

Systemic Opioid Elimination After Implantation of an Intrathecal Drug Delivery System Significantly Reduced Health-Care Expenditures

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Objective: To compare health-care expenditures over a 12-month horizon for chronic pain patients with implanted intrathecal drug delivery systems (IDDS) who eliminated or continued systemic opioids postimplant.

Methods: Claims data from commercial and Medicare databases were searched for patients who had an IDDS, used systemic opioids before implant, and had 12 months pre- and 13 months postimplant continuous medical and pharmacy coverage. The number and characteristics of patients who eliminated or continued systemic opioids were determined at four times postimplant: 30 days (allowing a systemic opioid washout period), 120 days, 150 days, and 210 days. Multivariable models evaluated the effect of eliminating opioids on health-care expenditures at each of those times.

Results: Three hundred eighty-nine patients met inclusion criteria, and 51% completely eliminated systemic opioids (12% within the 30-day washout and an additional 39% by the end of the one-year horizon). Systemic opioid elimination within 120 to 210 days postimplant was associated with a reduction of \$3,388 to \$4,465 in inpatient and outpatient expenditures, and \$4,689 to \$5,571 in inpatient, outpatient, and drug expenditures.

Conclusions: Fifty-one percent of patients completely eliminated systemic opioids in the year after IDDS implant. This elimination resulted in a 10% to 17% reduction in yearly inpatient, outpatient, and drug expenditures.

Keywords: Chronic pain, database review, health-care expenditure, intrathecal drug delivery, opioid

Conflict of Interest: Dr. Hatheway consults for and has received honoraria for speaking engagements and travel from Medtronic, plc. Dr. Hatheway has not received any honoraria, consulting, nor travel in relation to this project. Dr. Hatheway is also a speaker for Insys Pharmaceuticals. Dr. Caraway has served/serves on the Scientific Advisory Board for Medtronic, plc. and Spinal Modulation. Dr. Caraway is an employee of Nevro Corp. Dr. Caraway consults for Medtronic, plc. and Jazz Pharmaceuticals and has received honoraria for speaking engagements and research. Dr. Caraway has not received any honoraria, consulting, nor travel in relation to this project. Dr. David is an academic affiliate of CTI Clinical Trial and Consulting Services, who is consulting for Medtronic, plc. Candace Gunnarsson is an employee of CTI Clinical Trial and Consulting Services, which is a paid consultant to Medtronic, plc., the study sponsor. Jennifer Hinnenthal is an employee of Medtronic, plc and owns stock in the company. Amanda Ernst is an employee of Medtronic, plc and owns stock in the company. Dr. Saulino has served on a speakers bureau, received research grants and fellowship support from Medtronic plc. Dr. Saulino has not received any honoraria, consulting, nor travel in relation to this project.

INTRODUCTION

At least 100 million Americans suffer from chronic pain, more than the number affected by cancer, diabetes, and heart disease combined (1). The Institute of Medicine estimated that the incremental annual cost of health care due to pain ranged from \$560 to \$635 billion in 2010 U.S. dollars (2). Medical management of chronic pain usually begins conservatively with over-the-counter and prescription medications, including systemic opioids. Unfortunately, systemic opioid use can be complicated by inadequate analgesia, intolerable side-effects (3,4), opioid-induced hyperalgesia (5), rapid dose escalation, misuse, diversion, addiction, and overdose (6).

In 1991, the Food and Drug Administration (FDA) approved a concentrated form of morphine (Infumorph® Sterile Solution, Baxter Healthcare Corp., Deerfield, IL, USA) specifically developed for intrathecal administration via a continuous microinfusion device. Intrathecal drug delivery (IDD), as part of a pain management continuum,

provides an alternate route of opioid administration. Rather than widespread systemic distribution of drug with activity at undesired peripheral mu receptors, IDD targets the physiologically relevant

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spinal dorsal horn mu receptors. For this reason, IDD is often referred to as targeted drug delivery (TDD). TDD has been used successfully in long-term pain management for patients with failed back syndrome, complex regional pain syndrome, spinal stenosis, cancer pain, osteoporosis with compression fractures, and peripheral neuropathies (7). Inherent in the development of an IDD system (IDDS) was the assumption that it delivers drug(s) in a more effective manner, allowing for the elimination or dramatic reduction of systemic medications (such as oral opioids or transdermal patches) after implantation and dose titration. However, in clinical practice intrathecal delivery of morphine sulfate has been used both as a sole agent and an adjuvant route of opioid administration.

