

Variation in the Cost of Medications for the Treatment of Colorectal Cancer

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Colorectal cancer (CRC) is the second leading cause of death and the third most common malignancy in the United States.¹ The mounting costs associated with recent advances in cancer detection and treatment are troubling, and increasing attention is being paid to cost-effective analyses.²⁻⁷ Schrag⁸ noted that, in the decade leading up to 2004, the introduction of new life-extending therapies had led to a 340-fold increase in the cost of chemotherapy compared with traditional regimens.

A brief historical overview of CRC regimen development places these rising treatment costs in context.^{4,5} The original standard treatment for CRC included several regimens containing 5-fluorouracil (5-FU) and leucovorin calcium (LV), with varying administration schedules.⁹ With the addition of irinotecan hydrochloride and oxaliplatin to the pharmacopeia, new regimens such as fluorouracil-LV-irinotecan hydrochloride (FOLFIRI) and fluorouracil-LV-oxaliplatin (FOLFOX) were developed.^{10,11} Most recently, monoclonal antibodies have been included in treatment regimens.¹²⁻¹⁴ Initially, the survival time without chemotherapy was 8 months and increased to 12 months with the use of 5-FU; patients can now expect to survive beyond 21 months because of the incorporation of cetuximab and bevacizumab into regimens.^{8,12-14} These new life-extending agents are now considered standard therapy, placing a greater economic burden on the healthcare system not only because of higher costs per drug but also because of their expanded use. For example, expenditures for oxaliplatin, part of the FOLFOX regimen, grew by 72% in 2004.¹⁵

The literature contains limited studies on the costs of chemotherapy for CRC. A recent review by Meropol and Schulman¹⁶ provided costs of common regimens in the treatment of CRC for 6 months of treatment and noted the wide variation of costs among regimens. The present study expands on these findings by including the costs of regimens and supportive agents on a per-cycle basis and use basis, respectively, as well as insight into the utilization of these regimens across the United States. Many recent studies have design limitations that restrict the generalizability of their findings. Investigations based on the average wholesale price of drugs, not the average sale price used by Medicare for reimbursement purposes, do not accurately represent the cost of treatment from a socioeconomic perspective.^{8,17} An estimate of the overall cost of treatment for CRC by Paramore et al¹⁸ did not

Objective: To evaluate the economic burden of colorectal cancer (CRC) treatment on the healthcare system as treatment costs have risen 340-fold during the past 5 years.

Study Design: Nationwide registry.

Methods: Patients with CRC (N = 421) were selected from an observational prospective patient registry of US oncology clinics. The 8 most commonly prescribed regimens were identified. Standard dosing schedules were set for these regimens based on a literature review and expert CRC oncologist input. Each chemotherapeutic regimen was broken down into its component agents, and regimen costs were calculated by summing the costs of each agent per regimen. Price-per-milligram costs were calculated from Health Care Financing Administration Common Procedural Coding System codes for specific drugs. Patient population, temporal, and regional trends were studied among standard regimens.

Results: The most common regimens were 5-fluorouracil-leucovorin calcium (5-FU/LV) (147 patients [34.9%]), fluorouracil-leucovorin-irinotecan hydrochloride (FOLFIRI) (111 patients [26.4%]), and fluorouracil-leucovorin-oxaliplatin (103 patients [24.5%]). The remaining 60 patients (14.3%) received irinotecan, capecitabine, and oxaliplatin; oxaliplatin; irinotecan in combination with oxaliplatin; or a miscellaneous regimen. The largest cost differential for 6 cycles of planned treatment was \$35,971 between FOLFIRI (\$36,999) and 5-FU/LV (\$1028). On a per-week basis, treatment costs may differ by more than 91 times. Patient utilization of growth factors, ancillary medications, and monoclonal antibodies added significant costs.

Conclusions: The costs of CRC regimens varied considerably. Trends in treatment regimens have changed notably over time, with newer agents and supportive drugs adding substantially to treatment costs.

