

Preventing chemotherapy-induced nausea and vomiting: the economic implications of choosing antiemetics

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Unfortunately, despite significant improvements in controlling acute emesis with first-generation serotonin receptor antagonists, recent population-based data show that both acute and delayed nausea and vomiting after emetogenic chemotherapy remain a concern for patients and healthcare providers. The needs of patients seen in community oncology practices vary, and the costs of delivering essential care to meet those needs also vary considerably. Given the profound changes in health-care reimbursement enacted in 2005 under the Medicare Modernization Act, we conducted an analysis of the economic and practice implications of choosing an antiemetic regimen for patients undergoing chemotherapy in this new reimbursement environment. Economic analyses of common oncology conditions and treatments can help community-based medical oncology practices examine and understand the effects of changing oncology reimbursement policies on the patient, payer, and provider. Such considerations may ultimately help us efficiently deliver the highest quality care possible to our patients.

Chemotherapy-induced nausea and vomiting (CINV) remains one of the most common side effects of chemotherapy and is usually cited by patients as one of the adverse effects they dread most.^{1,2} Recent data from chemotherapy-experienced women with ovarian cancer who have received multiple prior cycles of carboplatin or cisplatin plus paclitaxel-based chemotherapy indicate that they rank complete control of acute and delayed CINV near remission of their disease and perfect health. In marked contrast, these same chemotherapy-experienced patients rank poorly controlled acute or delayed CINV as a health state close to where they rank death.³ From the patients' perspective, recent studies also indicate that poorly controlled CINV interferes with their physical, emotional, cognitive, and role functioning.^{4,5}

Despite the improvements made over the past 14 years in controlling acute emesis with first-generation serotonin (5-HT₃) receptor antagonists, both acute and delayed CINV remain a substantial clinical problem. Grunberg and colleagues recently published population-based data indicating that on the day of moderately emetogenic chemotherapy, 13% of patients vomit and 37% of patients complain of nausea.⁶ Control of delayed CINV was even worse, with 53% of patients complaining of

nausea and 28% of patients vomiting.⁶ This population based-research is supported by other data demonstrating that despite compliance with the antiemetic guidelines of the Multinational Association of Supportive Care in Cancer or the American Society of Clinical Oncology, 50% of patients still experienced delayed CINV, even after adjustment for important prognostic factors of delayed CINV (namely, age, gender, emetogenic potential of the chemotherapy regimen, and the presence of acute CINV).^{7,8}

Economic considerations in CINV

Economic analyses of medical care need to explicitly indicate the perspective of the analysis.⁹ Important perspectives to consider in any economic analysis include those of the stakeholders. Typically, these perspectives include society, where a cost-

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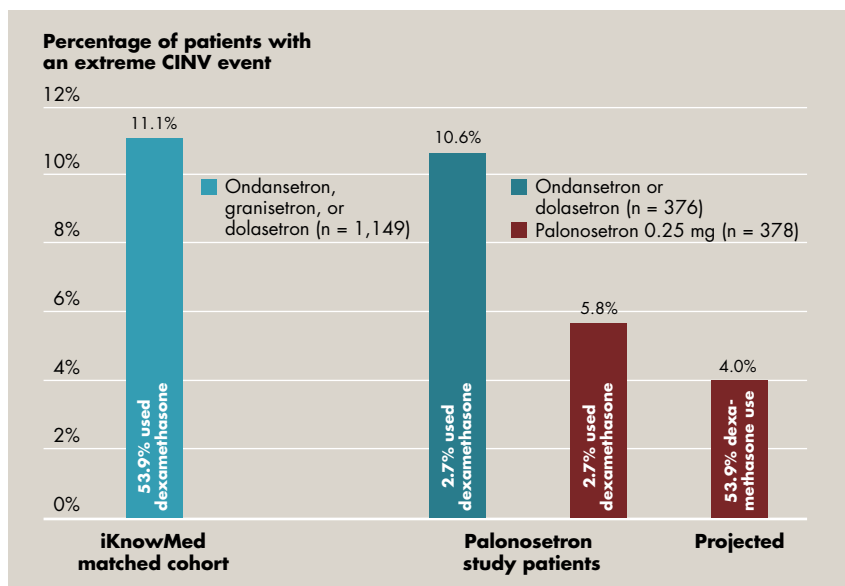


FIGURE 1 One in nine patients receiving a first-generation 5-HT₃ receptor antagonist has poorly controlled chemotherapy-induced nausea and vomiting (CINV) and consumes further healthcare resources. Use of palonosetron 0.25 mg reduces this extreme CINV event (see text for definition) by 48%–64%.

effectiveness analysis or cost-utility analysis is considered the gold standard; the payer perspective, which is commonly conducted from a cost-minimization perspective; and a patient perspective, which can be done using a willingness-to-pay methodology or a complicated cost-utility method with techniques such as a standard gamble or time trade-off approach. These perspectives and methods are beyond the scope of this report. Rarely is an economic analysis conducted from the perspective of one of the key stakeholders in the healthcare-industrial complex, that of the practicing physician who actually has an intimate and unique role in the delivery of healthcare.