We analyzed aggregated health-care expenditures over a one-year time horizon for chronic pain patients with IDDS by comparing those patients who completely eliminated systemic opioid use within 30, 120, 150, or 210 days postimplant with those patients who continued to use any amount of systemic opioids as an adjuvant to intrathecal delivery. The FDA-approved indications for IDDS include the chronic epidural/intrathecal infusion of Infumorph (preservative-free morphine sulfate sterile solution) for chronic intractable pain or Prialt® (ziconotide intrathecal infusion; Jazz Pharmaceuticals, Inc., Dublin, Ireland) for severe chronic pain.

METHODS

We analyzed data from the Truven Health MarketScan® Commercial Claims (Truven Health Analytics Inc., Ann Arbor, MI, USA) and Medicare Supplemental Databases for the years 2008 to 2011. The databases include records from more than 170 million unique patients enrolled since 1995 in employer-sponsored and public health insurance plans, and capture claims from hospital stays, outpatient visits, and pharmacies. These databases are nationally representative and include data from 150 employers and 21 health plans, representing 130 unique carriers. All of the databases were fully HIPAA compliant, and extracted data and planned analyses were deemed exempt from review by the New England Institutional Review Board (exemption #14–243).

Patients were identified for inclusion if they had: 1) a record of a complete IDDS implantation (pump and catheter) on the same service date; 2) a record of systemic opioid use prior to implant; and 3) 12 months pre- and 13 months postimplant continuous health plan and pharmacy enrollment. Patients were excluded from the analysis if they had: 1) a diagnosis of cancer at any time during the study period; 2) a diagnosis of spasticity on the implant date; or 3) a record of IDD-related procedures in the year before implant.

Defining Opioid Elimination

We counted the number and calculated the percent of patients who eliminated/continued systemic opioids during the study. Systemic opioid discontinuation was determined by identifying applicable prescription claims including medication type, dosing, and number of days' supply. Elimination was signaled by the patient's last systemic opioid prescription or refill from the claims data, with elimination recorded on the first day after that prescription supply ran out. By this definition, patients who decreased their systemic opioid intake but had not completely eliminated their use of systemic opioids were included in the "continued" group for the health-care expenditure multivariate analysis.

For the multivariate analysis, discontinuation was evaluated at four different times: 1) up to 30 days (considered a washout period

for systemic opioids prescribed before implant or after implant for procedure pain); 2) 120 days postimplant (washout + 90 days); 3) 150 days (washout + 120 days); and 4) 210 days (washout + 180 days). If a patient's last systemic opioid prescription ran out on day 100 postimplant, that patient would be counted as using systemic opioids at 120 days but as having eliminated systemic opioids at 150 and 210 days. Patients who had an additional systemic opioid refill within 60 days after the study period (washout + 365 days) were censored to 365 days.

Defining Expenditures

The dependent variable was a patient's total health-care expenditures over a one-year time horizon measured in two different ways: 1) inpatient and outpatient expenditures only; and 2) inpatient, outpatient, and drug expenditures. Inpatient and outpatient expenditures for both groups included office visits, radiology, laboratory tests, etc. When aggregating a patient's expenditures, the one-year (365 days) time horizon did not start until after the 30-day, postimplant washout period.

