Lifetime and Treatment-Phase Costs Associated With Colorectal Cancer: Evidence from SEER-Medicare Data

KATHLEEN LANG,* LISA M. LINES,* DAVID W. LEE,‡ JONATHAN R. KORN,* CRAIG C. EARLE,§ and JOSEPH MENZIN*

*Boston Health Economics, Inc., Waltham, Massachusetts; ‡GE Healthcare, Waukesha, Wisconsin; and §Harvard Medical School, Boston, Massachusetts

Background & Aims: This study provides detailed estimates of lifetime and phase-specific colorectal cancer (CRC) treatment costs. Methods: This retrospective cohort study included patients aged 66 years and older, newly diagnosed with CRC in a Surveillance Epidemiology and End Results (SEER) registry (1996–2002), matched 1:1 (by age, sex, and geographic region) to patients without cancer from a 5% sample of Medicare beneficiaries. The Kaplan–Meier sample average estimator was used to estimate observed 10-year costs, which then were extrapolated to 25 years. A secondary analysis computed costs on a per-survival-year basis to adjust for differences in mortality by stage and age. Costs were expressed in 2006 US$, with future costs discounted 3% per year. Results: Our sample included 56,838 CRC patients (41,256 colon cancer [CC] patients and 15,582 rectal cancer [RC] patients; mean ± SD age, 77.7 ± 7.1 y; 55% women; and 86% white). Lifetime excess costs were $29,500 for CC and $26,500 for RC patients. Per survival year, stage IV CRC patients incurred $31,000 in excess costs compared with $3000 for stage 0 patients. CRC patients incurred excess costs of $33,500 in the initial phase, $4500/y in the continuing phase, and $14,500 in the terminal phase. RC patients had lower costs than CC patients in the initial phase, but higher costs in both the continuing and terminal phases. Conclusions: Excess costs associated with CRC are striking and vary considerably by treatment phase, cancer subtype, and stage at diagnosis. Interventions aimed at earlier diagnosis and prevention have the potential to reduce cancer-related health care costs.

Currently available estimates of the cost of colorectal cancer (CRC) vary widely and are outdated. This study extends previous research by estimating lifetime and phase-specific CRC-related costs by cancer subtype, age, and stage at diagnosis using the most current data available. Representative CRC cost data are needed because they are used to evaluate technologies aimed at early detection and prevention. Further, age-specific CRC cost data are important because the aggressiveness of treatment and screening guidelines are age-dependent. Finally, understanding costs by stage at diagnosis is important from a public health perspective because it affects economic evaluations of new colorectal screening technologies. The goal of screening is to affect a positive shift in stage at detection from late to early stage. The economic benefit of this stage shift is measured in the incremental cost reduction in detecting CRC earlier.

Methods

Data Sources

This study used 3 data sources: (1) the linked Surveillance Epidemiology and End Results (SEER)–Medicare database (a collaborative effort of the National Cancer Institute, the SEER registries, and the Centers for Medicare and Medicaid Services); (2) the SEER*Stat database, containing clinical and survival data from the SEER registries; and (3) survival data for the general population from US life-tables.

SEER is a US cancer surveillance system consisting of population-based tumor registries designed to track incidence and survival. The registries routinely collect information from multiple reporting sources about newly diagnosed cancer patients in geographically defined areas representing approximately 25% of the US population. Complete details of the linkage of the SEER and Medicare data have been described elsewhere.

Patient Selection

Colorectal cancer cohort. All patients aged 66 years and older with a new diagnosis of malignant adenocarcinoma of the colon or rectum (ie, presence of a SEER cancer site recode value between 15 and 27 and one of the following International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3) histology codes: 8140, 8210-11, 8220-21, 8260-63, 8470, 8480-81, and 8490) reported to a SEER registry between January 1, 1996, and December 31, 2002, were identified for possible inclusion in the CRC cohort. The index date for each patient was defined as the date of CRC diagnosis. Patients were required to have a full 12 months of data available pre-index.