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categorize costs on a regimen-specific basis, for which there are likely to be significant variations. Costs of CRC treatment were also examined in several studies¹⁹⁻²³ conducted outside the United States, where drug prices and healthcare systems are highly regulated. Last, several cost-effective analyses attempted to compare the treatment costs for 2 or more specific options but failed to provide a comprehensive review of the costs for all contemporary treatment options.^{2,19-21,24}

Few studies have included the costs of commonly used ancillary drugs, leading to a gross underestimation of treatment costs, as supportive agents (erythropoietin alfa, darbepoetin alfa, and pegfilgrastim) constitute the 3 largest drug expenditures within clinics and 3 of the top 4 expenditures within hospitals.¹⁵ Supportive agents (eg, antiemetics and antidiarrheals) are especially important in the treatment of CRC. Krzyzanowska et al²⁵ recently noted that patients with CRC were hospitalized because of treatment-related toxic effects more often than patients with any other tumor type. Furthermore, the use of ancillary agents not only improves patients' quality of life but also may maximize treatment outcomes, as in the case of patients receiving full relative dose intensity (RDI) when treated with myeloid growth factors.²⁶⁻³¹

Such rapidly increasing costs have raised ethical questions regarding whether such sums of money should be dedicated to treatments that may prolong life by several months but not offer any increased cure rate.^{7,8} This study was undertaken to demonstrate the variation in costs of CRC chemotherapy based on patterns observed among a contemporary cohort of US patients. This information will inform healthcare providers, policy makers, and third-party reimbursement services, allowing them to form evidence-based responses to the pressing socioeconomic issue of CRC care management. In addition, this analysis presents the utilization patterns for the most common CRC regimens.

METHODS

Study Design

Data for this analysis were obtained from a prospective observational registry of patients with cancer initiating a chemotherapy regimen at 115 ambulatory centers across the United States. The patient registry was created to study the epidemiology of chemotherapy-induced toxic effects and their treatment. Treatment sites were randomly selected after being stratified by treatment volume and geographic region. Adult patients (≥ 18 years) were enrolled at each site if they were initiating chemotherapy involving myelosuppressive agents and were expected by the enrolling oncologist to be able to complete at least 4 cycles of treatment. Excluded from the study were patients likely to experience a secondary cause

of myelosuppression such as the following: patients receiving concurrent cytotoxic, biologic, or immunologic therapy for other noncancer conditions; patients having a diagnosis of conditions known to cause neutropenia; and patients having a diagnosis of acute leukemia or myeloma. Patients were not eligible if they were pregnant or lactating, had an active infection requiring treatment, were concurrently participating in a blinded clinical trial, or had a history of stem cell transplantation. Information collected included patient demographics, cancer stage, and chemotherapeutic and major supportive agents used in treatment. The study was approved by a central institutional review board, and all patients signed an informed consent.

A detailed case-report form was used to collect a comprehensive list of variables, including patient demographics, medical history, and clinical variables across 4 cycles of chemotherapy. On enrollment, patients were asked about any prior cancer care (surgery or chemotherapy) that could have affected their current treatment plan or their risk of chemotherapy toxic effects.

Data collection, study design, and interpretation were conducted by the Awareness of Neutropenia in Chemotherapy study group. The study group received funding from Amgen Inc. The funding agency had no involvement in site selection, data collection, or interpretation of the data. The present CRC subanalysis was not funded.

Patients With CRC

Registry patients diagnosed as having CRC between March 2002 and March 2005 ($N = 421$) were selected for this secondary analysis. The 8 most commonly prescribed regimens were identified within the patient population. Standard dosing schedules were set for these regimens based on a literature review and on expert CRC oncologist (AAK) input (**Table 1**). Patients were grouped according to myelosuppressive agents received, irrespective of dosage or cycle duration. For example, patients who received regimens containing 5-FU, LV, and irinotecan were all categorized into the irinotecan, fluorouracil, and LV (IFL)/FOLFIRI group to allow the application of standard regimens and dosages across both groups. The delivery of 5-FU/LV was not classified in the database as infusion or bolus dose; therefore, this regimen and the calculated doses reflect intravenous nonbolus delivery.