Statistical Analyses

To investigate the effect of eliminating systemic opioids on yearly health-care expenditures, costs for patients who eliminated or continued systemic opioids at 30 days, 120 days, 150 days, and 210 days were compared using cross-sectional multivariable models. We controlled for a number of important potential confounders. The first was expenditures preintervention, including inpatient and outpatient expenditures, with or without drug expenditures, during the 12 months before implantation. We included two Current Procedural Terminology (CPT) codes associated with IDDS trials, the first for bolus injection (CPT 62311) and the other for indwelling-catheter, continuous infusion (CPT 62319) of diagnostic or therapeutic substances (8). Medicare requires a catheter trial as a condition of reimbursement. In addition we controlled for a number of patient demographics, including patient age group (ages 0–29, 30–39, 40–49, 50–59, 60–69, 70–79, 80 years and older), gender, census region (Midwest, Northeast, South, and West), and a diagnosis of sleep apnea. Obstructive sleep apnea has been linked with increased vulnerability to the respiratory-depressant effects of opioids (7). Exploratory analyses of other comorbidities and the type of prescribing physicians indicated that they had little effect, given the limited sample size and numerous variables under consideration.

Regression models took the following form:

$$Exp_{i,post} = \alpha + \beta_1 \cdot Early_i + \beta_2 \cdot Exp_{i,pre} + \beta_3 \cdot CPT_i + \beta_4 \cdot X_{i,pre} + \varepsilon_i$$

where the dependent variable, $Exp_{i,post}$ is health-care expenditure in the 12 months postimplant; the variable of interest is $Early_i$, with β_1 being the coefficient of interest; $Exp_{i,pre}$ is health-care expenditure in the 12 months presurgery; CPT_i are the two CPT codes; and $X_{i,pre}$ is a vector of patient demographics including age group, region, gender, and a diagnosis of sleep apnea. Analyses were conducted using Stata® MP/12 software (StataCorp LP, College Station, TX, USA), and a P value of ≤ 0.05 was considered statistically significant.

RESULTS

The databases included 94,145,711 possible patients; 5,205 with a record of IDDS-related procedures were initially identified, 389 of

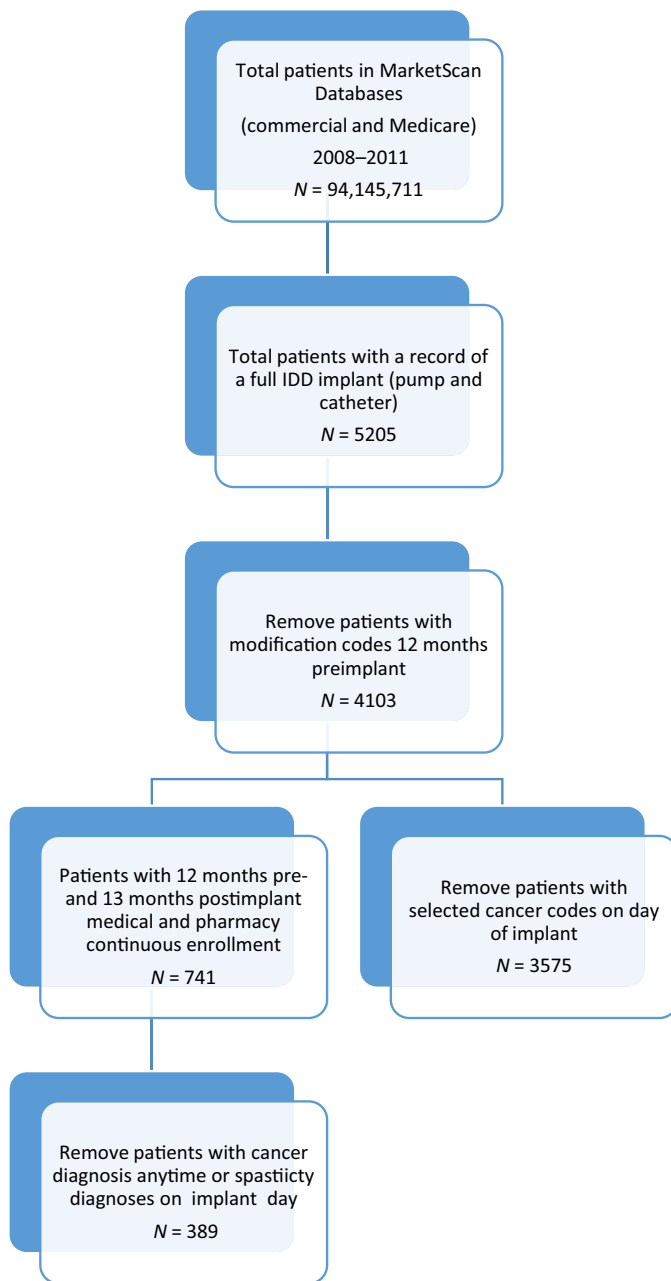


Figure 1. Database search strategy.

