Did Changes in Drug Reimbursement After the Medicare Modernization Act Affect Chemotherapy Prescribing?

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ABSTRACT

Purpose

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) decreased fee-for-service (FFS) payments for outpatient chemotherapy. We assessed how this policy affected chemotherapy in FFS settings versus in integrated health networks (IHNs).

Patients and Methods

We examined 5,831 chemotherapy regimens for 3,613 patients from 2003 to 2006 with colorectal cancer (CRC) or lung cancers in the Cancer Care Outcomes Research Surveillance Consortium. Patients were from four geographically defined regions, seven large health maintenance organizations, and 15 Veterans Affairs Medical Centers. The outcome of interest was receipt of chemotherapy that included at least one drug for which reimbursement declined after the MMA.

Results

The odds of receiving an MMA-affected drug were lower in the post-MMA era: the odds ratio (OR) was 0.73 (95% CI, 0.59 to 0.89). Important differences across cancers were detected: for CRC, the OR was 0.65 (95% CI, 0.46 to 0.92); for non-small-cell lung cancer (NSCLC), the OR was 1.60 (95% CI, 1.09 to 2.35); and for small-cell lung cancer, the OR was 0.63 (95% CI, 0.34 to 1.16). After the MMA, FFS patients were less likely to receive MMA-affected drugs: OR, 0.73 (95% CI, 0.59 to 0.89). No pre- versus post-MMA difference in the use of MMA-affected drugs was detected among IHN patients: OR, 1.01 (95% CI, 0.66 to 1.56). Patients with CRC were less likely to receive an MMA-affected drug in both FFS and IHN settings in the post- versus pre-MMA era, whereas patients with NSCLC were the opposite: OR, 1.60 (95% CI, 1.09 to 2.35) for FFS and 6.33 (95% CI, 2.09 to 19.11) for IHNs post- versus pre-MMA.

Conclusion

Changes in reimbursement after the passage of MMA appear to have had less of an impact on prescribing patterns in FFS settings than the introduction of new drugs and clinical evidence as well as other factors driving adoption of new practice patterns.

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INTRODUCTION

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) reduced Medicare reimbursements for covered outpatient prescription drugs (from 95% to 85% of the average wholesale price [AWP]). In 2005, the Centers for Medicare and Medicaid Services instituted a new payment system that reimbursed fee-for-service (FFS) providers for drugs at the national average sales price from the quarters 6 months earlier plus 6%. Before MMA, Medicare reimbursed FFS oncology practices for specified antineoplastic drugs administered to Medicare patients in their offices at

95% of the AWP. Medical oncologists were often able to purchase chemotherapy drugs for substantially less than AWP. The Government Accountability Office found that many chemotherapy drugs were available at discounts of 20% or more on average, although for some drugs, the discounts were much greater.¹ The Medicare Payment Advisory Commission found that larger oncology practices were able to obtain lower drug prices than smaller practices.²

Ostensibly, this change in financial incentives for prescribing high-cost outpatient chemotherapy was expected to slow the rapid increase in Medicare expenditures for these agents. MMA did reduce

revenues to oncology practices that administered significant volumes of chemotherapy agents. This change, however, had no immediate effects on Medicare capitation payments to Medicare Advantage health plans; the average adjusted per capita cost index that forms the base for risk-adjusted per capita payment of Medicare Advantage plans is a rolling average, so the effects of MMA rollbacks of reimbursement for chemotherapy agents were not felt by health maintenance organizations (HMOs) for at least 2 years. MMA had no effect on the Veterans Health Administration (VHA), which directly purchases drugs and does not profit on drugs administered to veterans. Physicians in group-model HMOs and VHA settings were typically salaried and, thus, would not be affected by the MMA reimbursement changes. MMA provided a natural before-and-after/no change experiment for testing the effects of cost-saving financial incentives faced by FFS medical oncologists on their patterns of chemotherapy prescribing.

We used data from the Cancer Care Outcomes Research and Surveillance (CanCORS) study, a population-based study designed to assess the quality of cancer care to improve our understanding of how policy changes impact providers' use of chemotherapy drugs.³⁻⁵ We compared the impact of MMA on patients treated in FFS settings with those treated in capitated HMOs and the VHA system. For this study, we grouped HMO and VHA oncologists together as Integrated Health Networks (IHNs). HMOs participating in CanCORS were vertically integrated prepaid group practices. We tested two hypotheses: (1) patients treated in FFS settings before April 2005 were more likely than patients treated in IHNs to receive chemotherapy regimens that included drugs for which reimbursements declined after MMA passage (the most profitable drugs for oncologists), and (2) the declines in use of drugs with lowered reimbursement rates after MMA were greater in FFS settings than in IHNs.