To ensure complete expenditure information for our sample, patients were excluded if at any time in the period 12 months before, or anytime after the index date, they were enrolled in a Medicare HMO, not eligible for both Medicare Part A and B benefits, or eligible for benefits under the end-stage renal disease program. We also excluded patients who had claims in the 12-month pre-index period indicating any other cancer, were diagnosed with CRC at the time of death or autopsy, or could not be matched to an appropriate comparator.

Comparison cohort. Comparison cohort patients were selected from Medicare enrollment files using a 5% random sample of Medicare beneficiaries residing in SEER areas who did not have cancer. One comparison patient of identical age, sex, and census region was matched randomly to each CRC patient and assigned the same index date (so that both patients were followed up over the same time period). As with CRC patients, comparators were not eligible for inclusion if they were enrolled in an HMO or were not eligible for Medicare Part A and B benefits at any point from 12 months before index through follow-up evaluation. These

Abbreviations used in this paper: CC, colon cancer; CRC, colorectal cancer; RC, rectal cancer.
patients were not required to have used services to be selected for inclusion, and they were allowed to develop cancers other than CRC after their index date. Patients in both cohorts were followed up from their index date until death or the end of the Medicare claims data (December 31, 2005).

**Statistical Analyses**

Baseline demographic and clinical characteristics of both study cohorts were evaluated, including Deyo–Charlson comorbidity scores. Health care costs included all Medicare payments, private insurer payments, and patient copayments and deductibles for covered services. Covered services included inpatient hospital services and skilled nursing facility stays, outpatient hospital services, physician and laboratory services, home health, and hospice care. Prescription drugs (including chemotherapy) administered in hospitals were included in inpatient expenditures. Outpatient chemotherapy costs were included in outpatient expenditures; oral prescription drugs administered on an outpatient basis were excluded because they were not covered by Medicare at the time of the study.

Excess costs attributable to CRC were defined as the difference in costs between CRC and matched comparison patients. We used this definition to minimize bias caused by coding inconsistencies and omissions associated with relying on a sum of expenditures for medical events with a cancer diagnosis code. For example, treatment for the side effects of cancer therapy should be included in the cost of cancer treatment but may not be coded with a cancer diagnosis. In addition, patients may be treated for cancer-related conditions and other conditions in the same medical encounter, in which case it is impossible to determine from the claims the cost of the cancer-related portion of the encounter.

**Estimation of lifetime costs.** Patients in our SEER–Medicare analysis were accrued between 1996 and 2002 and were followed up through 2005 (the end of the SEER–Medicare database), for a maximum of 10 years of follow-up evaluation, a time horizon unlikely to be adequate for evaluating lifetime costs among patients diagnosed with less-advanced cancer or for comparison patients. Thus, modeling techniques for the analysis of censored cost data were used to estimate lifetime health care costs attributable to CRC.

Costs for years 1 through 10 were estimated directly from observable SEER–Medicare data for CRC patients and controls using the nonparametric Kaplan–Meier Sample Average estimator. The Kaplan–Meier Sample Average computes costs by summing expected costs incurred per time interval, calculated as the product of the probability of surviving to that time interval, and the sample average cost among survivors to the start of that interval.

The Kaplan–Meier Sample Average estimator is calculated by using the following formula:

\[ C_t = \sum_{y=1}^{10} P_y C_y, \]

Where \( t \) is the post–index-date month, \( P_y \) is the survival probability, and \( C_y \) is the mean actual costs in period \( t \) among beneficiaries surviving to month \( t \). The Kaplan–Meier Sample Average estimator minimizes the bias associated with censored data by dividing the time period into short intervals. This calculation provides a nonparametric estimate of the average costs for patients with variable lengths of follow-up evaluation.

Costs for years 11 through 25 were extrapolated for both cohorts using the assumption that cohort-specific average annual medical care costs were constant for years beyond the available data until the year before the final year of life (ie, continuing costs). These continuing-phase costs were estimated from the subset of patients in each cohort who lived at least 3 years as the average annual cost for years between year 1 and the final year of life, exclusive. In addition, we assumed that medical care costs in the final year of life (ie, terminal costs) for patients who lived beyond the 10-year study period were the same, regardless of time from diagnosis; terminal costs were thus estimated as the average final-year cost among cases in the relevant cohort who died at least 2 years after the index date.