whom met all of the inclusion criteria and had complete records pre- and postimplant (Fig. 1). Of the 389 patients who met the inclusion criteria and had complete records, 51% completely eliminated systemic opioid usage postimplant; 12% eliminated systemic opioids within the 30-day washout period, and an additional 39% did so at various times throughout the one-year time horizon. The remaining 49% of patients continued using systemic opioids postimplant. Figure 2 graphs patient discontinuation of opioids after implant (day 0) for one year from the end of the washout period (30 days).

Table 1 provides summary statistics for dependent and control variables. The table summarizes the number and percentage of patients who eliminated/continued systemic opioids at each time for each variable. At the end of the 30-day washout, 46 of 343 patients (12%) had eliminated systemic opioids. At 120 days a

cumulative 70 of 319 patients (18%) had eliminated systemic opioids. At 150 days a cumulative 74 of 315 patients (19%) had eliminated systemic opioids. At 210 days a cumulative 82 of 307 patients (21%) had eliminated systemic opioids.

Table 2 summarizes the results from the multivariable analysis. The baseline one-year health-care expenditures after washout, controlling for all procedure and patient variables previously described, varied between \$30,700 and \$32,168. Since some patients had missing records for drug expenditure, the sample for this measure shrunk from 389 patients to 363 patients. This helps explain why, in some cases, average health-care expenditures with drugs were lower than expenditures without drugs.

The economic effects of eliminating systemic opioids during the washout period were small and not statistically significant (Table 2). Eliminating systemic opioids within 120, 150, or 210 days postimplant was associated with savings of \$3,388 to \$4,465 in inpatient and outpatient expenditures, a 10% to 14% reduction. When pharmacy expenditures were added to the inpatient and outpatient expenditures, savings ranged from \$4,689 to \$5,571, a 14% to 17% reduction. Patients who eliminated systemic opioids had significantly lower total yearly expenditures (inpatient/outpatient/drug) than those who continued at 120, 150, and 210 days.

The full regression analyses indicated that patients who eliminated systemic opioids postimplant appeared more likely to be in the 30–39 years or the >80 years age groups and far less likely to be in the 50–59 years age group. They also were more likely to reside in the Midwest and less likely to reside in the South or West, and more likely to have a diagnosis of sleep apnea.

DISCUSSION

Health-Care Utilization

Patients in our database sample, not surprisingly, were high users of health care. Their constant annual costs (ranging from \$30,700 to \$32,740; Table 2) were approximately three times the age-adjusted annual health-care expenditure per person in the U.S. in 2012 (approximately \$11,660 for the age distribution of our sample) (9). Gore et al. documented health-care costs that were significantly higher ($p < 0.0001$) in patients with pain than those without (10). They studied the clinical comorbidities, treatment patterns and health-care costs of patients with chronic low back pain, and found that estimated annual direct medical costs were $\$8,386 \pm \$17,507$ in the chronic pain group compared with $\$3,607 \pm \$10,845$ in the control group without chronic pain. The higher costs were attributed to greater resource utilization, primarily pharmacotherapy (including opioids). Best practices in IDD call for eliminating systemic opioids if possible, or reducing them by at least 50% if elimination is not feasible (11). To the extent that this recommendation is implemented, it will lower the costs of IDD therapy. Indeed, the savings of systemic opioid elimination by 120, 180, and 210 days postimplant were significant in our study.