Given the recent changes in healthcare reimbursement in the practice of medical oncology enacted in January 2005 under the Medicare Modernization Act, we undertook an economic analysis of one of the most common decisions made by office-based medical oncologists: the implications of choosing an antiemetic for patients receiving non-cisplatin, moderately emetogenic chemotherapy. This anal-

ysis was based, in part, on a recent presentation at a peer-reviewed poster session at the 2004 American Society of Health-System Pharmacists Mid-year Clinical Meeting, but updated using the new 2005 reimbursement system.

Study population

Vanscoy and colleagues presented a matched-case controlled analysis of 1,149 patients treated in the United States from 1999 through 2003, prior to the commercial introduction of palonosetron (Aloxi).¹⁰ Briefly, using the data from the pivotal phase III trials of palonosetron compared with either ondansetron (Zofran) 32 mg or dolasetron (Anzemet) 100 mg in patients receiving moderately emetogenic chemotherapy, they identified an oncology network (Matrix Oncology) using an electronic medical record (Oncology Metrics and iKnowMed) and created a cohort of controls after matching patients on cancer diagnosis, chemotherapy regimen, age, gender, prior chemotherapy experience, and the use of dexamethasone, as part of the

antiemetic regimen, on day 1 prior to chemotherapy.

The only variable in the matched cohort that was statistically different from the characteristics of the patients in the pivotal palonosetron phase III trials was the proportion of patients who received dexamethasone on day 1 prior to receiving moderately emetogenic chemotherapy. In the matched cohort, 53.9% received dexamethasone, compared with 2.7% of patients in the pivotal palonosetron trials ($P < 0.001$).

It was assumed that patients who experience nausea and vomiting at home but seek no further care are not considered to be an added expense to payers. Therefore, the investigators focused on patients who sought further care for poorly controlled symptoms, as this consequently impacts the labor expense for an oncologist's office and consumes further healthcare resources, ultimately impacting payers.

Defining an 'extreme CINV event'

Patients in the matched cohort were followed for the first 5 days after receiving moderately emetogenic chemotherapy for documentation in the electronic medical record of unscheduled visits or calls to the oncology practice for management of failed CINV prophylaxis, defined as an "extreme CINV event." These extreme CINV events included visits to the practice on days 2–5 post chemotherapy for intravenous or intramuscular rescue medication, reported nausea and vomiting coded as NCI-CTC (National Cancer Institute–Common Toxicity Criteria) toxicity grade 2 or higher, unscheduled hydration visits due to CINV, unscheduled office visits for evaluation or management of CINV, telephone calls to the practice with complaints of nausea and vomiting, or documented switching of outpatient antiemetics on days 2–5 after chemotherapy.

TABLE 1

Estimated labor time and costs

Task	Cost (\$)	Mean time (minutes)	Number of tasks (mean)	Number of staff (mean)
Extreme CINV event				
Phone service (call from patient)	28.02 ^a	14.08	3.3	1.25
Front desk	2.57 ^a	9.91	9.65	2.7
Phlebotomy	6.21 ^a	18.32	16.55	2.2
Laboratory	6.80 ^a	20.60	8.25	2.0
Nurse practitioner evaluation ^b	32.79 ^a	45.18	13.36	4.27
Level III/IV physician evaluation ^b	67.37 ^a	52.23	17.15	3.7
Triage	20.36 ^a	33.85	13.1	3.3
IV antiemetic rescue medication	30.87 ^a	59.29	18.17	2.3
Schedule	6.34 ^a	19.51	9.8	2.7
Billing	8.94 ^a	27.24	10.8	3.2
Dose-dense AC chemotherapy administration				
Front desk	2.57 ^a	9.91	9.65	2.7
Phlebotomy	6.21 ^a	18.32	16.55	2.2
Laboratory	6.80 ^a	20.60	8.25	2.0
Level III/IV physician evaluation	67.37 ^a	52.23	17.15	3.7
Triage	20.36 ^a	33.85	13.1	3.3
Chemotherapy	30.87 ^a	76.46	22.4	2.3
Schedule	6.34 ^a	19.51	9.8	2.7
Billing	8.94 ^a	27.24	10.8	3.2
Task summaries				
Extreme CINV Event Level III/IV physician evaluation and management ^b	193.44 ^c	255.03	93.25	9.95
Extreme CINV Event Nurse practitioner evaluation and management ^b	155.75 ^c	247.98	83.8	9.95
Dose-dense AC chemotherapy administration visit	163.00 ^c	258.12	84.95	9.15

AC = doxorubicin/cyclophosphamide; CINV = chemotherapy-induced nausea and vomiting

^aCost in 2003 US \$. ^bFor any given patient, service could be provided by either an advanced practice provider or a physician.