PATIENTS AND METHODS

Study Population and Data

The CanCORS study investigated the quality of cancer-related health care delivered to a population- and health system–based cohort of more than 10,000 patients newly diagnosed with colorectal cancer (CRC) or lung cancer between 2003 and 2005. Details of the design and purpose of the study are described elsewhere.³⁻⁵ Participants resided in Northern California, Los Angeles County, North Carolina, Iowa, or Alabama, or were members of one of several large HMOs (located in California, Hawaii, Massachusetts, Michigan, Oregon, and Washington State) or 15 VHA Medical Centers.⁶ Human subjects committees at all participating institutions approved the study.

From 2003 to 2005, each study site identified newly diagnosed lung cancers and CRCs within 8 weeks of diagnosis. Data were derived from the CanCORS patient surveys, cancer registries, and medical record abstraction (87% of patients consented to medical record abstraction).⁷ Our analysis included the 3,613 CanCORS participants who received any chemotherapy and consented to medical record abstraction. We documented the number of chemotherapy agents administered and their timing from medical record data through 15 months after diagnosis.⁸ The CanCORS sample is representative of all US patients with lung cancers or CRC as captured by the National Cancer Institute's SEER Program.⁶

Clinical variables, including the Adult Comorbidity Evaluation 27 comorbidity index,^{9,10} cancer stage, and chemotherapy drugs, were obtained from detailed inpatient and outpatient medical record reviews; when not available from medical records, stage was obtained from cancer registries.

Dependent Variables

The dependent variable of interest was patient receipt of a chemotherapy regimen containing a drug that experienced a decline in Medicare reimbursement after the implementation of MMA. The unit of analysis was the chemotherapy regimen. We extracted data from the Centers for Medicare and Medicaid Services Web site regarding the 2004 and 2005 reimbursements per unit dose for all anticancer drugs, including both cytotoxic and biologic agents administered to CanCORS patients. We identified the year of initial US Food and Drug Administration approval for each drug affected by MMA. Our primary dependent variable reflected regimens with any decline in reimbursement for a drug after the implementation of MMA, defined as an "MMA-affected drug"; exploratory analyses suggested no differences on the basis of larger or smaller payment declines. Oral chemotherapy drugs not administered in a physician's office were excluded from our analysis. Chemotherapy administrations were counted by multiday or multiweek cycles rather than daily administrations.

Independent Variables

Independent variables included the time period in which care was delivered (pre- v post-MMA) and care system (IHN v FFS). Adjustment variables included patient characteristics; cancer site (non-small-cell lung cancer (NSCLC), small-cell lung cancer (SCLC), or CRC; cancer stage according to the American Joint Committee on Cancer (sixth edition); and first-line versus second- or later-line chemotherapy regimens (defined by receipt of a new drug or gap of 90 days in receipt of chemotherapy). Because the evidence supporting the drug choices used as initial therapy is generally more robust than that for second- and later-line regimens, we hypothesized that more substitution away from relatively less profitable drugs (drugs most affected by MMA) would occur in selecting later lines of therapy.

We used logistic regression with generalized estimating equations to account for clustering of regimens within patients to predict receipt of a chemotherapy regimen containing a drug with a decline in reimbursement, with pre- versus post-MMA and FFS- versus IHN-enrolled patients (binary variable) as primary predictors of interest. Each model was adjusted for patient and clinical characteristics and line of therapy. We assessed the effects of interactions between pre- versus post-MMA periods, FFS versus IHN, type of cancer, and age at diagnosis (age ≥ 65 v < 65 years).

The final analytic sample included 5,831 treatment regimens received by 3,613 patients. The intraclass correlation was 0.18, with 1.6 regimens per cluster on average, resulting in an effective sample size of 5,260.¹¹ With 86% of regimens containing an MMA-affected drug and 80% of regimens administered pre-MMA, we were able to detect a minimal odds ratio (OR) of 1.33 with 80% power at an α level of .05. The minimally detectable OR for the analysis, including the interaction term, was 2.37.^{12,13}

RESULTS

The sample description and unadjusted comparisons between patients with their first chemotherapy regimen in the pre-MMA period (2003 to the first quarter [Q1] of 2005) versus patients with their first regimen in the post-MMA period (Q2 2005 through 2006) are provided in Table 1. Because the timing of study enrollment varied across CanCORS sites, patients whose first regimen was after MMA differed from other patients on race/ethnicity, sex, stage at diagnosis, comorbidity, and type of health system; greater numbers of IHN versus FFS patients were in the post-MMA period because of delays in starting recruitment at some of the IHN sites. We adjusted for these factors in our multivariable analyses.

