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Original Research Article

Systemic Opioid Prescribing Patterns and Total Cost of Care in Patients Initiating Spinal Cord Stimulation Therapy: A Retrospective Analysis

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Abstract

Background. Few studies have evaluated patterns of systemic opioid use among patients initiating spinal cord stimulation therapy for chronic pain. This study evaluated systemic opioid discontinuation and/or dose reduction and total health care cost after the start of spinal cord stimulation therapy. **Methods.** Using a commercial insurance claims database (2008–2017), we analyzed opioid utilization patterns in patients initiating spinal cord stimulation therapy over a 1-year baseline and 2-year follow-up. The primary end point was defined as either discontinuation ($\geq$365-day gap between prescription fills or total days' supply in follow-up $\leq$30 days) or $\geq$50% reduction in average daily morphine milligram equivalent dose. "Costs" were defined as total payer plus patient out-of-pocket payments. **Results.** A total of 5,878 patients met the selection criteria. Of these, 152 (2.6%) showed no opioid prescription data at any point in the study period. Among patients with one or more prescriptions, 42.0% met the primary end point (22.0% discontinued, and 20.0% reduced their dose by 50% or more). Mean total adjusted costs were significantly reduced in years 1 and 2 of follow-up relative to baseline (excluding device insertion costs). The average time to breakeven when accounting for device trial and permanent insertion cost was 3.1 years among those who met the composite end point and 4.2 years among those who did not. **Conclusions.** This analysis shows that among patients who continued spinal cord stimulation therapy for at least 2 years, a significant proportion were able to reduce and/or discontinue systemic opioid use, with costs after the start of therapy significantly reduced relative to baseline.

Key Words: Spinal Cord Stimulation; Opioids; Discontinuation

Introduction

Prescription opioid misuse, opioid use disorder, and opioid overdose have grown to epidemic levels in the United States. In 2018 alone, 67,367 deaths in the United States were attributed to opioid overdose, accounting for more than two thirds of all drug overdose deaths [1]. In an effort to mitigate this epidemic, the U.S. Centers for Disease Control (CDC), Department of Veterans Affairs, Department of Defense, American Pain Society, and American Academy of Pain Medicine have released guidelines for safe opioid prescribing. These guidelines share similar recommendations, emphasizing a shift toward pharmacological and nonpharmacological alternatives for chronic pain and tasking providers to carefully

weigh the specific clinical risks and benefits of systemic opioids before prescribing [2–4].

Spinal cord stimulation (SCS) is a nonpharmacological pain management option for control of chronic, intractable pain of the trunk or limbs [5–13]. Although several prior studies have shown a significant correlation between SCS therapy and a reduction in the use of systemic opioids, these findings were generally included as secondary or exploratory end points and also provided insufficient information on how opioid use data were collected [5–13].

Thus, although SCS therapy represents a promising avenue for reducing reliance on opioid analgesia for chronic, intractable pain, the current supporting evidence is of limited quality. The present study evaluated systemic opioid discontinuation and/or dose reduction among patients who initiated SCS therapy, without explantation, in a large, nationally representative dataset of commercial insurance claims. Furthermore, we evaluated the economic impact, from a payer and patient perspective, of initiating SCS therapy.

Methods

Study Overview

This was a retrospective analysis of health care claims data from the IBM Truven MarketScan® Research Databases. We identified patients with chronic, non–cancer-related pain who were newly implanted with an SCS device and with no evidence of a device explantation procedure. Systemic opioid dosing, medical resource use, and payer costs were summarized from 1 year before the start of SCS through 2 years' follow-up.

Data Source and Study Ethics

These research databases include de-identified, patient-level health care claims information on more than 135 million patients, or approximately 40% of the U.S. population, inclusive of information from approximately 100 self-insured employers and 12 commercial health plans nationally. These databases include information on medical claims (services rendered in an inpatient or outpatient setting), pharmacy claims, basic patient demographics, and plan enrollment information. Health care encounter information is reported with *International Statistical Classification of Diseases* (ICD)–9 and –10 diagnosis codes and procedure codes, current procedural terminology procedure codes, and medication national drug codes. Pharmacy prescription-level details include the number of units, days' supply, strength, and route of administration. All information in this data source is based on formal diagnosis and procedure codes listed on a medical visit claim or National Drug Code on a pharmacy prescription fill billed to a payer. Therefore, patient-reported outcomes such as pain and functional status were not captured. Because the database is a de-identified, closed system of administrative claims and is compliant with the Health Insurance Portability and Accountability Act (HIPAA), this study did not require Institutional Review Board approval. A data analysis and statistical analysis plan was written and agreed to by all authors before study execution.

Patient Selection

We identified all patients in the database with a record of SCS generator implantation and lead insertion during the same visit between 2009 and 2015, which allowed for a full 1-year baseline and 2-year follow-up (2008 as the first baseline year and 2016–2017 as the last follow-up years). We restricted analyses to include patients 18 years of age and older, with no history of prior permanent SCS implantation, no SCS removal procedure in follow-up (defined as the presence of a facility or physician procedure code for both generator and lead removal during the same visit), and no evidence of use of an intrathecal drug delivery system at any time during the study period (Figure 1). All patients were required to have had continuous health plan enrollment, including pharmacy benefits, from baseline through follow-up. To maximize sample size, up to a 30-day gap in insurance coverage was allowed during the baseline year. All codes used for patient selection are summarized in Appendix A.

Given that total health care utilization for cancer-related pain is high [14–16], as well as the possibility that patients could develop cancer-related pain in areas not covered by implanted SCS devices, we considered patients with cancer to be a clinically and economically dissimilar group to those initiating treatment for chronic non-cancer pain. Therefore, patients with active cancer diagnoses, defined as the presence of one inpatient or at least two outpatient visits with a diagnosis of cancer during the study period, were excluded.

Study Measures

Study Period

The index date for analysis was defined as the admission date for SCS generator and lead implantation. Baseline was defined as the 1-year period before the index date. For opioid utilization measures, follow-up was defined as the index admission date through 2 years, with the index visit included to account for prescriptions related to post-operative pain. For medical resource use and cost study measures, follow-up started on the day after the index visit discharge to evaluate index visit costs (i.e., SCS device plus insertion procedure) and follow-up costs separately.

Patient Demographic and Clinical Characteristics

Patient demographics, such as age, sex, census region, Charlson Comorbidity Index score, and history of clinical conditions (mood disorders, psychoses, opioid abuse, alcohol abuse, and tobacco abuse), were evaluated in the

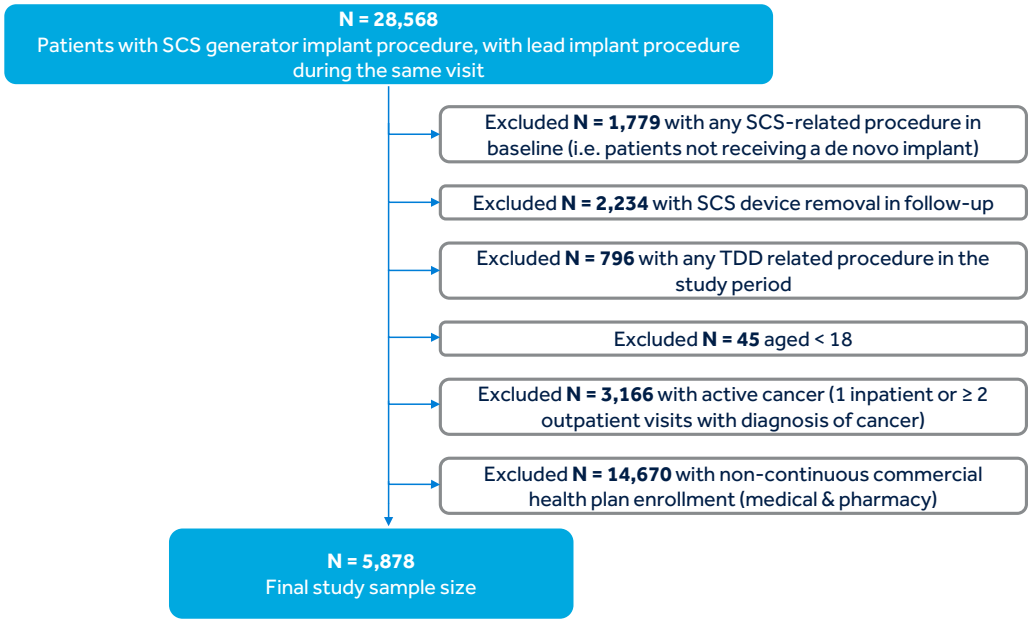


Figure 1. Patient selection. TDD = targeted drug delivery.