Cost of IDD vs. Conventional Pain Management

Because conventional systemic pharmacotherapy is noninvasive and reversible, it has typically been considered earlier in the pain-treatment continuum than IDD. Certainly the initial cost of implantation is higher than the cost of instituting pharmacotherapy. Yet a recent retrospective database analysis of 555 noncancer pain patients who received an IDDS found that it was less costly than conventional pain therapy (12). Costs in the year following implantation were \$17,317 more per patient than conventional

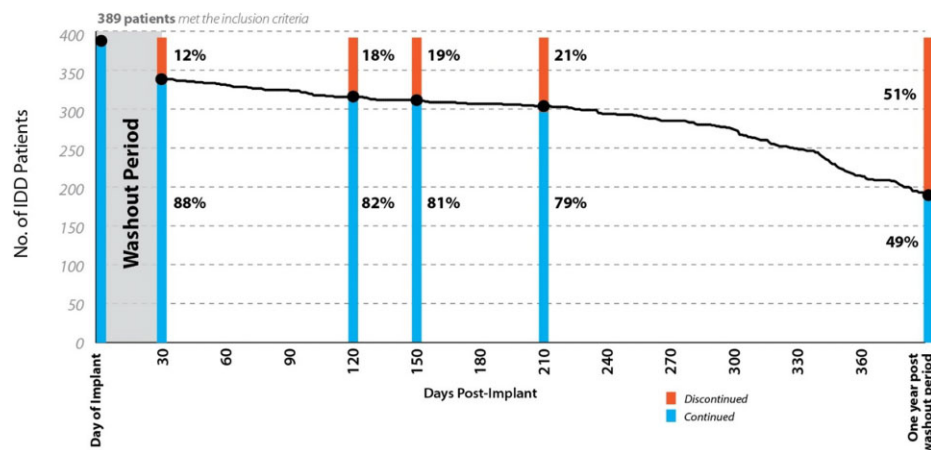


Figure 2. Patients who continued or eliminated systemic opioids after implantation of an intrathecal drug delivery system (IDDS). The number of patients who continued any amount of systemic opioids after IDDS implantation steadily decreased over the study period. A year after the washout period, 51% of patients had eliminated systemic opioids and 49% of patients continued taking systemic opioids. Reprinted with the permission of Medtronic, Inc. © 2014.

Table 1. Summary Statistics for Patients Who Eliminated/Continued Systemic Opioids Within 210 Days After Implantation of an Intrathecal Drug Delivery System (% or U.S. Dollars [SE]).

	30 days		120 days		150 days		210 days	
	Eliminated	Continued	Eliminated	Continued	Eliminated	Continued	Eliminated	Continued
No. of patients (%)	46 (11.8)	343 (88.2)	70 (18)	319 (82)	74 (19)	315 (81)	82 (21.1)	307 (78.9)
Female, %	65.2	58.6	57.1	59.9	58.1	59.7	58.5	59.6
Age in years, %								
<30	2.2	1.4	1.5	1.6	1.3	1.6	1.3	1.6
30–39	6.5	5.5	7.1	5.3	9.4	4.8	9.7	4.6
40–49	17.4	16.9	18.6	16.6	17.6	16.8	18.3	16.6
50–59	15.2	30.9	20.0	31.0	20.3	31.1	19.5	31.6
60–69	26.1	22.2	22.8	22.6	23.0	22.5	20.7	23.1
70–79	21.7	15.2	18.6	15.4	17.6	15.6	20.7	14.7
>80	10.9	7.9	11.4	7.5	10.8	7.6	9.8	7.8
Type of trial, %								
Bolus (CPT 63211)	50.0	53.9	42.9	55.8	41.9	56.2	43.9	56.0
Continuous (CPT 62319)	23.9	35.3	27.1	35.4	25.7	35.9	29.3	35.2
Census region, %								
Midwest	45.7	29.2	41.5	28.9	41.9	28.5	36.6	28.3
Northeast	4.3	5.8	7.1	5.3	6.7	5.4	7.3	5.2
South	41.3	48.1	41.4	48.6	41.9	48.6	40.2	49.2
West	8.7	16.9	10.0	17.2	9.5	17.5	15.9	17.3
Sleep apnea diagnosis, %	15.2	10.8	17.1	10.0	17.6	9.8	15.8	10.1
Pretreatment inpatient/outpatient expenditures	\$17,775 [27,078]	\$24,877 [34,564]	\$17,998 [27,329]	\$25,362 [34,974]	\$18,047 [26,727]	\$25,444 [35,161]	\$17,413 [25,765]	\$25,806 [35,484]
Pretreatment inpatient/outpatient/drug expenditures	\$22,324 [29,657]	\$32,847 [38,483]	\$23,558 [29,310]	\$33,378 [39,095]	\$23,252 [28,731]	\$33,545 [39,247]	\$22,601 [27,860]	\$33,992 [39,569]
Posttreatment inpatient/outpatient expenditures	\$19,632 [13,004]	\$21,386 [18,560]	\$17,717 [12,748]	\$21,938 [18,876]	\$17,691 [12,475]	\$21,997 [18,976]	\$17,069 [12,337]	\$22,276 [19,085]
Posttreatment inpatient/outpatient/drug expenditures	\$19,822 [10,583]	\$22,001 [18,621]	\$17,481 [10,957]	\$22,620 [18,925]	\$17,499 [10,718]	\$22,684 [19,028]	\$16,916 [10,709]	\$22,968 [19,143]

