxA, FolfiriA, or bevacizumab alone had significantly higher costs for CRC treatment. Recently, the "new drugs" have been widely used to treat CRC patients in developed countries, which is why CRC patients in developed countries have higher costs for survival. It was estimated that CRC patients may pay approximately $3,000 per dose in order to get 6 months of survival.[16]

TABLE 5 Determinants of Colorectal Cancer Treatment Costs[a]

Factors	Groups	Estimate	Standard Error	Wald Chi-square	*P* Value
Age	51-60/18-50	-0.040	0.021	3.50	0.059
	61-64/18-50	-0.087	0.029	8.87	0.003
Sex	Male/female	0.078	0.019	17.22	<0.001
Year	2006/2005	0.087	0.031	7.66	0.006
	2007/2005	0.001	0.031	0.00	0.976
	2008/2005	-0.029	0.033	0.75	0.387
	2009/2005	-0.066	0.043	2.35	0.126
Region	Northeast/other	0.121	0.036	11.22	<0.001
	North Central/other	0.046	0.022	4.24	0.039
	West/other	0.113	0.029	15.69	<0.001
Insurance plan	Comprehensive/PPO	-0.087	0.035	6.07	0.014
	Others/PPO	0.103	0.045	5.25	0.022
	Point of service/PPO	0.048	0.028	2.97	0.085
Charlson Comorbidity Score	1/0	0.075	0.026	8.67	0.003
	2/0	0.108	0.049	4.75	0.029
	3+/0	0.347	0.080	19.03	<0.001
Post-index metastasis	Yes/No	0.622	0.020	969.80	<0.001
Pre-index surgery	Yes/No	-0.056	0.020	7.76	0.005
Post-index surgery	Yes/No	0.261	0.032	67.6	<0.001
Post-index radiation	Yes/No	0.170	0.025	46.59	<0.001
Follow-up days		2.0E-4	1.0E-5	34.83	<0.001
Days between diagnosis and treatment	Less than 30/30-59	0.061	0.028	4.87	0.027
	60-89/30-59	-0.017	0.025	0.46	0.497
	90+/30-59	0.011	0.027	0.17	0.678
FOLFOX[b]	Yes/No	-0.065	0.026	6.58	0.010
FolfoxA[c]	Yes/No	0.343	0.034	99.66	<0.001
FolfiriA[d]	Yes/No	0.355	0.075	22.68	<0.001
Bevacizumab alone	Yes/No	0.233	0.070	11.06	<0.001
5-fluorouracil	Yes/No	-0.176	0.031	32.91	<0.001

[a]*Other factors with P>0.05 included pre-index metastatic diseases, index colon cancer (vs. rectal cancer), and Folfiri (FU/LV plus irinotecan).*
[b]*FOLFOX is FU/LV (fluorouracil/leucovorin) plus oxaliplatin.*
[c]*FolfoxA is FOLFOX plus bevacizumab.*
[d]*FolfiriA is FU/LV plus irinotecan plus bevacizumab.*
E = E notation; PPO = preferred provider organization.

This study indicated that the annualized total cost of care in newly diagnosed CRC patients increased by 17.6% annually from 2005 to 2009. The dominant reason may be the development of new regimens over time, as new drugs for CRC treatment were created and integrated into the systemic therapy with higher prices in the market. Additionally, more examinations and surgeries using modern technology were implemented over the time period studied. Other relevant factors could also affect the change of treatment costs for CRC patients simultaneously. Insured compared with uninsured participants were significantly more likely to have ever completed CRC screening.[17] The CRC patients with noncomprehensive insurance plans could have higher medical costs. Patients who waited less than 30 days between diagnosis and treatment cost more than those who waited between 30-59 days, which could be interpreted that the patients who received their treatments earlier were sicker so that they had higher costs. Also, the cost change could be associated with the age-specified ratios of CRC patients, which has been an increasing trend among the younger population since 2004.[18] Additionally, CRC patients often have diverse comorbidities, which could lead to a similar increasing trend of treatment costs in recent years.