Chemotherapeutic Drug Costs

Each regimen was broken down into its component chemotherapy agents, and regimen costs were calculated by summing the cost of each drug in the regimen. Because the registry did not contain drug cost data, the regimen cost calculations were taken from Medicare Part B average sale price–based payment

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Table 1. Standard Dosages and Schedules for Myelosuppressive Agents

Regimen	Drug Dosage, mg/m ² (Doses Delivered per Cycle) ^a					Cycle Length, d	Planned Treatment Cycles	Estimated Cost of Regimen per Cycle (per wk), \$	Estimated Total Myelosuppressive Drug Cost, \$
	Leucovorin Calcium	Fluorouracil	Irinotecan Hydrochloride	Oxaliplatin	Capecitabine				
5-FU/LV ⁹	500 (6)	500 (6)	—	—	—	56	6	171 (21)	1028
IFL/FOLFIRI ¹⁰	20 (4)	500 (4)	125 (4)	—	—	42	6	6338 (1056)	38,027
FOLFOX ¹¹	200 (2)	400 Intravenous bolus (2), 600 (2)	—	85 (1)	—	14	6	2931 (1465)	17,584
Irinotecan ³⁴	—	—	125 (4)	—	—	42	4	6322 (1054)	25,287
CapeOX ³³	—	—	—	130 (1)	2000 Oral (14)	21	6	5791 (1930)	34,744
Oxaliplatin ³⁵	—	—	—	85 (1)	—	14	4	2898 (1449)	11,593
Irinotecan in combination with oxaliplatin ³²	—	—	200 (1)	85 (1)	—	21	5	5427 (1809)	27,134

5-FU/LV indicates 5-fluorouracil/leucovorin; IFL/FOLFIRI, fluorouracil/leucovorin/irinotecan; FOLFOX, fluorouracil/leucovorin/oxaliplatin; CapeOX, capecitabine/oxaliplatin.

^aDoses are by intravenous infusion unless otherwise indicated.

limit files available from the Centers for Medicare & Medicaid Services, effective January 2006.³² Price-per-milligram costs were calculated from individual Health Care Financing Administration Common Procedural Coding System (HCPCS) codes for specific drugs. The price per milligram for each major myelosuppressive agent in a regimen was then multiplied by the total dosage received per cycle, based on published standard treatments.^{9-11,33-36}

The amount of drugs administered based on patient body surface area (BSA) was estimated using a patient BSA of 2.0 m², while doses determined by body weight were calculated based on a patient weighing 80 kg. Unit drug prices (eg, cost per milligram) were calculated by dividing the HCPCS total reimbursement by the respective billable package size. This price per basic unit was used to allow for a more precise calculation of drug costs per regimen. The price per basic unit was then multiplied by the amount of drug administered for each chemotherapeutic cycle based on the appropriate BSA or patient weight. The price per cycle was then multiplied by the mean number of cycles the patient was expected to receive according to registry data. Price estimates reflect the costs of the drug only; hospitalization and administration costs were not considered in the cost estimates. Lower total treatment costs could be expected with the use of oral medications.

Costs of Other Commonly Used Drugs

The price for other commonly prescribed drugs was calculated using the price per basic unit of drug, derived as already described for the chemotherapeutic agents. Price per unit

was then multiplied by the number of units in the published standard dosage and the mean patient weight.³⁷ Except for the monoclonal antibody cetuximab, which was calculated using the standard BSA of 2.0 m², all other commonly prescribed drug prices were calculated based on patient weight. Hematopoietic growth factor costs were based on the price expected per cycle utilization.³⁸ Supportive drug prices were based on dosages for single events. The price for the use of both hematopoietic growth factors and other supportive drugs was excluded from the total per-cycle drug cost because many of these agents are only required on an individualized patient basis.

The RDIs were calculated for all major myelosuppressive agents involved in therapy as the ratio of actual dose received per unit of time to standard reference dose per unit of time expected for each drug and cycle. The overall regimen RDI represents the mean of the myelosuppressive drugs across all observed treatment cycles. The RDIs were then categorized as 85% or less (partial dose intensity) or as greater than 85% (full dose intensity). In some instances, a patient's reported treatment regimen did not correspond to any published standard treatment. In these instances, the RDI could not be calculated.