baseline period [17]. The pain-related diagnosis listed on the index date and all pain-related diagnoses in the baseline period were summarized. Many patients had more than one pain diagnosis present. Therefore, we broadly summarized all pain-related diagnoses rather than categorizing patients as receiving SCS for a specific indication. We also summarized the number of unique pain diagnoses present.

Prescription Utilization

We evaluated the use of potentially pain-related, non-opioid medications in the baseline period, including the presence of any prescription for medications commonly used for the treatment of chronic pain, such as skeletal muscle relaxants, anticonvulsants, benzodiazepines, tricyclic or selective serotonin and/or norepinephrine reuptake inhibitor (SSNRI) antidepressants, or prescription-strength nonsteroidal anti-inflammatory drugs (NSAIDs).

All pharmacy fills for systemic opioid prescriptions were evaluated, inclusive of oral and patch opioid formulations. For simplicity, we will refer to "systemic opioids" as simply "opioids" hereafter. Prescription-level details included the National Drug Code, strength, days' supply, and number of units. To compare opioid dosing levels before and after the start of SCS therapy, all opioid prescriptions were converted to the morphine-equivalent dose, expressed in morphine milligram equivalents (MMEs), through the use of conversion factors published by the CDC or literature sources when CDC conversions were not available (Appendix B). An average daily MME of >500 was considered an outlier value and was excluded from MME calculations (ranging from 0.1% to 1.0% of patients, dependent on the time period) because of possible miscoding of claims pertaining to days' supply, strength, or number of units per prescription fill, all of which are required for every prescription fill for an accurate estimate of average daily MME.

Composite End Point: Opioid Dose Reduction and Discontinuation

Patients were defined as discontinuing systemic opioid therapy if there was evidence of a 365-day gap between systemic opioid prescription fills. Our reasoning for this retrospective definition of discontinuation was based on the following: In theory, the maximum days' supply for any one opioid prescription fill would be 90 days. Therefore, a minimum gap of 90 days between when the last prescription supply ran out and any subsequent prescription fill could suggest discontinuation. To account for either pro re nata (PRN) dosing or prescriptions for acute events such as surgery, we further (i.e., more conservatively) defined discontinuation as either a 365-day gap between prescription fills or a total days' supply over the 2-year follow-up of ≤30 days. The date of discontinuation was defined as the last days' supply of the last prescription filled before the gap in therapy, or the last observed days' supply in follow-up if no further prescription was observed, whichever occurred first.

Among patients with at least one opioid prescription in the baseline or follow-up periods, the percent reduction in average daily dose was evaluated. The proportion of patients achieving ≥50% dose reduction in either year 1 or year 2 of follow-up relative to baseline was summarized, with a 50% reduction defined as the difference in the average daily MME over either year 1 or year 2 of follow-up relative to the 1-year baseline time period.

Finally, a composite end point of dose reduction or discontinuation was defined as the proportion of patients who achieved full opioid discontinuation *or* who reached at least a 50% dose reduction relative to baseline.

Medical Resource Use and Health Care Payments (Costs)
The percentage of patients with an all-cause medical visit by place of service (inpatient, emergency department, outpatient hospital, ambulatory surgery center, clinic/office), as well as the cumulative number of visits by place of service, were summarized over time (baseline year, follow-up year 1, follow-up year 2) and compared across patients who met or did not meet the cumulative end point.

Similarly, total all-cause commercial insurer payments (hereafter termed "costs") and patient out-of-pocket (OOP) costs were evaluated over the baseline and follow-up periods and compared across patients who met or did not meet the composite end point. Costs were analyzed from an "all-cause" perspective, i.e., costs incurred from all medical visits and pharmacy prescription fills. These include payments both related and potentially unrelated to SCS therapy. All visits to any place of service (including laboratory costs) were included, as were all prescription fills (not limited to opioids). We did not attempt to determine which visits were related to pain or SCS, given the risk of introducing bias in retrospectively determining what was considered a therapy-related or more broadly pain-related medical visit. In subgroup analyses, cost trends in the baseline and follow-up periods were compared across the following patient profiles: full opioid discontinuation, MME reduction ≥75% compared with baseline, MME reduction 50–74%, MME reduction 1–49%, no change or an increase in MME, and no opioid use at any time in the study period.

Statistical Analyses

Logistic regression analysis was conducted to evaluate factors significantly correlated with achieving the composite end point. The following were included as model covariates: age group, gender, census region, Charlson Comorbidity Index score group, history of a diagnosis of opioid abuse, alcohol abuse, psychoses and mood disorder, number of historical pain-related diagnoses and specific pain diagnosis types present, baseline non-opioid pain-related medication use, and average daily MME in baseline.

A difference-in-difference repeated-measures linear model was constructed to compare the incremental total cost savings (payer plus patient OOP) of achieving or not achieving the composite end point over follow-up years 1 and 2, relative to baseline [18]. The covariates listed previously were included. The resulting significance of the difference-in-difference covariate indicated whether achieving the composite end point had a significant impact on total costs after the start of SCS relative to baseline. In subgroup analysis, a second difference-in-difference model was run to compare differences in total cost over follow-up vs. baseline in multiple patient groups categorized by MME reduction status.

Sample selection and creation of analytic variables were performed with the Instant Health Data (IHD) platform (BHE, Boston, MA). Regression analyses were undertaken with SAS, version 9.4 (Cary, NC). Comparisons of baseline characteristics across patients meeting or not meeting the composite end point were calculated with the *t* test test for normally distributed continuous variables, the Wilcoxon-Mann-Whitney test for skewed variables, and the chi-squared test for categorical variables.

Results

Demographic and Clinical Characteristics

A total of 5,848 patients met study selection criteria. Of the starting population, 7.8% were excluded because of device removal during follow-up. A small proportion of patients (2.6%) had no opioid prescription at any point in the baseline or follow-up periods and by definition were not included in calculation of the primary end point. Among patients with any opioid prescription during the study period, 42.0% met the composite end point of opioid discontinuation (22.0%) or ≥50% dose reduction (20.0%). Mean patient age among those meeting the end point was slightly older than that of those who did not (56.8 vs. 54.8 years, $P < 0.001$). The majority of patients (>40%) resided in the South, with a relatively even distribution of number of patients by implantation year (11–17%); see Table 1.

Comorbidity burden as measured by the Charlson Comorbidity Index score was not significantly different among patients who met the composite end point and those who did not meet it. History of diagnosed opioid abuse, tobacco use, mood disorder, and psychoses were also similar. In univariate comparison, patients who met the composite end point had a slightly lower incidence of the following pain-related diagnoses: degenerative radiculitis, general chronic pain disorder, and failed back surgery syndrome. However, though statistically significant, the absolute differences in incidence were small (Table 1). Similarly, slightly fewer patients who met the composite end point had four or more pain-related diagnosis types present, and the absolute difference was small (30.0% vs. 33.0%, $P = 0.019$).