We used the following formula to estimate costs in years 11 to 25:

\[ C^*_y = \sum_{y=11}^{25} \hat{P}_y \hat{C}_y, \]

Here, \( \hat{P}_y \) is the probability of surviving to year \( y \). For CRC patients, this survival probability was estimated for years 11 to 16 using SEER*Stat data and for years 17 to 25 by fitting SEER data from 1988 to 2004 to a Weibull model. US life tables from the National Center for Health Statistics provided survival probabilities for controls. \( \hat{C}_y \) is the expected cost in year \( y \), computed as a weighted average of the annual cost for cases dying in year \( y \) (ie, terminal cost) and those surviving through year \( y \) (ie, continuing cost). Total lifetime costs in each cohort are calculated by summing cohort-specific estimates of \( C^*_y \) and \( C^*_y \).

Lifetime excess costs among CRC patients were reported overall and per year of survival, by stage, age at diagnosis, and cancer subsite, in 2006 US dollars, with future costs discounted at 3% per year. Estimates of lifetime costs per survival year were calculated by dividing the estimate of expected lifetime costs for each age- and stage-specific group by the expected years of survival for that group.

**Phase-specific cost estimates for the entire colorectal cancer population.** Our lifetime cost estimation required estimates of continuing and terminal costs for CRC patients who survived at least 10 years. For completeness, we also estimated phase-specific costs for the entire CRC population (ie, short-term and long-term survivors). These costs were estimated as follows: (1) terminal costs were assigned first and were calculated as the average cost in the final year of life, with all costs considered terminal for patients living fewer than 13 months after diagnosis; (2) initial costs were calculated as the average costs in the initial (up to 1 year) period after diagnosis and before the last year of life and were calculated among those who lived at least 13 months after diagnosis; and (3) continuing costs included the period between the first and last year of life for patients with at least 25 months of survival, and were reported on a per-year basis.

**Results**

**Patient Characteristics**

We identified 56,838 CRC patients (41,256 colon cancer [CC], 15,582 rectal cancer [RC]) who met our selection criteria. Demographic and clinical characteristics for CC patients, RC pa-
tients, the combined CRC cohort, and the comparison cohort are presented in Table 1. The mean ± SD age was 77.7 ± 7.1 years; about 55% of patients in both cohorts were women and 86% were white.

**Lifetime Cost Estimates**

Total lifetime cancer-related costs were $28,500, with an inverted U-shaped pattern by stage and a U-shaped pattern by age (Table 2). Excess costs for RC patients were somewhat higher than costs for CC patients for stages I to III and substantially lower for stage 0. CC costs were $42,000 for stage 0, $45,000 for stage I, $43,000 for stage II, and $41,000 for stage III. Among RC patients, excess costs for stages I to III were approximately 50% greater than for stage 0 ($47,000 for stage I, $49,000 for stage 2, and $46,500 for stage III vs $30,000 for
stage 0). Excess costs among stage IV patients were negative, reflecting patients’ shorter life expectancy and the incorporation of future medical costs of comparison patients who outlive CRC patients.

On a per-survival-year basis, excess CRC costs were approximately 9 times greater for patients diagnosed at stage IV versus stage 0 (Figure 1). Excess CC costs per survival year were approximately 3 times greater for stage IV than for stage III. Excess RC costs per survival year were approximately 2 times greater for stage IV than for stage II. Compared with costs for CC, costs for RC were similar for stages 0 and I, somewhat higher for stages II to III, and substantially lower for stage IV. Across all stages, excess costs per year of survival were highest among the oldest patients.

Table 3 reports lifetime cancer-related health care costs per year of survival for combinations of age and stage at diagnosis. Within stage, costs increase monotonically with age up to stage III, but the difference is more pronounced in early stage disease. Within age, costs increase monotonically with stage, with the increase most pronounced in younger patients.