^cCost in 2005 US \$ based upon 2003 salaries from time-and-motion studies inflated to 2005 costs using Consumer Price Index–Medical rate of 4.4%.

As phone calls and office visits were not captured in the palonosetron phase III trials, an extreme CINV event, which would have triggered an office visit in the United States, was assumed based on patient diary reports. This created a linkage between the two data sets. Extreme CINV events were identified using daily diary nausea and vomiting data for patients in the phase III trial receiving palonosetron 0.25 mg, ondansetron 32 mg, or dolasetron 100 mg and were defined as either (1) patients

with severe nausea and more than two emetic episodes on any day and severe nausea the following day or (2) patients with more than five emetic episodes on any day and moderate or severe nausea the following day.

It was assumed that patients in the United States with this severity of CINV on days 2–5 after moderately emetogenic chemotherapy would, at a minimum, call their physicians office to report their problems with CINV. Based upon these definitions of extreme CINV events, Vanscoy

and colleagues reported that one in every nine patients (11.1%) receiving dolasetron, ondansetron, or granisetron (Kytril) prior to moderately emetogenic chemotherapy required further care for failed CINV prophylaxis (Figure 1).¹⁰ The rate of extreme CINV events, using the definition applied to the pivotal palonosetron phase III trials data, for ondansetron and dolasetron was similar (10.6%), indicating the validity of the two definitions of extreme CINV events. The rate of extreme CINV events for pa-

TABLE 2
Estimated costs and reimbursement

ICD-9 Code	Description	Labor or cost (\$)	Revenue (\$)
Management of Extreme CINV Event			
99213	Office visit	Labor	49.38
36415	Venipuncture	Labor	3.00
80048	Metabolic panel	Labor	9.64
G0345	Intravenous infusion 1 hour	Labor	64.80
G0346	Intravenous infusion each additional hour x 2	Labor	41.38
J7030	Normal saline, 1,000 cc	8.90	11.23
G0354	Intravenous push rescue antiemetic	Labor	27.71
Total			198.24 ^a
Administration of dose-dense AC chemotherapy			
G0359	Cyclophosphamide IV over 1 hour	Labor	177.61
G0358	Doxorubicin IV push	Labor	72.99
G0346	Intravenous infusion 1 hour	Labor	20.69
J7030	Normal saline, 1,000 cc	8.90	11.23
G0354	Intravenous push palonosetron	Labor	27.71
G0354	Intravenous push dexamethasone	Labor	27.71
G9021-9032	Demonstration project	Labor	130.00
99213	Established patient visit	Labor	49.38
Total			508.42 ^a

AC = doxorubicin/cyclophosphamide; CINV = chemotherapy-induced nausea and vomiting

^aNet revenue before deduction of labor costs

tients receiving palonosetron 0.25 mg was reduced to 5.8%—almost half the rate observed in patients treated with ondansetron or dolasetron (Figure 1). Vanscoy et al reported that if 53.9% of the palonosetron-treated patients had received dexamethasone on day 1, the improvement in complete response rate on day 1 would have reduced the extreme CINV event rate by 64% to 4.0%.¹⁰

Estimating impact on labor costs

To understand the impact of these extreme CINV events on operational efficiency and potential revenue of an outpatient oncology practice, we identified a network that used rigorous time-and-motion studies to establish a database of labor costs (Accelerat-

ed Community Oncology Research Network/Supportive Oncology Services). We asked them to estimate the amount of time it would take their employees to manage one of these extreme CINV events if the patient was entirely managed in the office. Since a finite labor pool cannot take care of two types of patients simultaneously, we also had them identify their labor costs for treating a patient with dose-dense doxorubicin/cyclophosphamide (AC) chemotherapy for breast cancer. This allowed a comparison of the labor costs and potential reimbursement for the same labor for two types of patients commonly seen in the community oncology setting. Labor costs were then inflated for 2004 and 2005 using the Consumer Price Index—Medical as estimated from the Bureau of Labor

Statistics Web site.¹¹ Reimbursement was estimated using national averages from the new Centers for Medicare & Medicaid Services (CMS) 2005 reimbursement system under the Medicare Modernization Act,¹² using G-codes and the CMS demonstration project (see page 132), thereby avoiding the variations from practice to practice associated with drug purchasing and reimbursement.