Baseline Medication Use

Incidence of any prescription fill for adjunctive non-opioid medications during the 1-year baseline period was significantly lower for all medication classes (muscle relaxants, anticonvulsants, benzodiazepine, and antidepressants) among those who met the composite end point than among those who did not (Table 2). Incidence of prescription-strength NSAID medications was similar across groups in the baseline period ($P = 0.408$). Among those with at least one opioid prescription in the baseline

Table 1. Demographic and clinical characteristics

	Met Composite End Point	Did Not Meet Composite End Point	*P* Value
Sample size, n (%)	2,403 (42.0)	3,323 (58.0)	
Age			
Mean ± SD	56.8 ± 13.9	54.8 ± 12.6	<0.001
Median	56	54	
Age group, %			
<50 y	30.0	34.7	0.0002
50–59 y	30.0	33.3	0.0091
60–69 y	20.1	17.8	0.0323
70–79 y	13.5	11.0	0.0042
≥80 y	6.5	3.3	<0.001
Female, %	61.1	61.9	0.5361
Region, %			
Northeast	10.9	8.8	0.0074
South	43.2	48.0	0.0003
Midwest	31.6	29.1	0.0490
West	14.1	13.4	0.4878
Missing	0.2	0.7	0.0324
Year of SCS implantation, %			
2009	16.3	15.9	0.7017
2010	17.1	16.9	0.7981
2011	12.4	14.6	0.0190
2012	15.1	16.7	0.1193
2013	13.2	12.7	0.5562
2014	14.1	12.6	0.0909
2015	11.7	10.8	0.2942
Charlson Comorbidity Index group, %			
0	60.9	62.9	0.1224
1	23.0	22.2	0.5096
≥2	16.1	14.8	0.2017
History of diagnosis, %			
Opioid abuse	4.3	4.9	0.3123
Tobacco use	13.2	12.8	0.6838
Mood disorder	18.6	19.0	0.7675
Mental health diagnoses[a]	7.1	6.7	0.5657
Pain diagnosis type, %[b]			
Radicular syndrome nondegenerative	79.5	80.1	0.5838
Radiculitis degenerative	65.5	68.6	0.015
Chronic pain disorders, general[c]	64.8	68.4	0.0049
FBSS	54.8	58.8	0.0023
CRPS I	9.9	9.6	0.7349
Peripheral neuropathy	8.1	8.1	1
CRPS II	3.4	3.1	0.5586
Arachnoiditis or epidural fibrosis	2.7	2.8	0.8415
Number of pain diagnosis types, %			
1	9.2	6.9	0.0014
2	23.2	22.6	0.6217
3	36.2	36.8	0.6223
≥4	30.0	33.0	0.0194
N/A: other chronic pain diagnosis, %	1.4	0.7	0.0143

CRPS= complex regional pain syndrome; FBSS= failed back surgery syndrome; SD= standard deviation.

[a]Mental health diagnoses included dementia, alcohol disorders, drug disorders, delirium, psychotic disorders, paranoia, paraphrenia, depressive type, and autism spectrum disorder.

[b]Pain diagnoses were not mutually exclusive.

[c]General chronic pain diagnoses included central pain disorder, chronic pain disorder, and other chronic pain.

period, the mean baseline average daily MME dose was 11.2 mg/day lower among those who met the composite end point in follow-up than among those who did not (44.0 vs. 55.2 mg/day, $P < 0.001$). Similarly, the mean number of treated days (the number of days in the 1-year baseline period with opioid supply available, based on total days' opioid supply filled) was significantly lower among patients who met the composite end point in follow-up (164 vs. 245 days, $P < 0.0001$).

Follow-Up Opioid Medication Use

Among patients with at least one opioid prescription during the study period, 22.0% discontinued opioid use in follow-up, while an additional 20.0% achieved ≥50%

Table 2. Baseline medication use

	Met Composite End Point*	Did Not Meet Composite End Point	*P* Value
Baseline non-opioid prescription use, %			
Skeletal muscle relaxant	48.8	57.0	<0.0001
Anticonvulsant	73.1	79.1	<0.0001
Benzodiazepine	34.2	38.3	0.0014
Antidepressant (SSNRI or tricyclic)	58.5	63.0	0.0007
Prescription-strength NSAID	39.2	38.1	0.4080
Conditional on ≥1 opioid prescription in baseline period			
Average daily MME, mg/day			
Mean ± SD	44.0 ± 73.3	55.2 ± 68.8	<0.0001
Median (IQR)	14.8 (4.3–45.5)	31.7 (12.8–65.7)	
Baseline average daily MME group, %			
<20	14.4	17.8	<0.0001
20–49	57.5	35.8	<0.0001
50–89	18.6	30.2	<0.0001
≥90	9.5	16.2	0.0011
Baseline number of treated days with any opioid prescription			
Mean ± SD	164 ± 126.2	245 ± 108.5	<0.0001
Median (IQR)	149 (39–293)	288 (166–338)	

IQR= interquartile range; SD= standard deviation; SSNRI = selective serotonin and/or norepinephrine reuptake inhibitor.*Systemic opioid discontinuation or ≥ 50% reduction in average daily MME.

average daily MME dose reduction in either year 1 or year 2 of follow-up relative to the average daily dose over the 1-year baseline period (Figure 2). A total of 44.0% of patients achieved some level of dose reduction (regardless of whether or not it was a ≥50% reduction), whereas 34.0% of patients had no change or an increase in average daily dose relative to baseline.

Among all patients with at least one opioid prescription, the mean average daily MME 12 months before the start of SCS was 42 mg/day, which increased slightly to 46 mg/day in the immediate month before the start of SCS (Figure 3). Mean MME was reduced to 41 mg/day during month 1 of follow-up and was further reduced to 28 mg/day during month 2, remaining relatively steady at this value through the end of 2 years. Trends in the median MME were similar, increasing slightly over baseline, then decreasing to a steady value by month 2 of follow-up.

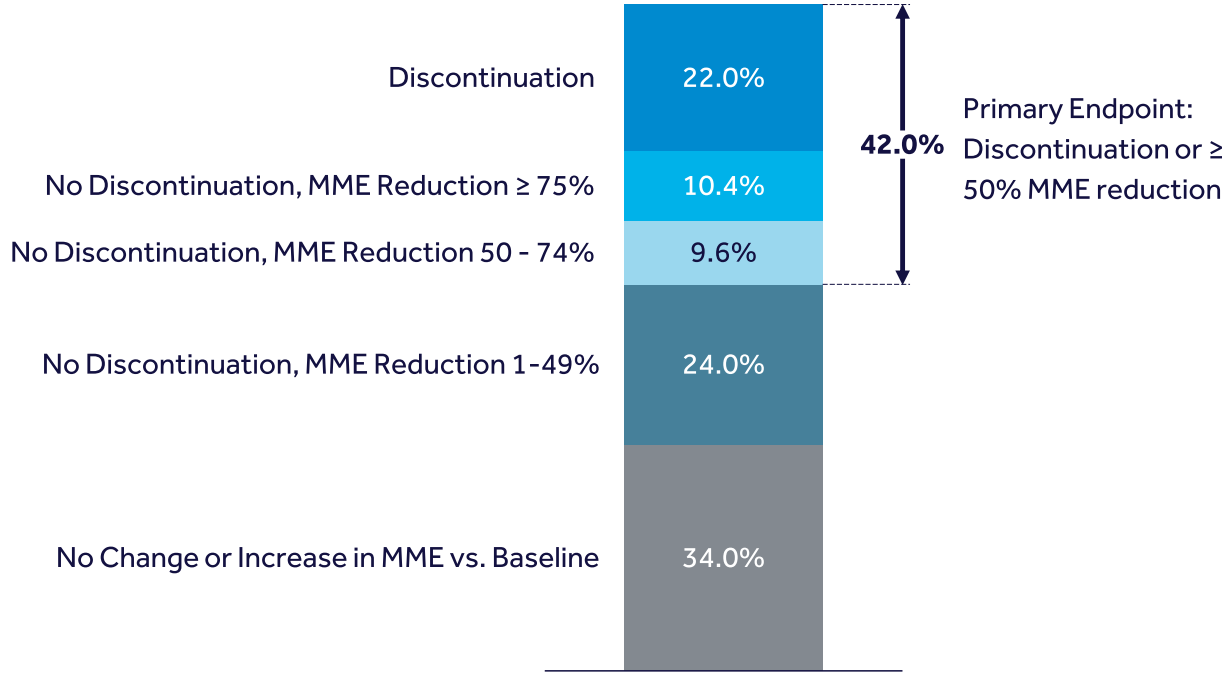
Factors Correlated with Achieving the Composite End Point