RESULTS

Patient and Treatment Demographics

The mean age of the population was 63 years (age range, 21-97 years), and the median age was 64 years. The 3 most common insurers among patients involved in the study were

■ **Table 2.** Demographics Among 421 Patients

Demographic	No. (%)	
	Male (n = 233)	Female (n = 188)
Age, y		
21-54	47 (20.2)	54 (28.7)
55-64	68 (29.2)	45 (23.9)
65-97	118 (50.6)	89 (47.3)
Subtotal (% of total)	233 (55.3)	188 (44.7)
Race/ethnicity (n = 419)		
White	353 (84.2)	
Black	49 (11.7)	
Asian	5 (1.2)	
Hispanic	9 (2.1)	
Native American	2 (0.5)	
Other	1 (0.2)	
Geographic region		
Northeast	66 (15.7)	
Central	143 (34.0)	
West	40 (9.5)	
South	172 (40.9)	
Tumor stage (n = 419)		
I	6 (1.4)	
II	72 (17.2)	
III	131 (31.3)	
IV	210 (50.1)	
Insurance		
Third party	223 (53.0)	
Health maintenance organization	29 (6.9)	
Medicare	152 (36.1)	
Medicaid	3 (0.7)	
Military or other	9 (2.1)	
Self or no report	5 (1.2)	
History of chemotherapy		
Yes	139 (33.0)	
No	282 (67.0)	
History of recent surgery within 1 mo of the study (n = 420)		
Yes	129 (30.7)	
No	291 (69.3)	

third parties (223 patients [53.0%]), followed by Medicare (152 patients [36.1%]) and health maintenance organizations (29 patients [6.9%]). Patients from the southern region of the United States comprised the largest group of the study (172 patients [40.9%]), followed by the central United States (143 patients [34.0%]), Northeast (66 patients [15.7%]), and West

higher use (29.7%) of FOLFOX in the South and markedly lower representation (2.5%) of FOLFOX in the West. Regimen proportions changed over time as new effective agents were approved and incorporated into practice (Figure 2). The most notable change was the increased use of FOLFOX, which started with a baseline of 0.0% utilization in March

(40 patients [9.5%]). Almost half of the patients (209 patients [49.6%]) were diagnosed as having stage I to stage III disease, and 282 patients (67.0%) were chemotherapy naive. The characteristics of the 421 patients are given in Table 2.

The most common regimens were 5-FU/LV (147 patients [34.9%]), IFL/FOLFIRI (111 patients [26.4%]), and FOLFOX (103 patients [24.5%]). The remaining 60 patients (14.3%) received irinotecan, capecitabine, and oxaliplatin (CapeOX); oxaliplatin, irinotecan in combination with oxaliplatin (IROX); or a miscellaneous regimen (Figure 1).³²⁻³⁴ These latter 4 small groups were collapsed into the category “other” for statistical analyses to ensure adequate sample sizes at each stratum. Of the patients receiving 5-FU/LV, 130 patients (88.4%) had no previous chemotherapy, and 87 patients (59.2%) were diagnosed as having early (stages I-III) disease. It was notable that 6 patients with stage I disease were receiving chemotherapy, including 3 patients receiving FOLFIRI, 2 receiving FOLFOX, and 1 receiving an uncatagorized regimen. Among all patients receiving FOLFOX, 51.5% had no previous chemotherapy, and 74.8% were diagnosed as having advanced (stage IV) disease. Of 210 patients diagnosed as having late-stage disease, 169 patients (80.5%) were administered oxaliplatin- or irinotecan-containing regimens.

Regimen Utilization Trends

Throughout all geographical regions, FOLFOX, 5-FU/LV, and IFL/FOLFIRI were the most commonly used regimens, except for somewhat

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2002 and rose to 61.1% of patients only 3 years later. Conversely, the use of 5-FU/LV decreased from 50.0% to 16.7% during the same period.