The effects of MMA on Medicare reimbursements for typical doses of 21 chemotherapy agents are depicted in Table 2. From 2003 onward, the overall share of MMA-affected agents declined continuously, starting from 95% of all treatment regimens in 2003 and declining to 80% by 2006 (Fig 1). The proportion of regimens that included

Table 1. Patient Characteristics (N = 3,613)

Characteristic	First Regimen				χ^2 P
	Pre-MMA*		Post-MMA		
	No.	%	No.	%	
Age at diagnosis (years)					
< 65	1,601	50	210	51	.954
65-74	973	30	123	30	
75+	625	20	81	20	
Race/ethnicity					
White	2,208	69	273	66	< .001
Non-Hispanic black	464	15	96	23	
Hispanic	201	6	13	3	
Other	326	10	32	8	
Sex					
Female	1,279	40	91	22	< .001
Male	1,920	60	323	78	
Cancer type					
CRC	1,413	44	161	39	.076
NSCLC	1,422	44	208	50	
SCLC	364	11	45	11	
Stage at diagnosis					
I-III	1,939	61	272	66	.046
IV	1,260	39	142	34	
Comorbidity (ACE-27)					
None	802	25	77	19	.023
Mild	1,267	40	170	41	
Moderate	625	20	97	23	
Severe	505	16	70	17	
IHN (HMO/VHA)					
No	2,522	79	292	71	< .001
Yes	677	21	122	29	

Abbreviations: ACE-27, Adult Comorbidity Evaluation 27; CRC, colorectal cancer; HMO, health maintenance organization; IHN, integrated health network; MMA, Medicare Prescription Drug, Improvement, and Modernization Act of 2003; NSCLC, non-small-cell lung cancer; SCLC, small-cell lung cancer; VHA, Veterans Health Administration.

*The cutoff for the impact of pre- and post-MMA impact was after the first quarter of 2005.

Table 2. Effects of MMA on Commonly Used Chemotherapy Drugs

Drug	Typical Daily Dose Reimbursement (\$)		Difference (\$)
	2004	2005	
Leucovorin	48.00	20.77	-27.23
Bevacizumab	4,571.70	3,996.84	-574.86
Carboplatin injection	1,521.96	839.05	-682.91
Cetuximab	10,177.92	9,239.13	-938.79
Cisplatin	257.64	67.65	-189.99
Cyclophosphamide	71.82	15.82	-56.00
Docetaxel	2,109.80	2,068.81	-40.99
Etoposide	102.51	33.84	-68.68
Fluorouracil	38.85	29.30	-9.56
Gemcitabine	2,853.20	3,232.33	379.13
Irinotecan	4,172.82	4,302.11	129.29
Oxaliplatin	4,495.40	4,430.36	-65.04
Paclitaxel	1,244.52	134.55	-1,109.97
Pemetrexed	4,306.83	3,771.06	-535.77
Topotecan	2,824.68	2,994.61	169.93
Vinorelbine	685.71	476.90	-208.81
Doxorubicin	89.76	58.84	-30.92
Doxorubicin liposome	3,168.54	3,245.61	77.07
Trastuzumab	2,912.56	3,000.20	87.64
Ifosfomide	1,210.95	429.27	-781.68
Mitomycin	185.64	77.30	-108.34

NOTE. Dollar amounts are for a daily dose, not a full multiday regimen.

Abbreviation: MMA, Medicare Prescription Drug, Improvement, and Modernization Act of 2003.

an MMA-affected drug declined from 2003 to 2006 by 17% in FFS practices and 6% in IHNs (Fig 2; Table A1, online only). In FFS, the sharpest decline occurred from Q1 to Q2 in 2005 (ie, pre- to post-MMA implementation), whereas IHN patients received increasing proportions of MMA-affected drugs at that time.

To provide support for our pre- or post-MMA classification, we estimated linear spline fits to the time series of proportions (on a log odds scale) of chemotherapy regimens that included drugs affected by MMA (Figs A1 and A2, online only). The piecewise linear spline regression segments joined at the end of Q1 2005. We performed statistical tests of the differences in trend slopes between pre- and post-MMA. Although the differences in slopes between FFS and IHN patients were not statistically significant, these analyses provided qualitative empirical evidence for our chosen temporal break point. Our spline regression results can be interpreted as showing the expected response of FFS physicians to the new lower payment levels. The observed increase in prescriptions for MMA-affected drugs by IHN physicians was surprising. The IHN-FFS use gap continued through 2006, suggesting continued inclusion of MMA-affected drugs in IHN chemotherapy formularies.

We estimated the odds of receiving chemotherapy containing an MMA-affected drug, adjusted for type of health system, first- versus

later-line drug regimen, whether a newly US Food and Drug Administration–approved drug was included in the regimen, type of cancer, and patient-level covariates for the entire sample and four subgroups: age 65 years or older, CRC, SCLC, and NSCLC (Table 3; two-way analyses are listed in Table A1). Cancer type, stage, and line of therapy

Fig 1. Decomposition of cancer drug regimens over time for Cancer Care Outcomes Research and Surveillance participants: proportions of regimens including drugs affected by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) versus regimens with only unaffected drugs overall. Q, quarter.