Findings from logistic regression analysis showed several demographic and clinical factors correlated with odds of meeting the composite end point. Older age (60–69 and >80, relative to age <50) was associated with higher odds of meeting the end point, whereas residing in the South was associated with lower odds (Table 3). Specific pain-related diagnosis was not significantly correlated with odds of meeting the end point (all $P > 0.05$). In an evaluation of medication factors, use of an anticonvulsant in the baseline period was associated with significantly lower odds of meeting the end point (odds ratio [OR] = 0.80, 95% confidence interval [CI]: 0.69–0.93, $P = 0.004$), whereas baseline prescription-strength NSAID use was associated with significantly higher odds (OR = 1.13, 95% CI: 1.01–1.27, $P = 0.037$). Not surprisingly, baseline average daily MME had the strongest association with meeting the composite end point in follow-up. Patients with an average MME of <20 mg/day had 1.92 the odds of meeting the composite end point relative to patients with an MME of ≥90 mg/day (OR = 1.92, 95% CI: 1.62–2.27, $P < 0.001$).

Adjusted Total Payments

In difference-in-difference adjusted regression analysis, after adjustment for patient demographic and clinical factors, total payer and patient OOP cost was significantly reduced in both years 1 and 2 of follow-up relative to baseline (excluding the costs of the SCS implant and the insertion procedure) among all patients, regardless of whether they met the composite end point (Figure 4). Among patients who met the composite end point, the mean adjusted reduction in total cost was –$13,508 (–40.6%) over year 1 of follow-up and –$14,041 (–42.2%) over year 2 of follow-up. Mean cost reduction was also significant among those who did not meet the composite end point, though the reduction was lower than among those who met the end point: –$11,310 (–31.6%) in year 1 and –$9,217 (–25.8%) in year 2. All reductions were significant (*P* values on difference-in-difference coefficients $P < 0.001$ for each model).

In an examination of patient subgroups by discontinuation status or MME reduction level, by year 2 of follow-up, the group with the largest percent reduction in adjusted cost relative to baseline was patients who completely discontinued opioids ($31,084 vs. $16,966; –45.4% reduction), followed by those with a 50–74% decline in average daily MME ($36,641 vs. $21,387; –41.6% reduction in cost), and those with no opioid use



[a]An additional N=152 (2.6% of all study patients) showed no opioid utilization at any time from baseline through 2-year follow-up; and were excluded from the proportions above.

Figure 2. Opioid utilization over 2-year follow-up. An additional n=152 (2.6% of all study patients) showed no opioid utilization at any time from baseline through 2-year follow-up and were excluded from the proportions in the figure.

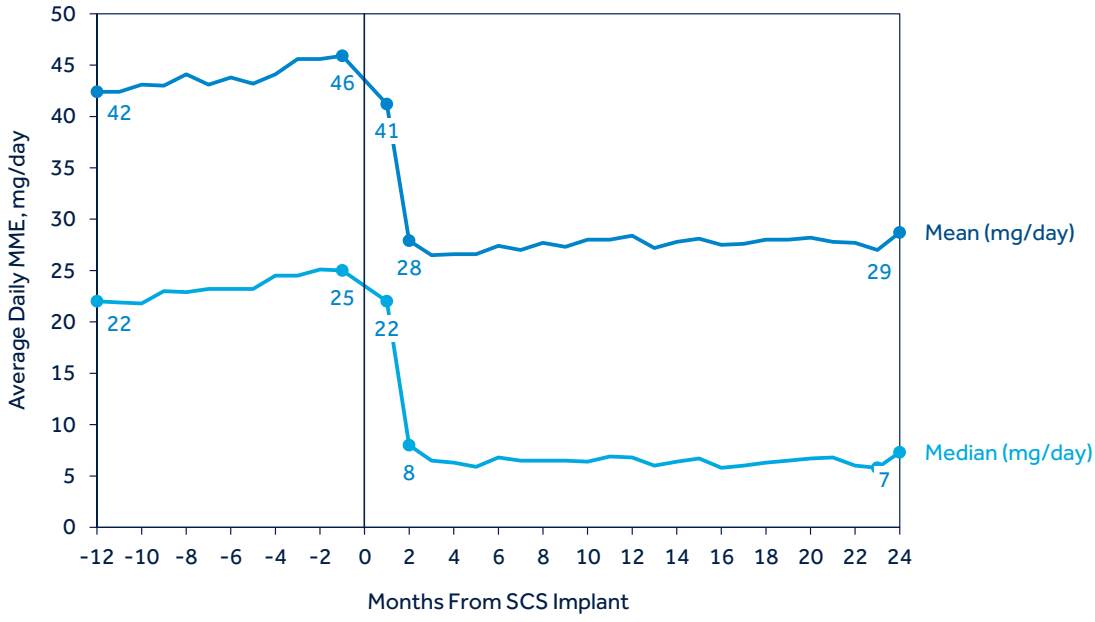


Figure 3. Mean and median MME (mg/day) by month from start of SCS.

at any point during the study period ($25,674 vs. $15,194; –40.8% reduction in cost; Figure 5).

The mean cost of an SCS trial procedure was $10,008, and the mean cost of device insertion was $33,080, for a total payer plus patient OOP cost associated with initiation of therapy of $43,088. The mean savings in years 1 and 2 of follow-up was $13,775 per year among those who met the composite end point and $10,268 for those who did not. When these are factored together, the average time to breakeven was 3.1 years among those who met the composite end point and 4.2 years among those who did not. Similarly, in an evaluation of time to

Table 3. Factors correlated with achieving the composite end point of opioid discontinuation or ≥50% dose reduction