Regimen Costs

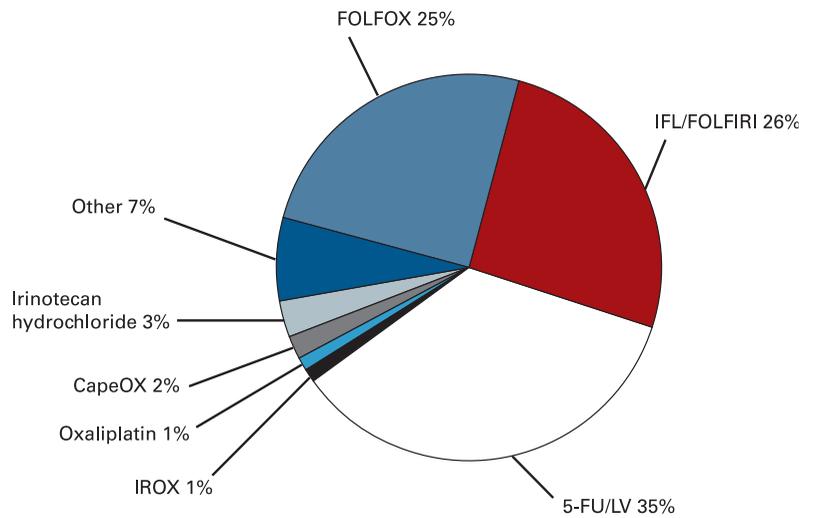
Regimen costs varied widely, and those containing oxaliplatin, irinotecan, and capecitabine were the most expensive. The largest cost differential was \$36,999, based on comparing \$38,027 (\$6338 per cycle) for IFL/FOLFIRI with an estimated \$1028 (\$171 per cycle) for 5-FU/LV, assuming the completion of a 6-cycle course of chemotherapy (Table 1). The most widely used regimen, FOLFOX, was estimated to cost \$2931 per cycle. Patients with late-stage disease tended to receive the more costly treatment regimens; just over 80.4% received regimens containing oxaliplatin or irinotecan. The median number of planned treatment cycles was determined for the patient population and was applied to per-cycle prices to derive the total price per regimen. After excluding 5-FU/LV because of its predominant role in early-stage disease, the treatment cost for late-stage disease varied by as much as \$26,434 between IFL/FOLFIRI and oxaliplatin and was at least 10 times the cost of 5-FU/LV. Treatment costs increased with the stage of disease because of adjuvant treatment agents and the increased use of ancillary agents (Figure 3).

Ancillary Drugs

Table 3 gives the costs of commonly prescribed drugs associated with CRC. Hematopoietic growth factors were frequently administered in conjunction with several of the myelosuppressive chemotherapeutic agents. Their use varied dramatically among regimens (Figure 3). Patients treated with FOLFOX showed the greatest growth factor utilization, with 22.3% of patients receiving darbepoetin alfa and 18.4% receiving erythropoietin alfa. Patients receiving FOLFOX also showed the greatest use of granulocyte colony-stimulating factors (G-CSFs), with 11.7% of patients receiving pegfilgrastim and 15.5% of patients receiving filgrastim. Patients who received 5-FU/LV tended to utilize growth factors less during the study.

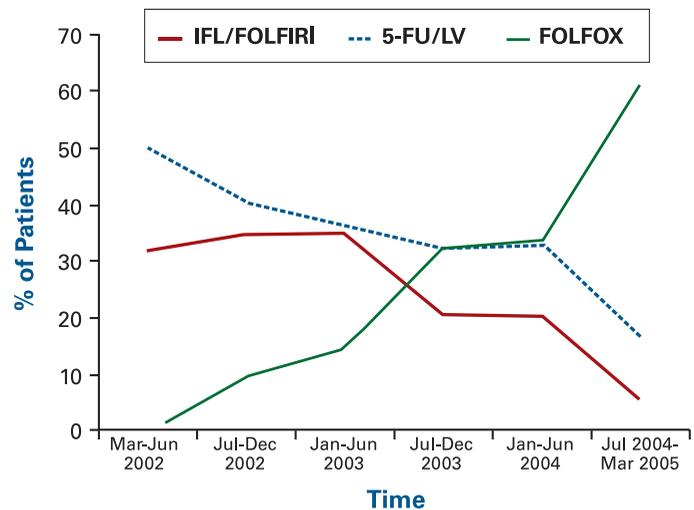
The G-CSFs increased treatment costs by \$1862 for a treatment cycle of filgrastim or by \$2093 for a treatment cycle of pegfilgrastim (Table 3). Erythropoiesis-stimulating