For the combined CRC cohort, costs for the 85+ group were approximately 50% and 30% higher than costs for the 66 to 74

Table 2. Excess Cancer-Related Lifetime Health Care Costs (2006 US$) by Cancer Subsite, Stage, and Age at Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>CC patients</th>
<th>RC patients</th>
<th>Combined CRC cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stages</td>
<td>$29,420</td>
<td>$26,544</td>
<td>$28,626</td>
</tr>
<tr>
<td>Stage 0</td>
<td>$42,127</td>
<td>$29,983</td>
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<td>Stage I</td>
<td>$45,094</td>
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<td>Stage II</td>
<td>$42,847</td>
<td>$49,020</td>
<td>$44,311</td>
</tr>
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<td>Stage III</td>
<td>$41,050</td>
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</tr>
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<td>Stage IV</td>
<td>$7428</td>
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<td>Unknown/unstaged</td>
<td>$25</td>
<td>$510</td>
<td>$474</td>
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<tr>
<td>All ages</td>
<td>$29,420</td>
<td>$26,544</td>
<td>$28,626</td>
</tr>
<tr>
<td>Age 66–74</td>
<td>$36,226</td>
<td>$26,790</td>
<td>$26,401</td>
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<td>Age 75–84</td>
<td>$22,815</td>
<td>$16,726</td>
<td>$21,167</td>
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<td>Age 85+</td>
<td>$27,309</td>
<td>$12,960</td>
<td>$23,799</td>
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NOTE. Survival probabilities beyond year 10 were estimated with SEER*Stat data (stage-specific survival data projected beyond year 16 with Weibull models). Future costs were discounted at 3% per year. Data from SEER-Medicare database, 1996-2005.

Figure 1. Excess lifetime cancer-related health care costs (2006 US$) per year of survival, by cancer subsite, and stage at diagnosis.

Table 3. Excess Lifetime Cancer-Related Health Care Costs (2006 US$) per Year of Survival and by Age and Stage at Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>All ages</th>
<th>Age 66–74</th>
<th>Age 75–84</th>
<th>Age 85+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage at diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CC patients</td>
<td>RC patients</td>
<td>Combined CRC cohort</td>
<td>CC patients</td>
<td>RC patients</td>
</tr>
<tr>
<td>All stages</td>
<td>$8,909</td>
<td>$8,713</td>
<td>$8,675</td>
<td>$9,151</td>
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<tr>
<td>Stage 0</td>
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<td>$3,210</td>
<td>$3,084</td>
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<td>Stage I</td>
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<td>Stage II</td>
<td>$1,783</td>
<td>$2,172</td>
<td>$2,217</td>
<td>$2,498</td>
</tr>
<tr>
<td>Stage III</td>
<td>$1,783</td>
<td>$2,172</td>
<td>$2,217</td>
<td>$2,498</td>
</tr>
<tr>
<td>Stage IV</td>
<td>$1,783</td>
<td>$2,172</td>
<td>$2,217</td>
<td>$2,498</td>
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<tr>
<td>Stage IV/unknown/unstaged</td>
<td>$7,675</td>
<td>$7,675</td>
<td>$7,675</td>
<td>$7,675</td>
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</table>

NOTE. Survival probabilities beyond year 10 were estimated with SEER*Stat data (stage-specific survival data projected beyond year 16 with Weibull models). Future costs were discounted at 3% per year. Data from SEER–Medicare database, 1996–2005.
and 75 to 84 age groups, respectively. For the CC cohort, costs for the 85+ age group were approximately 50% and 40% higher than costs for the 66 to 74 and 75 to 84 age groups, respectively. For the RC cohort, costs for the 85+ age group were approximately 20% and 10% higher than costs for the 66 to 74 and 75 to 84 age groups, respectively.

Across age groups, RC patients had less variation in costs than CC patients. Compared with CC patients, RC patients had higher costs for the 66 to 74 and 75 to 84 age groups and lower costs for the 85+ age group.