Limitations

There are several limitations that should be considered when interpreting this work. First, the study sample was restricted to CRC patients aged 18 to 64 years (working age) and did not include retired/older patients. Medical costs of CRC treatment among older patients could be different from the younger population.[19] In addition, a potential selection bias should also be recognized because this study used only the MarketScan claims database, which focused on the patients aged 18 to 64 years covered by commercial health plans. Hence, one should exercise caution in extrapolating the results of this study to

other populations with CRC, especially for the elderly population (over 65 years old). There are several other potential limitations with this study because of the claims data-based methodology. First, CRC was identified using ICD-9-CM codes and did not include information on patients based upon diagnostic tests. Second, to identify the cohorts, it was assumed that ICD-9-CM diagnosis codes were complete and accurate. Third, the database included only ICD-9-COM diagnosis codes that were reported with successfully reimbursed medical and pharmacy claims. Fourth, race/ethnicity, smoking status, and all of the other noncoded information (e.g., laboratory results) were not captured in this database. Fifth, this study also had limitations in classifying patients according to treatment line and describing instances where the algorithm could have failed in tracking a switch from one treatment line to another. Another limitation is the scope of generalizability of the study results. Treatments may have been influenced by the different formulary status of the treatments in the health plans. It is likely that treatments had similar accessibility to patients and prescribers.

Conclusion

Based on current evidence, randomized, prospective studies are needed in the future to confirm and disseminate the findings of clinical benefits of the new regimens in managing CRC.

Authors

BRIAN S. SEAL, RPh, MBA, PhD, is Director, U.S. Health Economics & Outcomes Research; CHARLIE KREILICK is Deputy Director, Data Analytics; and SUSAN H. FOLTZ BOKLAGE, MS, is Associate Director, Data Analytics, Bayer HealthCare Pharmaceuticals Inc., Wayne, New Jersey. SEAN D. SULLIVAN, PhD, is the Stergachis Family Professor and Director, Pharmaceutical Outcomes Research and Policy Program and Associate Dean for Research, University of Washington School of Pharmacy, Seattle, Washington; SCOTT RAMSEY, MD, PhD, is Member, Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, Washington; KENNETH M. SHERMOCK, PharmD, PhD, is Director, Center for Medication Quality and Outcomes, The Johns Hopkins Hospital, and Core Faculty, The Armstrong Institute for Patient Safety and Quality, Johns Hopkins Medicine, Baltimore, Maryland; and SATISH VALLURI, PhD, MPH, MS, is a former employee of Bayer HealthCare Pharmaceuticals and is Adjunct Faculty, University of Maryland, Baltimore, Maryland. JINMA REN, PhD, is Research Specialist, and CARL V. Asche, PhD, is Director and Research Professor, Center for Outcomes Research, University of Illinois College of Medicine, Peoria, Illlinois. SYAM SARMA, PhD, is a Consultant, Wilmington, North Carolina.

AUTHOR CORRESPONDENCE: Carl V. Asche, PhD, Center for Outcomes Research, University of Illinois College of Medicine, One Illini Dr., Peoria, IL 61656-1649. Tel.: 309.671.8461; Fax: 309.671.8438; E-mail: cva@uic.edu.

DISCLOSURES

Bayer HealthCare Pharmaceuticals Inc. funded this study. Asche was paid as a consultant as were Sullivan, Ramsey, Shermock, and Sarma. Ren is an employee of the University of Illinois College of Medicine, and Seal, Kreilick, Foltz Boklage, and Valluri are paid employees of Bayer HealthCare Pharmaceuticals Inc.

Study concept and design were contributed by Seal, Shermock, and Valluri, with assistance from Sullivan, Ramsey, Kreilick, Sarma, and Asche. Data were collected by Kreilick, Foltz Boklage, and Sarma, with assistance from Seal, Shermock, and Ren. Data interpretation was primarily the work of Sullivan, Ramsey, Seal, Shermock, and Valluri, with assistance from Kreilick, Foltz Boklage, Sarma, and Asche. The manuscript was written by Ren, Valluri, and Asche, with help from Seal, Sullivan, Ramsey, and Shermock. The manuscript was revised by Sullivan, Ramsey, Seal, and Asche, with help from Ren and Valluri.

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