management, but financial break-even occurred soon after the second year postimplant. In the lifetime analysis, projected over a 30-year horizon, IDD saved \$3,111 per patient annually compared to conventional management.

Kumar et al. came to a similar conclusion over a decade ago in their study of 67 patients with failed back syndrome who were treated with IDD ($N = 23$) or conventional pain therapy ($N = 44$) (13). Actual cumulative costs for IDD over a five-year period were CAN \$29,410 vs. \$38,000 for conventional pain therapy. The initial costs of IDD equipment were recovered by 28 months postimplant. The same group updated their economic analyses in 2013 and calcu-

lated that total costs were CAN \$61,442 for IDD and \$48,408 for conventional management over ten years (14). They determined the incremental cost-effectiveness ratio (ICER), which compares costs and health outcomes of two therapies. The IDD ICER was \$11,326 per quality-adjusted life year (QALY) gained. The probability of IDD being a cost-effective alternative to conventional management was 50% and 84% at willingness-to-pay (WTP) thresholds of \$14,200 and \$20,000, respectively. IDD fell well below the WTP threshold which, in the United States, typically ranges from \$50,000 to \$100,000/QALY; beyond that threshold, therapies are considered not to be cost-effective.

Table 2. The Economic Effect of Eliminating Systemic Opioids on Expenditures Within Seven Months of Implantation of an Intrathecal Drug Delivery System[†] (U.S. Dollars [SE]).

	Inpatient/outpatient expenditures				Inpatient/outpatient/drug expenditures			
	30 days	120 days	150 days	210 days	30 days	120 days	150 days	210 days
Reduction in expenditures	-478.4 [2,104]	-3,388* [1,935]	-3,577* [1,922]	-4,465** [1,861]	-1,383 [1,977]	-4,689** [1,869]	-4,782** [1,886]	-5,571*** [1,832]
Aggregated yearly expenditures	30,700*** [7,515]	31,761*** [7,704]	31,899*** [7,719]	32,168*** [7,763]	31,263*** [7,680]	32,415*** [7,882]	32,559*** [7,901]	32,740*** [7,939]
No. of patients	389	389	389	389	363	363	363	363
R-squared	0.091	0.096	0.097	0.101	0.102	0.11	0.111	0.116

[†]Multivariable model controlled for age, gender, census region, preimplant expenditures, type of intrathecal drug delivery trial (CPT 62311 or 62319), and diagnosis of sleep apnea.

Robust standard errors in brackets; * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$.

Successful IDD requires physician training, regular monitoring, and continuing management (11), all of which are associated with inherent cost. These studies, however, demonstrate that IDD has the potential to reduce longitudinal costs compared with conventional pharmacotherapy. Eliminating systemic opioids could lower the long-term costs of IDDS still further.

Opioid Elimination Studies

Patient safety also argues in favor of eliminating systemic opioid use after initiating IDD. Small, targeted intrathecal doses are associated with less drug-related toxicity than systemic opioids (15), whereas concomitant use of systemic opioids and IDD increases the risk of both morbidity and mortality (16). The elimination of systemic opioids after IDDS implantation also maintains the therapy under physician control, potentially reducing the chances of non-compliance, diversion, or abuse.