Fig 2. Decomposition of cancer drug regimens over time for Cancer Care Outcomes Research and Surveillance participants: proportions of regimens including drugs affected by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) versus regimens with only unaffected drugs by type of health system. FFS, fee-for-service; IHN, integrated health network; Q, quarter.

had an impact on the use of MMA-affected drugs in any chemotherapy regimen (regardless of whether administered pre- or post-MMA). In the full model, patients with NSCLC were less likely to have received a chemotherapy regimen with an MMA-affected drug than patients with CRC (OR, 0.81; 95% CI, 0.67 to 0.96); the OR for use of MMA-affected drugs among patients with SCLC was not statistically significant. Having stage IV NSCLC was associated with lower odds of use of an MMA-affected drug (OR, 0.61; 95% CI, 0.47 to 0.79) but not for SCLC or CRC. Use of MMA-affected drugs was lower in second- and subsequent-line regimens compared with first-line regimens for the entire sample, for patients age 65 years or older, and for all three cancer subgroups.

Compared with FFS patients, IHN patients were more likely to receive an MMA-affected drug (OR, 1.23; 95% CI, 0.98 to 1.54), but this varied across cancers. For CRC, the OR for use of MMA-affected drugs by IHN versus FFS patients was 1.53 (95% CI, 1.03 to 2.29), but no significant differences between IHNs and FFS settings were seen for NSCLC or SCLC.

The odds of receiving an MMA-affected drug were lower in the post-MMA era (OR, 0.73; 95% CI, 0.59 to 0.89), but varied by cancer type. Although use of MMA-affected drugs decreased for patients with CRC and SCLC in the post-MMA era, for patients with NSCLC, use of MMA drugs increased post-MMA (OR, 1.60; 95% CI, 1.09 to 2.35). In the interaction between health system and pre- or post-MMA era, FFS patients were less likely to receive an MMA-affected drug (OR, 0.73; 95% CI, 0.59 to 0.89); however, there was no difference in the use of MMA-affected drugs overall between pre- and post-MMA among patients in IHNs (OR, 1.01; 95% CI, 0.66 to 1.56). Again, variation was observed across cancers. Patients with CRC had decreased odds of using MMA-affected drugs in both FFS and IHNs post-MMA versus pre-MMA, whereas patients with NSCLC had increased odds post-MMA, with greater magnitude of the increase for IHNs than for FFS settings: OR was 1.60 (95% CI, 1.09 to 2.35) for FFS post- versus pre-MMA, and OR was 6.33 (95% CI, 2.09 to 19.11) for IHNs post- versus pre-MMA.

We estimated stratified models for first-line versus second-line regimens. Patients treated in IHNs were more likely than FFS patients to receive an MMA-affected drug, but the OR for second- and later-line regimens was not statistically significant. The effect of MMA timing differed between types of health systems after restricting the analysis to second- and later-lines of therapy: FFS oncologists were less likely to prescribe MMA-affected drugs for second-line and later regimens after MMA, whereas IHN oncologists were more likely to prescribe MMA-affected agents in second and later lines of therapy after MMA.

As a sensitivity analysis, we repeated our analysis with a three-level health plan variable—FFS, HMO, VHA—with interactions by MMA timing and health plan type. The results were confirmatory of our main analysis, and we did not observe any significant differences in the impacts of MMA on VHA and HMO patients (Figs A3 and A4, online only).

DISCUSSION

Contrary to our hypotheses that pre-MMA financial incentives led to greater use of MMA-affected agents (which tended to be the most profitable), the overall use of MMA-affected drugs was declining in both FFS settings and IHNs for patients with lung cancers and those with CRC before Q2 2005 (when MMA reduced chemotherapy payments). From Q2 2005 through 2006, use of MMA-affected drugs continued to decline among FFS patients, as expected, but use in IHN patients increased.

Further examination of patterns of chemotherapy use by cancer type revealed that patients with CRC experienced continuing declines in use of MMA-affected drugs by both FFS and IHN patients, whereas both FFS and IHN patients with NSCLC experienced strong increases in prescriptions for MMA-affected drugs, although the magnitude of the increase was greater in the IHNs than in the FFS setting.

The odds of receiving MMA-affected drugs in second-line regimens were considerably lower than in first-line regimens for all three cancers, and the odds of receiving an MMA-affected drug were lower in the post-MMA period for second and subsequent lines of therapy but not for first-line therapy. This variation suggests that many factors influence chemotherapy regimen selection over time, and although financial considerations may play a role they do not appear to be the most important consideration. The increase in the use of MMA-affected drugs for NSCLC from 2005 to 2006 in both FFS and IHN settings is at odds with the new reimbursement policy and may have been driven by the amount of substitution available in NSCLC compared with CRC and SCLC, new evidence supporting the use of adjuvant therapy for NSCLC, and availability of newly approved MMA-affected drugs such as pemetrexed and bevacizumab for patients with advanced disease.⁸ It is interesting to note that the increased odds of an MMA-affected drug for NSCLC was greater for IHN than for FFS patients. We cannot determine from our data whether this was related to the differences in financial incentives across settings or perhaps the organizational structures of IHNs, which may facilitate adoption of new therapies more rapidly as evidence emerges. One implication of our results is that a single policy instrument is unlikely to generate consistent patterns of response across all Medicare beneficiaries using the affected drugs.