**Phase-Specific Cost Estimates for the Entire Colorectal Cancer Population**

Examining both short- and long-term survivors, CRC-related initial phase costs were approximately $33,000, excess continuing phase costs were about $4500 per year, and excess terminal costs were more than $14,000 (Table 4). Initial-phase costs were slightly higher for CC patients, whereas continuing-phase costs were roughly one-third higher for RC versus CC and terminal costs were higher for RC patients by a small margin. Phase-specific costs were much higher for stages III and IV compared with stages 0 to II for all phases. However, little can be inferred from the difference in stage IV because these patients are treated continually for active disease. In all phases, costs were highest for the 66 to 74 age group and lowest for the 85+ age group. The biggest difference in costs by age occurred in the continuing phase, in which the 66 to 74 age group had costs approximately two-thirds higher than that of the 75 to 84 age group.

**Discussion**

This study evaluated lifetime and phase-specific excess costs among elderly patients with CRC in the United States. We found that lifetime CRC-related costs are substantial and vary by cancer subsite, stage at diagnosis, age at diagnosis, and treatment phase. Excess lifetime costs show an inverted U-shaped pattern by stage at diagnosis, and a U-shaped pattern by age at diagnosis for both CC and RC. Costs for RC patients are lower than costs for CC patients in stage 0, higher in stages I to III, and lower in stage IV. On a per-survival-year basis, costs are substantially higher for both RC and CC patients diagnosed in stage IV versus any other stage. RC patients had lower costs than CC patients in the initial phase, but higher costs than CC patients in both the continuing and terminal phases.

Our findings regarding excess costs associated with CRC are broadly consistent with 2 previous studies. Etzioni et al analyzed excess lifetime costs of care for CRC patients using data from SEER–Medicare (1986–1994) using a methodology similar to ours (ie, subtracting total lifetime costs for a noncancer control group from lifetime costs for CRC patients). Brown et al used 5 years of SEER–Medicare data (1990–1994) to estimate phase-specific (initial, continuing, and terminal) costs and to project total lifetime costs associated with CRC, not accounting for future medical costs that would have been incurred in the absence of cancer. Because their study did not account for future medical costs, our estimates of excess costs are somewhat lower. Total costs in our study for both cancer patients and comparison patients are higher for all stages and cancer subsites, which we would expect given our use of data that includes more recent advances in CRC treatment (eg, irinotecan) and the inflation in the cost of health care services that has occurred during the decade between data sources.

One previous study found much higher estimates of CRC-related direct medical costs. This study used an administrative claims database, which included patients insured by private or Medicare supplemental health plans. The investigators found that Medicare beneficiaries had considerably lower monthly expenditures than patients with commercial insurance, likely explaining our difference in findings. An additional study found that 41% to 55% of patients who were diagnosed with CRC more than 5 years ago were still receiving treatment, well past the time when CRC patients are traditionally thought of as cured.

Table 4. Initial, Continuing, and Terminal Cancer-Related Health Care Costs (2006 US$) by Cancer Subsite, Stage, and Age

<table>
<thead>
<tr>
<th>Age, y</th>
<th>CC</th>
<th>RC</th>
<th>All patients</th>
<th>CC</th>
<th>RC</th>
<th>All patients</th>
<th>CC</th>
<th>RC</th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>66–74</td>
<td>$33,980</td>
<td>$35,002</td>
<td>$34,282</td>
<td>$3277</td>
<td>$4166</td>
<td>$3503</td>
<td>$13,457</td>
<td>$14,273</td>
<td>$13,675</td>
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<tr>
<td>75–84</td>
<td>$33,401</td>
<td>$31,741</td>
<td>$32,967</td>
<td>$3277</td>
<td>$4166</td>
<td>$3503</td>
<td>$13,457</td>
<td>$14,273</td>
<td>$13,675</td>
</tr>
<tr>
<td>85+</td>
<td>$32,966</td>
<td>$27,982</td>
<td>$31,869</td>
<td>$2261</td>
<td>$3534</td>
<td>$2502</td>
<td>$12,273</td>
<td>$12,571</td>
<td>$12,346</td>
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</tbody>
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*Initial costs were defined as average costs in the initial (up to 1 year) period after diagnosis and before the last year of life and were calculated among only those who lived at least 13 months after diagnosis.