The multicenter National Outcomes Registry for Low Back Pain prospectively collected data on 166 patients enrolled by 36 physicians between February 1999 and February 2000. Of these patients, 136 were implanted after trial and 72 were available at one-year follow-up (17). At six months, 65% ($N = 108$) of IDD patients had decreased or discontinued their use of systemic opioids, and at 12 months 42% ($N = 75$) had done so. At 12 months more than 65% of patients had an Oswestry Disability Index score decrease of at least one level, 80% were satisfied with their therapy, and 87% said they would undergo the procedure again for the same results.

So why do some patients continue on systemic opioids after IDDS implantation? Many clinicians worry that opioid taper and discontinuation will be unacceptable to patients with chronic pain. Only recently has the peer-reviewed literature included protocols for systemic opioid elimination and analysis of the results. A retrospective chart review of 99 consecutive patients demonstrated that systemic opioids were required by 90% of this cohort prior to implantation but the percentage fell to 32% by one month postimplant, and only 16% required any systemic opioids at one year postimplant (18). The patients were told in advance that the goal of IDD is pain relief as well as functional improvement. They learned that the IDDS is an alternate route of delivery for pain medication, and they agreed to try to discontinue systemic opioids or the IDD trial would not proceed. To treat breakthrough pain, the myPTM[®] Personal Therapy Manager (Medtronic Inc., Minneapolis, MN) facilitated patient-activated dosing, within physician-set limits.

Other studies of TDD have employed different pre- and postimplant systemic opioid management protocols. In a prospective study of 61 consecutive patients with a three-year follow-up, patients were told that daily systemic opioid use would be eliminated before and restricted following IDDS implantation (19). They were gradually weaned off 50% of their oral opioids over three to five weeks before trial. After a successful trial they continued to wean off *all* oral opioids over an additional three to five weeks, and remained opioid-free for seven to ten days before pump implantation. The intrathecal opioid dose at six months was 1.4 morphine equivalent/day and remained virtually unchanged for 36 months. Oral opioid use at three months averaged 3.8 mg morphine equivalent/patient/day, significantly less compared with an average daily dose of 126.7 mg before the IDDS trial. The oral opioids used after implant were not used daily, and allowed patients a sense of control according to the authors. A similar sense of control has been reported for TDD patients who have access to the myPTM system (20,21). Patients in the three-year study achieved clinically significant improvements in pain, mood, function, enjoyment, and perceived global improvement that persisted throughout the study (19). Side-effects, including wound infection, pruritus, peripheral edema, and seroma, were mild, likely due to the lower doses of both systemic and intrathecal opioids after implantation.

A smaller study of 22 patients included systemic opioid taper and a five-week opioid-free period before trial (22). Following a successful IDDS trial during week 6, patients remained opioid-free for 10 to 14 days before permanent implantation and never resumed systemic opioid therapy thereafter. A year after implantation the mean visual analog scale (VAS) for pain was significantly lower (7.3 ± 1.9 before opioid taper, 7.15 after opioid-free period, and 3.9 ± 2.6 a year postimplant), and function, evaluated by physical and occupational therapists, had improved. In addition, analgesia was maintained with microgram doses, with a dose-response relationship for effective analgesia of $\leq 400 \mu\text{g}$ intrathecal morphine; most patients achieved analgesia with doses in the 100 to 200 μg range. These lower effective doses would be expected to enhance patient safety.

Taken together, these studies suggest that opioid elimination after IDDS implantation not only reduces expenditures but also can be accomplished in a wide variety of patients with chronic pain from varied etiologies while maintaining pain relief, improving function, enhancing patient safety, and achieving patient satisfaction.

Strengths and Limitations of This Study

By contrast to the single-center studies with small numbers of patients, the current analyses draw on large, national, multicenter databases that reflect diverse patient demographics (census region, age, gender) and pain etiologies, many types of treating physicians, various systemic opioid management protocols, and a variety of public or private insurance plans. Still, 51% of the patients completely eliminated systemic opioid use in the first year after implantation, and total expenditures were significantly lower for those patients who did. The mechanisms behind these significant reductions were not addressed in our study but should be considered for future research, especially if a larger sample size can be obtained. They may be attributed to a reduction in utilization across all sites or specific sites, as well as a reduction in intensity of care (e.g., fewer procedures).