In the decade since MMA was passed, the aggregate cost of cancer care has increased by as much as 66%, despite a slight decline in cancer

Table 3. Odds of Receiving Combination Chemotherapy That Included Drugs Affected by MMA: Analysis of 5,831 Total Regimens Initiated From 2003 to 2006

Variable	Full Model				Age 65 Years or Older Only				Cancer Subgroups											
	No.	OR	95% CI	P	No.	OR	95% CI	P	CRC				SCLC				NSCLC			
									No.	OR	95% CI	P	No.	OR	95% CI	P	No.	OR	95% CI	P
Total patients	3,613				1,802				1,574				409			1,630				
Total regimens	5,831				2,727				2,517				674			2,640				
MMA timing																				
Pre-MMA (ref.)	1.00				1.00				1.00				1.00			1.00				
Post-MMA	0.73	0.59 to 0.89	.002		0.87	0.64 to 1.18	.378		0.65	0.46 to 0.92	.02		0.63	0.34 to 1.16	.14	1.60	1.09 to 2.35	.02		
Health plan																				
FFS (ref.)	1.00				1.00				1.00				1.00			1.00				
IHN	1.23	0.98 to 1.54	.078		1.05	0.78 to 1.40	.762		1.53	1.03 to 2.29	.04		0.63	0.31 to 1.27	.20	1.15	0.83 to 1.58	.41		
Regimen order																				
First (ref.)	1.00				1.00				1.00				1.00			1.00				
Follow-up	0.28	0.24 to 0.33	< .001		0.33	0.26 to 0.41	< .001		0.74	0.58 to 0.95	.02		0.02	0.01 to 0.06	< .001	0.17	0.13 to 0.22	< .001		
Age at diagnosis (years)																				
< 65 (ref.)	1.00				—				1.00				1.00			1.00				
65-74	0.69	0.57 to 0.83	< .001		—				0.77	0.57 to 1.05	.10		0.90	0.49 to 1.67	.74	0.60	0.44 to 0.80	< .001		
75+	0.46	0.37 to 0.56	< .001		—				0.39	0.28 to 0.55	< .001		0.76	0.36 to 1.62	.48	0.42	0.30 to 0.58	< .001		
Race/ethnicity																				
White (ref.)	1.00				1.00				1.00				1.00			1.00				
Hispanic	0.74	0.53 to 1.04	.079		0.66	0.41 to 1.05	.083		0.69	0.45 to 1.05	.08		0.76	0.27 to 2.12	.60	0.70	0.38 to 1.29	.25		
Non-Hispanic black	1.04	0.82 to 1.31	.77		0.90	0.64 to 1.26	.528		0.89	0.63 to 1.25	.49		0.63	0.29 to 1.38	.25	1.55	0.99 to 2.42	.06		
Other	0.84	0.65 to 1.10	.205		0.99	0.66 to 1.48	.954		0.87	0.56 to 1.34	.52		0.76	0.39 to 1.49	.43	1.11	0.71 to 1.72	.65		
Sex																				
Male (ref.)	1.00				1.00				1.00				1.00			1.00				
Female	0.92	0.78 to 1.08	.313		0.88	0.70 to 1.10	.256		0.88	0.67 to 1.16	.38		0.71	0.44 to 1.14	.16	1.09	0.83 to 1.43	.55		
Cancer type																				
CRC (ref.)	1.00				1.00				—				—			—				
NSCLC	0.81	0.67 to 0.98	.034		0.83	0.64 to 1.08	.168		—				—			—				
SCLC	0.84	0.65 to 1.09	.189		0.99	0.69 to 1.43	.968		—				—			—				
Stage at diagnosis																				
I-III (ref.)	1.00				1.00				1.00				1.00			1.00				
IV	0.81	0.69 to 0.95	.012		0.88	0.71 to 1.09	.236		1.11	0.85 to 1.46	.45		0.64	0.39 to 1.07	.09	0.61	0.47 to 0.79	< .001		
Comorbidity (ACE-27)																				
None (ref.)	1.00				1.00				1.00				1.00			1.00				
Mild	0.91	0.74 to 1.12	.365		0.76	0.54 to 1.08	.126		0.73	0.54 to 0.99	.04		0.82	0.42 to 1.61	.57	1.12	0.77 to 1.63	.56		
Moderate	0.86	0.67 to 1.09	.208		0.71	0.48 to 1.04	.077		0.85	0.58 to 1.26	.43		0.58	0.27 to 1.23	.16	0.96	0.62 to 1.49	.86		
Severe	0.92	0.70 to 1.20	.517		0.75	0.51 to 1.11	.152		0.75	0.47 to 1.22	.25		0.57	0.26 to 1.25	.16	0.96	0.63 to 1.47	.86		
New drug																				
No (ref.)	1.00				1.00				—				1.00			1.00				
Yes	0.71	0.54 to 0.94	.015		0.47	0.32 to 0.69	< .001		—				0.09	0.02 to 0.53	.01	0.03	0.01 to 0.05	< .001		
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Table 3. Odds of Receiving Combination Chemotherapy That Included Drugs Affected by MMA: Analysis of 5,831 Total Regimens Initiated From 2003 to 2006 (continued)