Parameter	Odds Ratio	95% CI	*P* Value
Age, y (vs. <50)			
50–59	1.01	0.88–1.17	0.8688
60–69	1.19	1.01–1.41	0.0425
70–79	1.12	0.91–1.37	0.2787
≥80	1.64	1.22–2.2	0.0011
Male	1.09	0.97–1.23	0.1519
Census region (vs. Northeast)			
South	0.79	0.64–0.97	0.0223
Midwest	0.90	0.73–1.11	0.3265
West	0.98	0.77–1.24	0.8516
Missing	0.43	0.17–1.11	0.0808
Charlson Comorbidity Index score (vs. 0)			
1	1.06	0.92–1.22	0.4179
2	1.09	0.92–1.28	0.3198
Year of SCS implantation (vs. 2015)			
2009	0.99	0.79–1.24	0.9508
2010	0.97	0.78–1.21	0.7984
2011	0.81	0.64–1.02	0.0787
2012	0.82	0.65–1.02	0.0760
2013	1.02	0.81–1.28	0.8710
2014	0.99	0.79–1.25	0.9381
History of diagnosis of:			
Opioid abuse	1.16	0.89–1.51	0.2778
Alcohol abuse	1.43	0.88–2.31	0.1497
Mental health diagnoses[a]	1.06	0.85–1.33	0.6022
Mood disorder	1.09	0.94–1.27	0.2383
Specific pain diagnosis (baseline through index); not mutually exclusive			
Chronic Pain Disorders—General†	0.93	0.68–1.27	0.6501
FBSS	0.92	0.68–1.24	0.5961
Radicular nondegenerative	1.14	0.84–1.56	0.4016
CRPS I	0.99	0.72–1.38	0.9757
Radicular degeneration	0.91	0.67–1.23	0.5276
Peripheral neuropathy	0.98	0.72–1.33	0.9087
CRPS II	1.09	0.74–1.6	0.6767
Arachnoiditis or epidural fibrosis	0.96	0.65–1.43	0.8517
Number of pain diagnosis types (above) present (vs. 1)			
2	0.88	0.61–1.26	0.4758
3	0.88	0.48–1.61	0.6744
≥4	0.92	0.38–2.27	0.8651
Other pain diagnosis	1.33	0.65–2.74	0.4391
Baseline non-opioid pain medication use (vs. no use)			
Skeletal muscle relaxant	0.94	0.83–1.06	0.2848
Anticonvulsant	0.80	0.69–0.93	0.0044
Benzodiazepine	1.08	0.94–1.23	0.2741
Antidepressant (SSNRI or tricyclic)	0.99	0.88–1.12	0.9060
Prescription-level NSAID	1.13	1.01–1.27	0.0372
Baseline average daily MME group (vs. ≥90 mg/day)			
<20	1.92	1.62–2.27	< 0.0001
20–49	0.76	0.63–0.92	0.0046
50–89	0.74	0.6–0.92	0.0059
Model fit statistics			
c-statistic	0.64		
Overall model *P* value	< 0.0001		

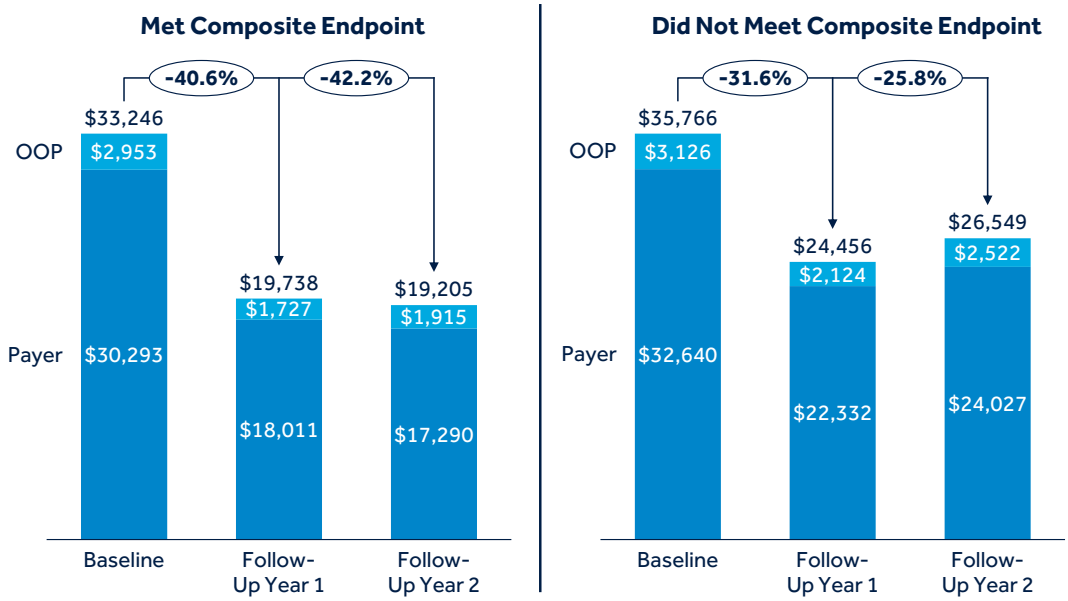
CRPS= complex regional pain syndrome; FBSS= failed back surgery syndrome; IQR= interquartile range; SD= standard deviation; SSNRI= selective serotonin and/or norepinephrine reuptake inhibitor.

[a]Mental health diagnoses included dementia, alcohol disorders, drug disorders, delirium, psychotic disorders, paranoia, paraphrenia, depressive type, and autism spectrum disorder.

breakeven in the subset of patients who completely discontinued opioid use in follow-up vs. those who did not, the average time to breakeven was similar, at 3.2 years among those who discontinued vs. 3.9 years among those who did not.

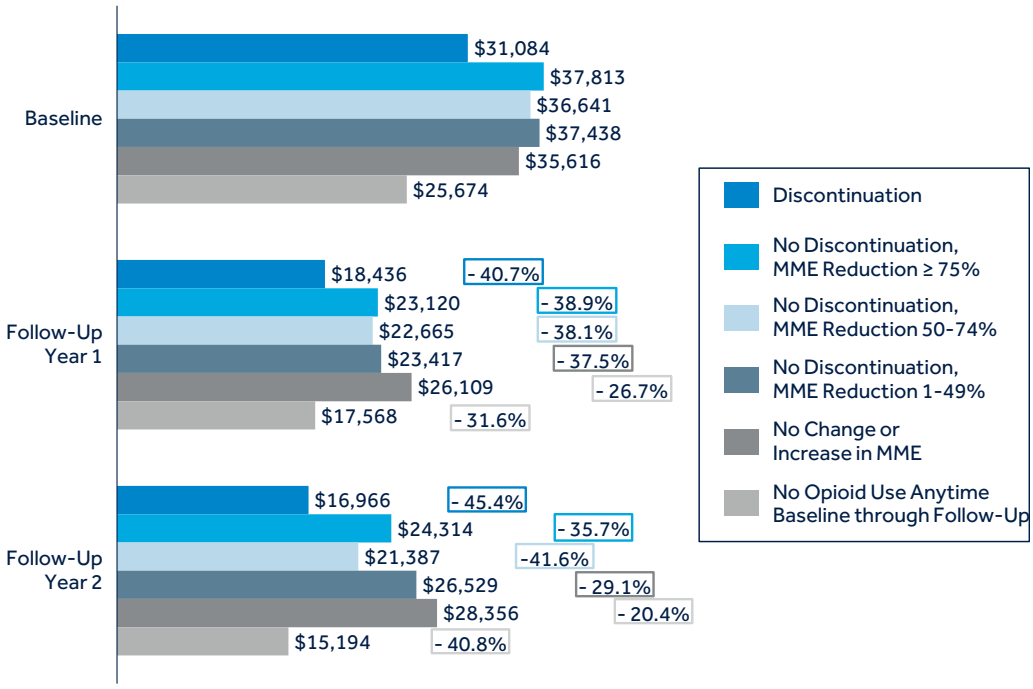
Discussion

This retrospective analysis of commercial claims data evaluated opioid medication use in the 1 year before and 2 years after the start of SCS therapy. Overall,



[a] Total payments exclude the cost of the SCS device and insertion procedure.

Figure 4. Adjusted total payments by composite end point. Total payments exclude the cost of the SCS device and insertion procedure.



[a] MME, morphine milligram equivalents

Figure 5. Adjusted total payments by follow-up opioid discontinuation and MME reduction status.

42.0% of patients met the composite end point; of those, 22.0% discontinued systemic opioid use altogether, and 20.0% achieved ≥50% dose reduction. All-cause total payer and patient OOP costs were significantly reduced in follow-up years 1 and 2 relative to the baseline year among all patient groups, with the exclusion of SCS insertion procedure–related costs.