■ **Figure 1.** Distribution of Common Colorectal Cancer Treatment Regimens Among 421 Patients



5-FU/LV indicates 5-fluorouracil/leucovorin; IFL/FOLFIRI, fluorouracil/leucovorin/irinotecan; FOLFOX, fluorouracil/leucovorin/oxaliplatin; CapeOX, capecitabine/oxaliplatin; IROX, irinotecan/oxaliplatin.

■ **Figure 2.** Time Trend of Patients Receiving the 3 Most Common Colorectal Cancer Treatment Regimens

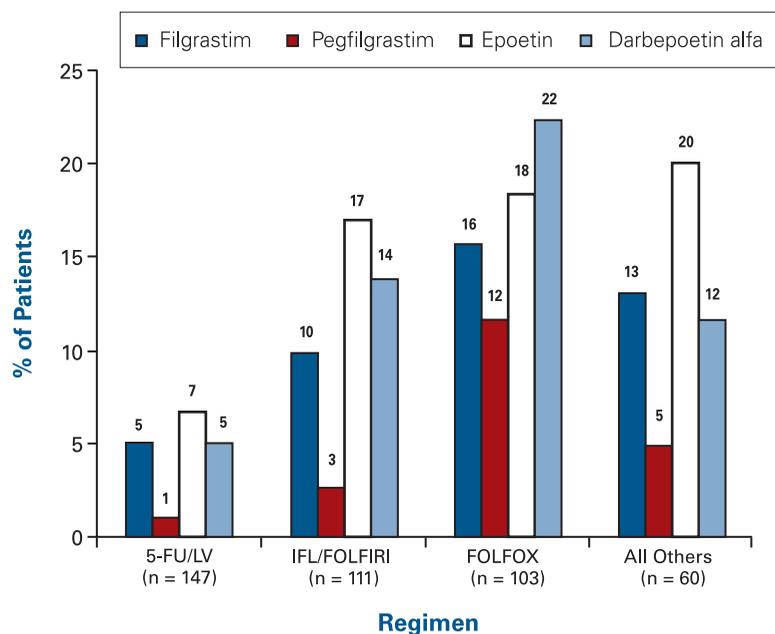


IFL/FOLFIRI indicates fluorouracil/leucovorin/irinotecan; 5-FU/LV, 5-fluorouracil/leucovorin; FOLFOX, fluorouracil/leucovorin/oxaliplatin.

glycoproteins, namely, erythropoietin alfa and darbepoetin alfa, added weekly costs of \$361 and \$299, respectively. Although utilization was not calculated for oprelvekin, the cost per 2-week cycle was estimated to be \$2768. Patients may have received growth factors at any time during their observed 4 cycles of treatment and may have been administered growth factors more than once during treatment.

Despite the high costs associated with G-CSFs, they may have an important role in compliance with planned

■ **Figure 3.** Utilization of Growth Factors Among Common Colorectal Cancer Treatment Regimens



5-FU/LV indicates 5-fluorouracil/leucovorin; IFL/FOLFIRI, fluorouracil/leucovorin/irinotecan; FOLFOX, fluorouracil/leucovorin/oxaliplatin.

courses of chemotherapy.^{38,39} In a univariate analysis, results showed that the overall number of chemotherapy cycles completed was statistically higher for patients who received G-CSFs ($P < .05$).⁴⁰ Patients who did not receive G-CSFs completed a mean of 3.19 cycles of chemotherapy compared with 3.53 cycles among patients who were administered 1 or more cycles of G-CSFs.

The RDI also varied across treatment regimens. The RDI values for 377 patients were recorded and calculated for each regimen throughout the 4 cycles of chemotherapy. Patients receiving 5-FU/LV showed a statistically significantly higher RDI than patients receiving all other regimens ($P < .001$). Among patients receiving 5-FU/LV, 76.1% of patients received full dose intensity (RDI, $>85\%$). Patients receiving other regimens had much lower rates of receiving full dose intensity.