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incidence rates. This is a result of population growth, increased survival rates, and increased intensity of cancer care.^{14,15} The impact of MMA on overall costs of cancer care is not understood, and studies are mixed in terms of its impact on use. If anything, overall use of chemotherapy increased unabated following MMA,¹⁶ although substantial unexplained regional variation has been observed.¹⁷⁻¹⁹ Use of chemotherapy at the end of life by hospital outpatient departments did not change post-MMA, but it dropped significantly in independent oncologist practices, in which up to 80% of practice revenue traditionally came from the profit margins from infused drugs.^{20,21}

After passage of MMA, independent community oncology practices saw substantial decreases in their revenues, which resulted in consolidations and acquisitions of practices by hospitals, many which are able to purchase chemotherapy drugs at discounted rates through the Federal 340B program.²² Although the full impact of these changes is not known, the shift of chemotherapy from community practices to hospital outpatient settings is associated with higher total costs for private payers.^{23,24} Further research is needed to understand the long-term effect of MMA and other efforts to slow the rising expenses for cancer care on access, quality, and cost of care from a patient-centered perspective.

Type of health care setting was not independent of geographic region in CanCORS. The HMOs participating in CanCORS were predominantly located in the North Central, Mountain, and Pacific regions of the United States, with one in the Northeast. Despite evidence of geographic variation in response to the MMA,¹⁶⁻¹⁹ we were unable to assess geographic differences by type of health system because we did not have sufficient overlap between the two constructs—HMOs and Veterans Affairs Medical Centers were not located in the same areas as the FFS patients. Another measurement challenge was potential confounding between IHNs and FFS settings because some population-based sites included an unknown number of IHN patients whom we could not identify. Our IHN sample did not contain FFS patients because we recruited from IHN enrollment files. Other limitations included the lack of information on the appropriateness of the choice of chemotherapy drugs used and the lack of data on costs of chemotherapy covered by third-party payers, the VHA, and HMOs, or the costs charged to patients. In addition, we did not assess whether the IHNs had formulary restrictions or institutional guidelines that could have influenced use of MMA-affected drugs. The decline in the number of patients over time, particularly in the IHNs, could also introduce measurement error.

In conclusion, before the MMA, both FFS and IHN oncologists prescribed chemotherapy agents whose reimbursements were going to be reduced by MMA at declining rates. After the implementation of MMA, IHN oncologists increased their use of MMA-affected agents, although FFS oncologists accelerated their decline in use of MMA-affected drugs before leveling off. These findings highlight the complexity of the decision process in selecting chemotherapy regimens. Although the potential profitability from drugs may be an important driver of physician behavior in the FFS system, other factors are also important. The change in reimbursement after MMA passage appears to have had less of an impact on prescribing patterns in FFS than the introduction of new drugs and clinical evidence as well as other factors driving adoption of new practice patterns.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Appendix**Table A1.** Impact of MMA on Chemotherapy Administration Counts of All Regimens Initiated

Regimens	No. for All Years	2004																2005				2005-Q4/ 2006	
		2003		Q1		Q2		Q3		Q4		Q1		Q2		Q3							
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Including only drugs unaffected by MMA	812	56	6	86	12	93	11	113	13	128	17	102	16	90	20	73	21	71	21				
Including drugs affected by MMA	5,019	818	94	647	88	716	89	755	87	629	83	538	84	371	80	271	79	274	79				
FFS																							
Including only drugs unaffected by MMA	659	40	6	64	12	72	12	97	14	108	17	79	16	77	22	61	23	61	23				
Including drugs affected by MMA	3,869	618	94	486	88	541	88	585	86	521	83	430	84	277	78	202	77	209	77				
IHN																							
Including only drugs unaffected by MMA	153	16	7	22	12	21	11	16	9	20	16	23	18	13	12	12	15	10	13				
Including drugs affected by MMA	1,150	200	93	161	88	175	89	170	91	108	84	108	82	94	88	69	85	65	87				

Abbreviations: FFS, fee-for-service; IHN, integrated health network; MMA, Medicare Prescription Drug, Improvement, and Modernization Act of 2003; Q, quarter.