We chose to limit this analysis to patients who did not undergo a device removal procedure during 2-year follow-up. By restricting the study population to those with no explantation, we sought to more closely estimate the impact on opioid utilization among "responders." Nonetheless, the definition of "responder" based solely on no explantation procedure is flawed, given the lack of pain or functional scores in administrative claims; however, it is the best proxy retrospectively. Given that it may be of interest to certain stakeholders to evaluate results among the total patient population starting SCS, inclusive of those with an explantation, we in sensitivity analyses examined the proportion meeting the primary end point. Results were quite similar, with the proportion meeting the primary end point numerically lower, as expected (40.8%, with 20.0% discontinuing and 19.9% with ≥50% dose reduction), as compared with our base case analysis restricted to patients with no removals (42.0%, with 22.0% discontinuing and 20.0% with dose reduction). Overall, the inclusion/exclusion of these patients had minimal impact on the primary end point.

Results from our multivariate analyses showed that older age and prior medication use were correlated with higher odds of meeting the composite end point. This is in agreement with findings that opioid misuse and abuse behaviors are inversely correlated with older age, potentially because of the higher risk and severity of opioid-induced side effects in older adults [19–21], as well as cultural and generational factors that may affect the motivation to discontinue use.

Prior use of anticonvulsant therapy was associated with lower odds of opioid discontinuation or lower odds of significant dose reduction after the start of SCS. We do not have a clear explanation for this finding. It is possible that patients on dual anticonvulsant/opioid therapy had more severe pain profiles at baseline that were not captured via MME dose alone (which was already independently controlled for in regression analyses). We did observe a slightly higher mean daily MME in the baseline period among patients with concomitant anticonvulsant use than among those with no use (51.6 vs. 47.1 mg/day, $P < 0.001$). More research is needed on the relationship of prior anticonvulsant use and its correlation with follow-up opioid use and cognitive function/status to fully explain findings in this study.

To date, there has been limited literature on trends in opioid use after the start of SCS therapy. Several single-center studies have assessed opioid use as a secondary end point; however, findings are limited by small sample sizes and reliance on patient recall for any opioid utilization (a binary end point in itself), with no details on opioid dosing [5, 6, 10, 22]. In the largest analysis to date, Sharan et al. evaluated 5,476 commercially insured patients in the Truven MarketScan database (2010–2014) who initiated SCS therapy [8]. The primary study finding was that higher opioid dose before the start of SCS was associated with significantly higher risk of therapy failure (defined as an explantation procedure) than that seen in patients at lower pre-SCS doses [8]. In the year leading up to SCS therapy, opioid use increased among 54% of patients, stayed the same for 21%, and decreased for 25% of patients, indicating significant variation in dosing patterns before the start of SCS. After the start of SCS therapy, a greater proportion of patients who continued SCS achieved an MME decrease (47%, n = 2,397) or had MME stay the same (23%, n = 1,167) relative to baseline levels vs. patients who had an SCS system explanted (decrease: 38%; stayed the same: 19%). High-dose opioid use (MME ≥90 mg/day) was associated with increased risk of device explantation (OR = 1.55, 95% CI: 1.14–2.12, $P = 0.005$). The authors concluded that earlier consideration of SCS before opioid usage escalates may improve outcomes with SCS therapy in that study [8].

Another analysis of the Truven dataset evaluated the effects of time from chronic pain diagnosis to the start of SCS therapy in a cohort of 762 patients [23]. The authors found that the median time from first diagnosis of chronic pain to the start SCS was 1.35 years. With every 1-year increase in time to SCS start, there was an associated 39% greater odds of being categorized in the "high" number of opioid prescription fills group. Similarly, a longer time from chronic pain diagnosis was significantly correlated with greater odds of being in the top tertile of total medical expenditures [23].

In a study more similar to our present analysis, Dougherty et al. evaluated data from a private health insurance company (2003–2014) to summarize opioid utilization among 145 patients starting SCS therapy [22]. The authors defined opioid discontinuation as no opioid prescription fill at any time in months 6 to 12 of follow-up and a dose reduction of >20% as a "meaningful" change relative to baseline [22]. Overall, 15.9% of patients discontinued opioid use, and 49.7% were categorized as experiencing a "meaningful" dose reduction [22]. The discontinuation and meaningful dose reduction proportions were different from those observed in our study (22.0% and 20%, respectively); however, we evaluated 2 years of follow-up rather than 1 year, and we more aggressively defined a meaningful dose reduction as ≥50%. We chose 50% as the threshold for "meaningful" dose reduction, given that this would likely have a larger impact on opioid-induced side effects than would a smaller dose reduction threshold. If we were to define meaningful dose reduction as ≥20%, the proportion meeting this modified dose reduction end point in our study would have been 34%, closer to that observed by Dougherty et al. [22]. Nonetheless, a minimal clinically important difference in opioid dose has not been defined for this population, so the ultimate definition of a meaningful dose reduction threshold is left up to individual patient experience of the magnitude of improvement in opioid-induced side effects experienced.

We observed 2.6% of patients with no opioid prescription fill at any point during the study period (1-year baseline through 2-year follow-up). These patients were not included in the calculations for the primary end point, given that, by definition, they could not discontinue or reduce opioid utilization. This proportion with no opioid prescription is quite low, as it is conceivable that a patient had at least one opioid fill during the study period for reasons potentially unrelated to SCS (e.g., control of postoperative pain). Therefore, it is not representative of the proportion using/not using opioids before the start of SCS. To more closely estimate that number, we post hoc evaluated the proportion with no opioid prescription fill limited to the 6 months before the start of SCS (13%). This proportion is closer to the percentage with no opioid use reported in prior retrospective analyses (17–20% in the 3 to 6 months leading up to start of SCS) [22, 24].

All opioid use trends in our present study and prior retrospective studies are inclusive of various patient profiles, including the specific indication, time living with pain, and pre-SCS patterns of opioid utilization. Generally speaking, as observed by Sharan et al. [8], Dougherty et al. [22], and our present analysis, patients' average daily opioid dose increased steadily before the start of SCS. Therefore, at a population level, we can infer there is no systematic approach to weaning opioid-dosing levels before the start of therapy. Given that higher doses increase the odds of therapy failure [8] and in our study are correlated with a lower odds of being able to completely discontinue opioids or reach a meaningful dose reduction, more consideration of and research on opioid weaning are needed before either SCS trial or the start of permanent therapy. This discussion of weaning is more common today with intrathecal drug delivery systems [25–27]. Nevertheless, given the underlying pharmacodynamics of opioid peak and trough medication levels, the potential effect of opioid weaning on therapy success should be similar, regardless of non-opioid interventional therapy applied. Future prospective research is needed to evaluate current best practices and outcomes after an opioid-weaning protocol before the start of SCS.

This study is limited by the nature of retrospective analyses of administrative claims data. Specifically, we do not have patient-reported information on pain scores or functional status over time. The requirement for continuous health plan enrollment led to a sample size reduction of approximately 51% (Figure 1). Although this exclusion was applied to ensure complete capture of all patient interactions with the health care system, it may introduce bias in the final study population evaluated. It is possible that patients disenrolled because of loss of employer coverage related to chronic pain, thereby potentially limiting our population to those with less severe or better-controlled pain who remained in the workforce and on their employer-sponsored insurance. Further analyses of patients with worker's compensation or other forms of health coverage are warranted.