In addition to growth factor use, other supportive care agents were frequently utilized and added substantial costs to the overall treatment (Table 3). Antiemetic cost estimates were based on the standard dose

■ **Table 3.** Estimated Costs of Commonly Prescribed Drugs

Drug	Oral		Injection	
	Dosage	Cost, \$	Dosage	Cost, \$
Hematopoietic Growth Factors				
Filgrastim	—	—	5 µg/kg (8 d)	1862
Pegfilgrastim	—	—	6 mg/cycle	2093
Erythropoietin alfa	—	—	40,000 U/wk	361
Darbepoetin alfa	—	—	100 µg/wk	299
Oprelvekin	—	—	50 µg/kg (2 wk)	2768
Antiemetics Per-Episode Cost				
Aprepitant	125 mg (d 1), 80 mg (d 2-3)	264	—	—
Palonosetron hydrochloride	—	—	0.25 mg	180
Dolasetron mesylate	100 mg	48	1.8 mg/kg	92
Ondansetron hydrochloride	24 mg	101	32 mg	119
Granisetron hydrochloride	2 mg	74	10 µg/kg	56
Monoclonal Antibodies				
Bevacizumab	—	—	5 mg/kg (2 wk)	2279 (For 14 d of treatment)
Cetuximab	—	—	400 mg/m ² (wk 1), 250 mg/m ² (wk 2-3)	6482 (For 14 d of treatment)

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recommended to be administered for a single episode of chemotherapy-induced nausea and vomiting.³⁷ Among the oral antiemetics, single-event costs ranged from \$74 for granisetron hydrochloride to \$264 for aprepitant.

Because of the time frame captured by the registry, monoclonal antibodies were not yet frequently utilized. Among all stages of disease, 23 patients (5.5%) reported the use of bevacizumab, and 5 patients (1.2%) reported the use of cetuximab. However, because these agents are now considered standard treatment, their cost was estimated from recommended treatment standards (Table 3). A 2-week treatment cycle of bevacizumab may cost an estimated \$2279, while patients receiving cetuximab may expect costs for an initial first-week loading dose and subsequent weekly doses to be \$6482.

DISCUSSION

Based on the prospective patient registry, many important patterns of chemotherapy choices and short-term outcomes can be observed. Patients with advanced CRC (stage IV) were treated with a greater range of regimens than patients with early-stage disease. Among the patients receiving 5-FU/LV, 84.9% of patients had stage I to stage III disease, while patients with stage IV disease were typically prescribed more expensive regimens containing oxaliplatin and irinotecan. Similarly, patients with a history of chemotherapy were more likely to be treated with regimens containing oxaliplatin or irinotecan. Patients receiving a regimen of 5-FU/LV achieved a significantly higher rate (76.1%) of full dose intensity (RDI >85%), despite having the lowest growth factor utilization.

Building on the patterns of care, the cost of treatment also showed significant variation on a per-cycle basis and for the complete treatment phase. Factors that affected the price of a specific treatment cycle included the specific drug used, the amount of drug administered, the number of times the drug was administered per regimen, and the patient's physical characteristics. On a per-cycle basis, the maximum difference in costs exceeded \$6000 between the 5-FU/LV and IFL/FOLFIRI regimens. To allow for the comparison of cycles that differ in length, the per-week cost also showed a corresponding cost differential. On a per-week basis, the largest difference in costs occurred between CapeOX (\$1930) and 5-FU/LV (\$21), representing more than a 91-fold difference. As might be expected, the total treatment costs dramatically increased as a function of the number of cycles typically prescribed, and the difference in total treatment costs varies by more than \$36,000 between IFL/FOLFIRI and 5-FU/LV.