Choice of Chemotherapy Drugs in Response to Payment Changes

Table A2. Multivariate Regression Analysis of the Odds of Receiving Combination Chemotherapy With Drugs Affected by MMA: 5,831 Total Regimens Initiated From 2003 to 2005

Covariate	Unadjusted Percentage of MMA Regimens	All Regimens			First-Line Regimens			Second- and Later-Line Regimens		
		OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
MMA timing										
Pre-MMA (ref.)	88	1.00		—	1.00		—	1.00		—
Post-MMA	80	0.73	0.59 to 0.89	.002	0.93	0.60 to 1.44	.738	0.69	0.54 to 0.88	.003
Health network type*										
FFS (ref.)	85	1.00		—	1.00		—	1.00		—
IHN	88	1.23	0.98 to 1.54	.078	1.66	1.14 to 2.44	.009	0.98	0.73 to 1.32	.895
Health network by MMA timing										
IHN (post-MMA v pre-MMA)	—	1.01	0.66 to 1.56	.967	0.62	0.29 to 1.32	.213	1.33	0.79 to 2.24	.276
FFS (post-MMA v pre-MMA)	—	0.73	0.59 to 0.89	.002	0.93	0.60 to 1.44	.738	0.69	0.54 to 0.88	.003
Interaction: IHN post-MMA–FFS post-MMA	—	1.39	0.87 to 2.21	.168	0.67	0.28 to 1.61	.370	1.92	1.10 to 3.36	.022
Regimen order										
First-line (ref.)	92	1.00		—	—		—	—		—
Follow-on and recurrent	77	0.28	0.24 to 0.33	< .001	—		—	—†		—
Newly FDA-approved drug included in regimen										
No (ref.)	87	1.00		—	1.00		—	1.00		—
Yes	77	0.71	0.54 to 0.94	.015	0.93	0.51 to 1.68	.806	0.57	0.41 to 0.77	< .001
Patient-level covariates										
Age at diagnosis (years)										
< 65 (ref.)	88	1.00		—	1.00		—	1.00		—
65-74	85	0.69	0.57 to 0.83	< .001	0.60	0.44 to 0.82	.002	0.72	0.57 to 0.91	.006
75+	82	0.46	0.37 to 0.56	< .001	0.33	0.24 to 0.45	< .001	0.56	0.41 to 0.75	< .001
Race/ethnicity (self-reported from patient survey)										
White (ref.)	86	1.00		—	1.00		—	1.00		—
Hispanic	83	0.74	0.53 to 1.04	.079	0.71	0.44 to 1.14	.158	0.80	0.50 to 1.28	.348
Non-Hispanic black	88	1.04	0.82 to 1.31	.770	0.94	0.65 to 1.34	.720	1.12	0.82 to 1.53	.486
Other	85	0.84	0.65 to 1.10	.205	0.84	0.54 to 1.31	.448	0.88	0.64 to 1.21	.433
Sex										
Male (ref.)	86	1.00		—	1.00		—	1.00		—
Female	86	0.92	0.78 to 1.08	.313	0.96	0.73 to 1.26	.777	0.91	0.74 to 1.13	.394
Cancer type										
CRC (ref.)	88	1.00		—	1.00		—	1.00		—
NSCLC	85	0.81	0.67 to 0.98	.034	2.29	1.71 to 3.05	< .001	0.38	0.29 to 0.50	< .001
SCLC	85	0.84	0.65 to 1.09	.189	12.30	4.91 to 30.81	< .001	0.27	0.19 to 0.39	< .001
Stage at diagnosis										
I-III (ref.)	88	1.00		—	1.00		—	1.00		—
IV	86	0.81	0.69 to 0.95	.012	0.89	0.68 to 1.18	.433	0.72	0.58 to 0.89	.002
Comorbidity (ACE-27)										
None (ref.)	88	1.00		—	1.00		—	1.00		—
Mild	86	0.91	0.74 to 1.12	.365	0.77	0.53 to 1.10	.152	0.97	0.74 to 1.26	.796
Moderate	85	0.86	0.67 to 1.09	.208	0.70	0.46 to 1.06	.094	0.94	0.69 to 1.27	.672
Severe	85	0.92	0.70 to 1.20	.517	0.53	0.34 to 0.81	.004	1.25	0.89 to 1.76	.202

NOTE. There were 6,098 regimens initiated over the period. Because of missing data on patient-level variables, 5,831 regimens remained for analysis. In stratified models, there were 3,517 first-line and 2,315 second- or later-line regimens. The study cohort was 3,613 chemotherapy recipients from Cancer Care Outcomes Research and Surveillance.

Abbreviations: ACE-27, Adult Comorbidity Evaluation 27; CRC, colorectal cancer; FDA, US Food and Drug Administration; FFS, fee for service; IHN, integrated health network; MMA, Medicare Prescription Drug, Improvement, and Modernization Act of 2003; NSCLC, non-small-cell lung cancer; OR, odds ratio; ref., reference; SCLC, small-cell lung cancer.

*IHNs include health maintenance organizations and the Veterans Health Administration.

†No difference reported because there was more than one possible difference to report. Only global test of interaction reported.