Additionally, given the nature of the dataset examined, we have information only on prescription medications filled and paid for with patients' commercial insurance. Any medications filled and paid for by other means (cash/self-pay) were not collected in this dataset, and therefore our estimates of systemic opioid dose reduction are sensitive to the proportion of patients not using their commercial insurance to fill prescriptions. To estimate our potential error rate in this analysis, we sent an inquiry to each state's Prescription Drug Monitoring Program. Of the 21 states supplying information, the proportion of all opioid prescription fills in 2018 that were paid for by self-payment was 10.3%. Notably, this percentage does not reflect the proportion of patients with existing commercial insurance who chose to fill a prescription via self-payment (the potential error rate in our study), but rather the payment method among *all* patients filling a prescription, regardless of insurance coverage. Therefore, we expect the proportion of prescription fills not captured in our commercial insurance claims–based dataset to be lower than state Prescription Drug Monitoring Program rates.

Time to breakeven estimates consider only the cost of the device itself. However, payments over follow-up were summarized on an all-cause basis, i.e., inclusive of all patient visits and not limited to pain-related costs, given the inherent difficulty in determining retrospectively which visits were primarily for pain management. Regardless of difficulties in classifying visits as pain related or not, restricting to only pain-related visits would not capture potential reductions in health care utilization as a secondary effect of improved pain control. We believe our all-cause approach to breakeven estimates is conservative relative to the values that would be derived from pain-specific payments. Exact time to breakeven estimates will vary by patient-specific intensity of care over follow-up, as well as individual health plan reimbursement rates.

Conclusion

This study showed that among patients who start SCS therapy, without device removal over 2-year follow-up, a significant proportion were able to reduce average daily systemic opioid dose by at least half relative to baseline levels and/or discontinue systemic opioid use altogether. Not only were these clinical benefits realized, but there were also significant savings in total all-cause payer and patient OOP costs relative to pre-SCS amounts, totaling approximately $14,000 by year 2 of follow-up among those who met the primary end point of opioid dose reduction or discontinuation and $9,000 even among patients not meeting this clinical end point. These results are specific to patients who did not choose to have a device removal procedure and who had at least 3 years of

continuous commercial health plan enrollment, which may not be representative of the entire patient population initiating SCS therapy.

In the current era of increased emphasis on reducing nonessential opioid use, SCS may represent an effective and economically viable option for reducing or eliminating opioid consumption for a large proportion of patients. Future prospective studies are warranted to further evaluate medication use after the start of SCS therapy.

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Appendices

Appendix A: Codes for Patient Selection

Appendix B: MME Conversion Factors

SCS Generator Insertion	
86.94	Insertion or replacement of single array neurostimulator pulse generator, not specified as rechargeable
86.95	Insertion or replacement of multiple array neurostimulator pulse generator, not specified as rechargeable
86.96	Insertion or replacement of other neurostimulator pulse generator
86.97	Insertion or replacement of single array rechargeable neurostimulator pulse generator
86.98	Insertion or replacement of multiple array (two or more) rechargeable neurostimulator pulse generator
0JH70BZ	Insertion of Single Array Stimulator Generator into Back Subcutaneous Tissue and Fascia, Open Approach
0JH70CZ	Insertion of Single Array Rechargeable Stimulator Generator into Back Subcutaneous Tissue and Fascia, Open Approach
0JH70DZ	Insertion of Multiple Array Stimulator Generator into Back Subcutaneous Tissue and Fascia, Open Approach
0JH70EZ	Insertion of Multiple Array Rechargeable Stimulator Generator into Back Subcutaneous Tissue and Fascia, Open Approach
0JH80BZ	Insertion of Single Array Stimulator Generator into Abdomen Subcutaneous Tissue and Fascia, Open Approach
0JH80CZ	Insertion of Single Array Rechargeable Stimulator Generator into Abdomen Subcutaneous Tissue and Fascia, Open Approach
0JH80DZ	Insertion of Multiple Array Stimulator Generator into Abdomen Subcutaneous Tissue and Fascia, Open Approach
0JH80EZ	Insertion of Multiple Array Rechargeable Stimulator Generator into Abdomen Subcutaneous Tissue and Fascia, Open Approach
63685	Insertion or replacement of spinal neurostimulator pulse generator or receiver, direct or inductive coupling
SCS generator removal	
86.05	Incision with removal of foreign body or device from skin and subcutaneous tissue
0JPT0MZ	Removal of Stimulator Generator from Trunk Subcutaneous Tissue and Fascia, Open Approach
0JPT3MZ	Removal of Stimulator Generator from Trunk Subcutaneous Tissue and Fascia, Percutaneous Approach
63688	Revision or removal of implanted spinal neurostimulator pulse generator or receiver
SCS generator revision	
86.09	Other incision of skin and subcutaneous tissue
0JWT0MZ	Revision of Stimulator Generator in Trunk Subcutaneous Tissue and Fascia, Open Approach
0JWT3MZ	Revision of Stimulator Generator in Trunk Subcutaneous Tissue and Fascia, Percutaneous Approach
0JWTXMZ	Revision of Stimulator Generator in Trunk Subcutaneous Tissue and Fascia, External Approach
SCS lead insertion	
03.93	Implantation or replacement of spinal neurostimulator lead(s)
00HU0MZ	Insertion of Neurostimulator Lead into Spinal Canal, Open Approach
00HU3MZ	Insertion of Neurostimulator Lead into Spinal Canal, Percutaneous Approach
00HV0MZ	Insertion of Neurostimulator Lead into Spinal Cord, Open Approach
00HV3MZ	Insertion of Neurostimulator Lead into Spinal Cord, Percutaneous Approach
63650	Percutaneous implantation of neurostimulator electrode array, epidural
63655	Laminectomy for implantation of neurostimulator electrodes, plate/paddle, epidural
SCS lead revision	
03.99	Other operations on spinal cord and spinal canal structures
00WU0MZ	Revision of Neurostimulator Lead in Spinal Canal, Open Approach
00WU3MZ	Revision of Neurostimulator Lead in Spinal Canal, Percutaneous Approach
00WV0MZ	Revision of Neurostimulator Lead in Spinal Cord, Open Approach
00WV3MZ	Revision of Neurostimulator Lead in Spinal Cord, Percutaneous Approach
63663	Revision including replacement, when performed, of spinal neurostimulator electrode percutaneous array(s), including fluoroscopy, when performed
63664	Revision including replacement, when performed, of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed
SCS lead removal	
03.94	Removal of spinal neurostimulator lead(s)
00HU0MZ	Insertion of Neurostimulator Lead into Spinal Canal, Open Approach
00HU3MZ	Insertion of Neurostimulator Lead into Spinal Canal, Percutaneous Approach
00HV0MZ	Insertion of Neurostimulator Lead into Spinal Cord, Open Approach
00HV3MZ	Insertion of Neurostimulator Lead into Spinal Cord, Percutaneous Approach

(continued)