The study had a number of limitations. It is crucial to note that the focus of this study was not to conduct a cost-benefit analysis for TDD vs. conventional medical management. That would have required a matched group of patients without IDDS, and analysis of additional clinical and financial benefits beyond the ones stemming from opioid discontinuation. Instead, we studied TDD patients pre- and postimplant and examined only their systemic opioid elimination/continuation, not their decreases in systemic opioid use. It is probable that within the 49% of patients who continued systemic opioids postimplant there was a sizable subgroup that decreased but did not completely eliminate systemic opioid usage. Moreover, there was no way to determine what systemic opioid tapering protocols, if any, the treating physicians may have used. Elimination was not confirmed by urine testing, so some patients in the opioid-elimination groups may have obtained and used systemic opioids. In addition, patients who had health-care coverage but paid cash for their medications had no pharmacy claims, and may have been included in the elimination groups. For patients in the continuation groups, we may have missed the individual benefits of decreasing systemic opioids, although the lower cost of less medication was captured in the economic analysis. In addition, the study did not determine which intrathecal medications were used, the means by which systemic opioid elimination saved money, or whether pain severity had an effect on opioid elimination or continuation.

CONCLUSIONS

Among chronic pain patients with an implanted IDDS, 51% eliminated systemic opioids by one year after washout. Systemic opioid elimination within 120, 150, or 210 days postimplant was associated with a 10% to 17% reduction in total yearly expenditures. Total estimated savings ranged from \$3,388 and \$4,465 in inpatient and outpatient expenditures, and from \$4,689 and \$5,571 in inpatient, outpatient, and drug expenditures. Given the enormous personal and societal burden of chronic pain, the quality-of-life, safety, economic, and public health incentives for eliminating or decreasing systemic opioid use deserve consideration.

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Authorship Statements

Dr. John Hatheway, Dr. David Caraway, and Dr. Michael Saulino provided input into the research design, interpreted data, critically reviewed and edited the paper, ensured the research and data were clinically relevant, and approved the final version. Dr. Candace Gunnarsson contributed to the design and interpretation of the study as well as drafting and critical review of the manuscript. Dr. Gunnarsson had complete access to the data and approved the final manuscript. Jennifer Hinnenthal provided input into the research design, interpreted the data, critically reviewed/edited the paper and approved the final version. Dr. Guy David contributed to the design, analysis, and interpretation of the study as well as drafting and critical review of the manuscript. Dr. David had complete access to the data and approved the final manuscript. Amanda Ernst provided input into research design, helped coordinate the analysis, interpreted analyzed data, edited and critically reviewed the paper, and approved the final version. Medtronic provided funding to the vendor for data analysis and to the medical writer for technical writing. All authors contributed significantly to the publication and approved the final content.

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COMMENTS

My fundamental concern about the results described is that, while cost savings and eventual recoupment of implant costs are demonstrated for 51% of the patients involved, there are 49% of

patients who get implanted and don't reduce their opioid intake. From a health system perspective this means that any cost savings from a "successful" implant is taken up by the unsuccessful implants and thus the ITP therapy is demonstrated to not be cost effective, overall. The study looks at a wide variety of diagnoses and treatments (in that the infusates used were not uniform) and most likely the means of determining who was an appropriate candidate for implantation in the first place. I believe it would be a stronger paper if some characteristic of pre-implant success could be identified or at least a stronger call was made for more rigorous screening so as to minimize the number of "unsuccessful" implants.

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Studies as these are extremely important in determining outcomes for patients in many cases. It seems as though multiple avenues have been pursued with the manuscript as far as determining the cost for the healthcare systems and insurance companies. Chronic pain has become such a societal problem, as far as costs go; many of these invasive treatments with little determined outcomes based data are becoming less and less approved by insurance companies. Studies such as these provide physicians in the academic and private sector the potential evidence that such treatments are a good option for patients in chronic pain.

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Comments not included in the Early View version of this paper.