Results

Based on data from 20 community oncology practices, the estimated average labor time to manage an extreme CINV event was 255 minutes, which translated into approximately \$175 in labor costs (in 2005 dollars). For a typical patient with breast cancer receiving dose-dense AC chemotherapy, estimated labor time was 258 minutes, or \$163 in labor costs. Details of the time and labor costs by unit of service are shown in Table 1.

The database of labor costs was developed in 2003; therefore, the individual tasks display the actual time involved for the unit of service, and the costs reflect 2003 dollars. The summary costs were inflated to 2005 costs by using a 4.4% rate of inflation for 2004 and again for 2005, as described previously. For an average patient, we assumed 50% of the extreme CINV events were managed by an advanced practice nurse, at a cost of \$155.75 per event, and 50% by a physician, at a cost of \$193.44 per event—hence, the “average cost” of \$175.

The reimbursement for these two separate units of oncology service is detailed in Table 2. Using just Medicare G-codes for hydration, the typical laboratory tests ordered as part of the evaluation and management of a patient with cancer who has CINV with dehydration and a level III office visit lead to an average reimbursement of approximately \$198. In comparison, for about the same amount of labor time, the reimburse-

ment under CMS for 2005 for a patient receiving dose-dense AC is approximately \$508.

Net revenue for these two scenarios, after consideration of the labor costs involved, is \$23.24 for an extreme CINV event and \$345.42 for evaluation and treatment of an established patient with breast cancer receiving dose-dense AC chemotherapy, more than a 14-fold difference. This disparity is graphically depicted in Figure 2. It is important to note that this net revenue does not take into consideration other costs, such as rent, utilities, non-medical care items necessary to operate a medical oncology practice, and the revenue or loss from drug margins, in either scenario.

Discussion

It is well recognized that change in reimbursement policy is one of the most important factors that influence medical practice patterns and subsequent resource utilization. The Medicare Modernization Act has dramatically changed the reimbursement policies for the practice of medical oncology in the United States. How this will ultimately impact access to care, practice patterns, resource utilization, and overall costs of cancer care remains to be determined.

It is increasingly clear, however, that in order to run an efficient and sustainable delivery system for providing essential oncology care, community-based medical oncology practices will need to have a thorough understanding of their internal cost structures in delivering various types of oncology services. Patients are not uniform in their needs, and the costs of delivering essential care to meet those needs can vary considerably. As an example, a patient with breast cancer who is highly educated and has an excellent social support network does not necessarily cost the practice the same to manage as a similar patient, matched for stage and extent of disease, who has language transla-

tion needs, transportation needs, and a limited social network.

This analysis of costs and reimbursement for a common, day-to-day decision in the practice of medical oncology serves to illustrate how a medical oncology practice might want to begin to examine its internal cost structure and make data-based decisions about how to operate efficiently in today's environment. CINV is a preventable side effect in the majority of patients receiving emetogenic chemotherapy, and the introduction of newer antiemetics over the past 2 years has served to highlight the true incidence of acute and delayed CINV and the unmet need that existed with first-generation 5-HT₃ receptor antagonists. Managing extreme CINV events is not only of significant clinical and economic consequence for the patient but also can have adverse economic consequences for the oncology practice. Economic analyses of these common oncology conditions will need to be conducted from multiple perspectives, including the patient, payer, society, and provider. Hopefully, this analysis will invite others to continue to examine the effect of changing oncology reimbursement policies on all the stakeholders in community cancer care.

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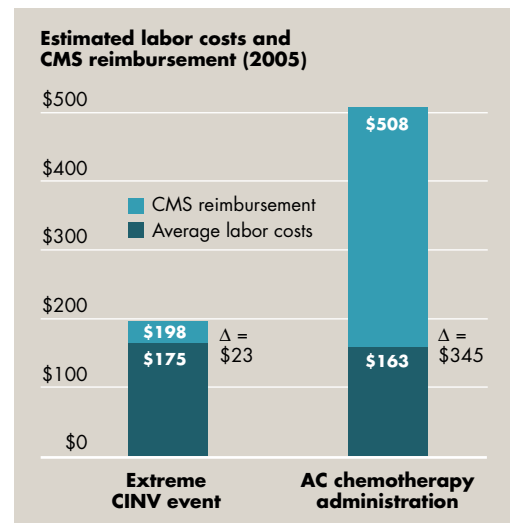


FIGURE 2 Net revenue for managing an extreme CINV event and dose-dense doxorubicin/cyclophosphamide (AC) chemotherapy. CINV = chemotherapy-induced nausea and vomiting; CMS = Centers for Medicare & Medicaid Services.

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