63661	Removal of spinal neurostimulator electrode percutaneous array(s), including fluoroscopy, when performed
63662	Removal of spinal neurostimulator electrode plate/paddle(s) placed via laminotomy or laminectomy, including fluoroscopy, when performed
Codes indicating presence or history of TDD	
03.9	Insertion of catheter into spinal canal for infusion of therapeutic or palliative substances
00HU33Z	Insertion of Infusion Device into Spinal Canal, Percutaneous Approach
62350	Implantation, revision or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable reservoir/infusion pump; without laminectomy
62351	Implantation, revision or repositioning of tunneled intrathecal or epidural catheter, for long-term medication administration via an external pump or implantable reservoir/infusion pump; with laminectomy
86.06	Insertion of totally implantable infusion pump
0JH80VZ	Insertion of Infusion Pump into Abdomen Subcutaneous Tissue and Fascia, Open Approach
62362	Implantation or replacement of device for intrathecal or epidural drug infusion; programmable pump, including preparation of pump, with or without programming
86.05	Incision with removal of foreign body or device from skin and subcutaneous tissue
00PU03Z	Removal of Infusion Device from Spinal Canal, Open Approach
00PU33Z	Removal of Infusion Device from Spinal Canal, Percutaneous Approach
00PU43Z	Removal of Infusion Device from Spinal Canal, Percutaneous Endoscopic Approach
00PUX3Z	Removal of Infusion Device from Spinal Canal, External Approach
0JPT0VZ	Removal of Infusion Pump from Trunk Subcutaneous Tissue and Fascia, Open Approach
0JPT3VZ	Removal of Infusion Pump from Trunk Subcutaneous Tissue and Fascia, Percutaneous Approach
62365	Removal of subcutaneous reservoir or pump, previously implanted for intrathecal or epidural infusion
62369	Electronic analysis of programmable, implanted pump for intrathecal or epidural drug infusion (includes evaluation of reservoir status, alarm status, drug prescription status); with reprogramming and refill
62370	Electronic analysis of programmable, implanted pump for intrathecal or epidural drug infusion (includes evaluation of reservoir status, alarm status, drug prescription status); with reprogramming and
95990	Refilling and maintenance of implantable pump or reservoir for drug delivery, spinal (intrathecal, epidural) or brain (intraventricular), includes electronic analysis of pump, when performed;
95991	Refilling and maintenance of implantable pump or reservoir for drug delivery, spinal (intrathecal, epidural) or brain (intraventricular), includes electronic analysis of pump, when performed
S9328	Home infusion therapy, implanted pump pain management infusion; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment
Cancer	
140.xx - 239.9x	
C00.0 - D49.9	

Name	Strength	Conversion Factor	Source
Alfentanil sc	mcg	30	Palliative Care guidelines 2016
Buprenorphine film	mcg/hr	12.6	CDC 2018 and CMS 2017 (footnote 4)
Buprenorphine film, extended release	mcg/hr	12.6	CDC 2018 and CMS 2017 (footnote 4)
Buprenorphine tablet	mg	30	CMS 2017
Buprenorphine iv/sc	mg/mL	33	Buprenorphine label
Buprenorphine solution	mg/mL	33	Buprenorphine label
Buprenorphine powder			N/A cannot assign conversion for powers (compounding)
Butorphanol iv/sc	mg	7	CDC 2018
Butorphanol solution	mg	7	CDC 2018
Butorphanol spray	mg	7	CDC 2018
Codeine tablet	mg	0.15	CDC 2018
Codeine capsule	mg	0.15	CDC 2018
Codeine iv/sc	mg	0.15	CDC 2018
Codeine solution	mg/day	0.15	CDC 2018
Codeine liquid	mg/day	0.15	CDC 2018
Codeine suspension	mg/day	0.15	CDC 2018
Fentanyl film or oral spray	mcg	0.18	CDC 2018
Fentanyl film, extended release	mcg	0.18	CDC 2018
Fentanyl film	mcg	0.18	CDC 2018
Fentanyl nasal spray	mcg	0.16	CDC 2018
Fentanyl spray	mcg	0.16	CDC 2018
Fentanyl patch	mcg/hr	7.2	CDC 2018 and CMS 2017 (footnote 8)
Fentanyl tablet	mcg	0.13	CDC 2018
Fentanyl lozenge	mcg	0.13	CDC 2018

(continued)

Name	Strength	Conversion Factor	Source
Fentanyl iv/sc	mcg	0.13	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Fentanyl solution	mcg	0.13	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Fentanyl solution, extended release	mcg	0.13	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Hydrocodone	mg	1	CDC 2018
Hydrocodone capsule, extended release	mg	1	CDC 2018
Hydrocodone tablet, extended release	mg	1	CDC 2018
Hydrocodone tablet	mg	1	CDC 2018
Hydrocodone capsule	mg	1	CDC 2018
Hydrocodone elixir	mg	1	CDC 2018
Hydrocodone liquid	mg	1	CDC 2018
Hydrocodone solution	mg	1	CDC 2018
Hydromorphone oral	mg	4	CDC 2018
Hydromorphone capsule, extended release	mg	4	CDC 2018
Hydromorphone tablet	mg	4	CDC 2018
Hydromorphone tablet, extended release	mg	4	CDC 2018
Hydromorphone iv/sc	mg	4	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Hydromorphone solution	mg	4	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Hydromorphone liquid	mg	4	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Levomethadyl acetate oral	mg	8	CDC 2018
Levomethadyl acetate iv/sc	mg	8	CDC 2018
Levorphanol oral	mg	11	CDC 2018
Levorphanol tablet	mg	11	CDC 2018
Levorphanol iv/sc	mg	11	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Levorphanol solution	mg	11	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Meperidine oral	mg	0.1	CDC 2018
Meperidine tablet	mg	0.1	CDC 2018
Meperidine capsule	mg	0.1	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Meperidine syrup	mg	0.1	CDC 2018
Meperidine iv/sc	mg	0.1	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Meperidine solution	mg	0.1	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Methadone tablet	mg	3	CDC 2018
Methadone tablet, dispersible	mg	3	CDC 2018
Methadone concentrate	mg	3	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Methadone solution	mg	3	CDC 2018
Methadone powder		3	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Methadone injectable solution	mg/mL	3	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Morphine oral	mg	1	CDC 2018
Morphine capsule, extended release	mg	1	CDC 2018
Morphine tablet	mg	1	CDC 2018
Morphine tablet, extended release	mg	1	CDC 2018
Morphine tablet, soluble	mg	1	CDC 2018
Morphine rectal	mg	1	CDC 2018
Morphine suppository	mg	1	CDC 2018
Morphine iv/sc	mg/mL	1	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Morphine solution	mg/mL	1	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Morphine liquid	mg/mL	1	Assumption—consistent with other routes of administration in CDC 2018 for opioid class

(continued)

Name	Strength	Conversion Factor	Source
Morphine concentrate	mg/mL	1	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Nalbuphine	mg/day	3	Nielsen 2015
Nalbuphine solution	mg/day	3	Nielsen 2015
Opium	mg	1	CDC 2018
Opium suppository	mg	1	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Oxycodone	mg	1.5	CDC 2018
Oxycodone capsule, extended release	mg	1.5	CDC 2018
Oxycodone capsule	mg	1.5	CDC 2018
Oxycodone tablet	mg	1.5	CDC 2018
Oxycodone tablet, extended release	mg	1.5	CDC 2018
Oxycodone concentrate	mg/ml	1.5	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Oxycodone solution	mg/ml	1.5	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Oxymorphone	mg	3	CDC 2018
Oxymorphone tablet	mg	3	CDC 2018
Oxymorphone tablet, extended release	mg	3	CDC 2018
Oxymorphone injectable solution			N/A cannot assign conversion for powers (compounding)
Oxymorphone suppository		3	Assumption—consistent with other routes of administration in CDC 2018 for opioid class
Pentazocine	mg	0.37	CDC 2018
Pentazocine tablet	mg	0.37	CDC 2018
Pentazocine solution	mg	0.37	CDC 2018
Propoxyphene capsule	mg	0.23	CDC 2018
Propoxyphene tablet	mg	0.23	CDC 2018
Sufentanil solution	mcg/day	2	ANZCA Opioid Dose Equivalence
Tapentadol tablet	Mg	0.4	CDC 2018
Tapentadol tablet, extended release	Mg	0.4	CDC 2018
Tramadol capsule, extended release	Mg	0.1	CDC 2018
Tramadol tablet	Mg	0.1	CDC 2018
Tramadol tablet, disintegrating	Mg	0.1	CDC 2018
Tramadol tablet, extended release	Mg	0.1	CDC 2018

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