The use of ancillary and supportive agents in treatment cannot simply be considered an additive cost of care. Al-

though expensive, G-CSFs help prevent dose reductions and improve delivery of full dose intensity, which is associated with improved survival rates for some cancers.^{26,29,31} Furthermore, drugs such as antiemetics have an important role in increasing quality of life in patients receiving highly emetogenic agents.⁴¹

Although this study was not a classic cost-effectiveness analysis, the objective of the study was to show that there is a notable difference in costs of contemporary CRC regimens in the United States without a commensurate improvement in survival times.⁸ As new, more effective treatment regimens begin to incorporate new drugs such as the monoclonal antibodies, the costs of treatment can be expected to continue escalating. However, although the use of monoclonal antibodies will increase costs significantly, the improvement in survival must also be considered.^{8,12-14}

There are several limitations to this research that should be acknowledged. Primarily, the data used for this post hoc analysis stem from a prospective observational study of ambulatory chemotherapy regimens for multiple tumor types across the United States. The data were not designed or powered to provide an outcomes analysis for CRC treatment. Therefore, a cost-per-life-saved analysis could not be calculated because the primary study design was not intended to follow up patients for more than 4 cycles of chemotherapy. Likewise, costs associated with placement, care, and complications associated with intravenous catheters used were not estimated but would further increase management costs in patients receiving intravenous chemotherapy infusions. The results presented herein suggest the value of a future case-control study designed to evaluate the outcomes resulting from specific colorectal treatment regimens.

Although our reported differences in total treatment costs are based on completion of 6 cycles, patients actually completed a mean of 2.9 cycles of treatment in the dataset. Also, the estimated treatment costs included only drug costs and did not include the resources related to dispensing, administration, and professional fees. Moreover, it is expected that the drug component will be the most significant cost driver for most of the treatment regimens. Costs were estimated based on current Medicare reimbursement limits and do not reflect any discounted or special contracted prices for drug acquisition. Using the national standard prices represents a maximum upper limit and is appropriate for considering costs from a societal perspective.³²

The total cost estimates reflect, at best, a cost during the most acute phase of CRC, namely, the treatment phase. Costs of care beyond this phase are not addressed by this research and have been shown to be considerable.¹⁸ Furthermore, the trends in the use of the newest agents and latest

Take-away Points

The development of new agents and regimens for the treatment of colorectal cancer has placed a serious economic burden on the healthcare system as treatment costs have risen 340-fold compared with traditional regimens during the past 5 years.

■ This nationwide study of oncology practices demonstrated a large variation in the use of modern chemotherapy regimens for colorectal cancer, resulting in dramatic differences in costs.

■ Based on completing a full course of chemotherapy, the total cost of chemotherapy may differ by as much as \$36,999 per patient depending on the regimen.

reus for Roche and Genentech. Dr Lyman reports serving as a consultant and having been a member of the speaker's bureau for Amgen, as well as receiving research grant support from Amgen and GlaxoSmithKline. Dr Scarpace reports having been a member of the speaker's bureau for Pfizer. The other authors (SAF, BSM, DAW, MSP, EC, LEC) report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

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advances in CRC chemotherapy treatment are not reflected in the registry. Perhaps the most significant limitation is the lack of longer-term patient outcomes, which would allow for the real-time calculation of cost per survival time. Although survival times could have been approximated using published estimates, there are many intervening variables that would make this method inaccurate. Following up the patients through the entire course of their disease and collecting costs in a closed healthcare system would be the only way to arrive at meaningful cost-effectiveness ratios.

CONCLUSIONS

As CRC treatment advances continue, it will be imperative to have contemporary and comprehensive estimates of the costs of treatment options. Sound estimates of costs are a necessary first step toward the evaluation of costs per additional gains in survival or quality of life. It is imperative to develop objective measures of cost-effectiveness to support patients, clinicians, and policymakers in their quest for a rational allocation of limited healthcare delivery resources.

This study revealed significant differences in the use of contemporary CRC regimens, including notable trends over time. The cost of CRC regimens varied considerably, with newer agents and supportive drugs adding substantially to treatment costs, particularly in late-stage disease. Based on completing a 6-cycle course of chemotherapy, the total cost of chemotherapy may differ by as much as \$36,999 per patient depending on the regimen. The use of new targeted therapies significantly adds to this cost disparity, but their role in optimal care must be considered.

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