*Continuing costs were defined as average annual costs in years beyond the initial year and before the last year of life and were calculated among only those patients who lived at least 25 months after diagnosis.

*Terminal costs were defined as average costs in the final year of life (all costs are considered terminal for patients living <13 months after diagnosis).
cured. This reinforces our findings that continuing costs are nearly $3500 higher for CRC patients than for the comparison cohort.

One recently published study of the phase-specific costs of cancer care using SEER-Medicare data from 1999 to 2003 found similar costs for the initial year of life ($32,101 for male CRC patients vs our estimate of $33,500 for all CRC patients). However, because of the methods used in matching terminal-phase cancer patients to continuing-phase controls, their estimates of terminal-phase costs were much higher than ours ($39,544 vs $14,500). Our continuing-phase cost estimate ($4500) was slightly higher than theirs ($2444 for men), possibly because of a different approach to annualizing the data.

Our results are consistent with previous studies showing that the costs of the last year of life are lower for older patients than for younger patients, reflecting the fact that older patients receive less aggressive treatment. This fact is important to remember when calculating cost-effectiveness ratios, especially for preventive care. When considering that terminal costs decrease with age, costs per quality-adjusted life years for preventive interventions may be lowered by a substantial amount for some patient groups.

Our study contributes to the existing literature on costs associated with CRC by evaluating the latest data, thus reflecting some of the recent changes in treatment patterns for CRC, such as the introduction of irinotecan and more use of multimodality therapy. This study reports colorectal cancer costs per survival year.

The substantially higher costs for later-stage cancers may indicate that these cancers receive more drastic or expensive treatments. If this is the case, it may be important to focus on earlier detection of CRC as a way to reduce medical expenditures. In addition, per-survival-year costs are lower for younger patients than for older patients. However, phase-specific costs are higher for younger patients, perhaps reflecting more aggressive treatments used in younger patients.

Although lifetime costs for RC are slightly lower than costs for CC patients for all stages combined, costs vary considerably by stage at diagnosis. For the later-stage cancers, RC patients have substantially higher costs than CC patients. Our results suggest that any discussion involving CRC patients would be improved by focusing on RC and CC patients separately.

Our findings will be useful in shaping policy discussions regarding CRC treatment, costs, and insurance coverage. In addition, our findings regarding stage- and phase-specific costs for the entire CC and RC populations can be used in economic models such as cost-effectiveness models evaluating the potential impact of new technologies to detect and treat CRC.

This study is subject to certain limitations that are common to all studies that rely on retrospective claims data, such as potential coding errors and incomplete data. Our use of the SEER-Medicare database, which includes complete claims only for Medicare-eligible patients aged 65 years and older, introduces additional limitations. Although the elderly comprise the majority of patients with CRC, this sample is not representative of all US patients, particularly those with other forms of health insurance (eg, managed care, private pay). Despite its limitations, SEER-Medicare data have been used in numerous published studies of colon cancer, as well as cancers of the breast, prostate, and lung, among others.

Only services covered by Medicare were included in this analysis, and at the time of this study, coverage for most oral prescription medications was not included. Because claims are available only through 2005, the most recent changes in CRC treatment patterns were not captured in the data. Until recently, a combination of fluorouracil and leucovorin was the standard of care for CRC; numerous other drugs have been approved for use in CRC patients since 2004, including oxaliplatin, bevacizumab, cetuximab, and panitumumab. These new cytotoxic and biologic agents used in cancer treatment are among the most expensive technologies in medical care, and the costs of these agents are substantially greater than costs for older drugs. The impact of more expensive drugs on the cost of CRC remains to be seen. If treatment is getting more expensive, our estimates of CRC-related costs may be lower than the current costs associated with the disease.

In conclusion, this study showed that excess costs associated with CRC are striking and vary considerably by treatment phase, cancer subsite, and stage at diagnosis. Within each treatment phase and on a per-survival-year basis, costs increase substantially for later-stage diagnoses. Interventions aimed at prevention and earlier detection of CRC have the potential to yield sizable economic benefits.

References
12. Etzioni R, Urban N, Baker M. Estimating the costs attributable to...