Table A3. Full Model with Three-Level Health Plan Variables (FFS, HMO, VHA)

Variable	OR	95% CI	P
MMA timing			
Pre-MMA (ref.)	1.00		
Post-MMA	0.65	0.49 to 0.85	< .001
Health plan			
FFS (ref.)	1.00		
HMO	1.23	0.98 to 1.55	.08
VHA	1.06	0.75 to 1.50	.74
Regimen order			
First (ref.)	1.00		
Follow-up	0.28	0.24 to 0.34	< .001
Age at diagnosis (years)			
< 65 (ref.)	1.00		
65-74	0.69	0.57 to 0.82	< .001
75+	0.46	0.37 to 0.57	< .001
Race/ethnicity			
White (ref.)	1.00		
Hispanic	0.75	0.54 to 1.04	.09
Non-Hispanic black	1.01	0.79 to 1.28	.94
Other	0.84	0.64 to 1.09	.19
Sex			
Male (ref.)	1.00		
Female	0.94	0.79 to 1.12	.52
Cancer type			
CRC (ref.)	1.00		
NSCLC	0.82	0.67 to 0.99	.04
SCLC	0.84	0.65 to 1.09	.18
Stage at diagnosis			
Stage I-III (ref.)	1.00		
IV	0.81	0.69 to 0.95	.01
Comorbidity (ACE-27)			
None (ref.)	1.00		
Mild	0.91	0.73 to 1.12	.35
Moderate	0.85	0.67 to 1.09	.20
Severe	0.91	0.70 to 1.19	.50
New drug			
No			
Yes	0.72	0.54 to 0.96	.02
Interaction: MMA timing by health plan			
Overall interaction effect	—		.20
FFS (post-MMA v pre-MMA)	0.65	0.49 to 0.85	< .001
IHN (post-MMA v pre-MMA)	1.01	0.65 to 1.55	.98
VHA (post-MMA v pre-MMA)	0.79	0.54 to 1.15	.22

Abbreviations: ACE-27, Adult Comorbidity Evaluation 27; CRC, colorectal cancer; FFS, fee-for-service; HMO, health maintenance organization; IHN, integrated health network; MMA, Medicare Prescription Drug, Improvement, and Modernization Act of 2003; NSCLC, non-small-cell lung cancer; OR, odds ratio; ref., reference; SCLC, small-cell lung cancer; VHA, Veterans Health Administration.

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Table A4. Full Model With Cancer Stage Variables

Variable	OR	95% CI	P
MMA timing			
Pre-MMA (ref.)	1.00		
Post-MMA	0.70	0.57 to 0.86	< .001
Health plan			
FFS (ref.)	1.00		
IHN	1.21	0.96 to 1.52	.10
Regimen order			
First (ref.)	1.00		
Follow-up	0.28	0.24 to 0.33	< .001
Age at diagnosis (years)			
< 65 (ref.)	1.00		
65-74	0.69	0.58 to 0.83	< .001
≥ 75	0.46	0.37 to 0.57	< .001
Race/ethnicity			
White (ref.)	1.00		
Hispanic	0.73	0.52 to 1.01	.06
Non-Hispanic black	1.03	0.81 to 1.31	.83
Other	0.85	0.65 to 1.10	.21
Sex			
Male (ref.)	1.00		
Female	0.92	0.78 to 1.09	.32
Cancer stage (type)			
I-III (CRC; ref.)	1.00		
I-III (NSCLC)	1.22	0.96 to 1.54	.10
I-III (SCLC)	1.20	0.82 to 1.75	.34
IV (NSCLC)	0.69	0.55 to 0.86	< .001
IV (SCLC)	0.76	0.57 to 1.01	.06
IV (CRC)	1.49	1.08 to 2.06	.02
Comorbidity (ACE-27)			
None (ref.)	1.00		
Mild	0.91	0.74 to 1.12	.38
Moderate	0.86	0.67 to 1.10	.22
Severe	0.90	0.69 to 1.18	.44
New drug			
No (ref.)			
Yes	0.63	0.47 to 0.84	< .001
Interaction: MMA timing by health plan			
Overall interaction effect	1.42	0.89 to 2.28	.14
FFS (post-MMA v pre-MMA)	0.70	0.57 to 0.86	< .001
IHN (post-MMA v pre-MMA)	1.00	0.65 to 1.54	.99

Abbreviations: ACE-27, Adult Comorbidity Evaluation 27; CRC, colorectal cancer; FFS, fee-for-service; IHN, integrated health network; MMA, Medicare Prescription Drug, Improvement, and Modernization Act of 2003; NSCLC, non-small-cell lung cancer; OR, odds ratio; ref., reference; SCLC, small-cell lung cancer.

Fig A1. Log odds of receipt of regimen containing drugs affected by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (unstratified). Q, quarter.

Fig A2. Log odds of receipt of regimen containing drugs affected by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (stratified by health plan). FFS, fee-for-service; IHN, integrated health network; Q, quarter.