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ORIGINAL RESEARCH

Long-Term Reductions in Opioid Medication Use After Spinal Stimulation: A Claims Analysis Among Commercially-Insured Population

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Purpose: Chronic, non-cancer pain significantly and negatively impacts patient quality of life. Neuromodulation is a major component of multi-modal interdisciplinary approaches to chronic pain management, which includes opioid and nonopioid medications. In randomized controlled trials, spinal cord stimulation (SCS) has been shown to reduce pain and decrease short-term opioid use for patients. This study sought to evaluate the effect of SCS on longer term opioid and non-opioid pain medication usage among patients over ≥3 years of follow-up.

Patients and Methods: Claims analysis was conducted using the Merative™ MarketScan® Commercial Database. Patients aged ≥18 who initiated SCS between 1/1/2010 and 3/31/2021 with ≥1 year of baseline data and ≥3 years of follow-up data were included. Opioid discontinuation, daily dose (DD) reduction, proportion of days covered (PDC), concomitant co-medication with benzodiazepines and/or gabapentinoids, and polypharmacy were evaluated during the baseline and follow-up periods. Adjusted logistic regression was used to evaluate the impact of baseline dosages on discontinuation and dose reduction.

Results: During follow-up, 60% of 2,669 SCS patients either discontinued opioid use or reduced opioid DD by at least 20% from baseline; another 15% reduced DD by 1–19%. Logistic regression showed patients with higher baseline dosages were less likely to discontinue opioids completely (odds ratio[OR] 95% confidence intervals[CI]: 0.31[0.18,0.54]) but more likely to reduce their daily dose (OR[CI]: 7.14[4.00,12.73], p<0.001). Mean PDC with opioids decreased from 0.58 (210 of 365 days) at baseline to 0.51 at year 3 (p<0.001). With SCS, co-medication with benzodiazepines decreased from 47.3% at baseline to 30.3% at year 3, co-medication with gabapentinoids reduced from 58.6% to 42.2%, and polypharmacy dropped from 15.6% to 9.6% (all p<0.001).

Conclusion: Approximately three-quarters of patients who received SCS therapy either discontinued or reduced systemic opioid use over the study period. SCS could assist in reducing long-term reliance on opioids and other pain medications to treat chronic non-cancer pain.

Keywords: chronic pain, opioid misuse, spinal cord stimulation, opioid medication

Introduction

Chronic, non-cancer pain affects approximately 20% of adults and significantly reduces patient quality of life.[1] Furthermore, up to 10% of adults suffer high-impact chronic pain with work limitations.[1] The management of chronic pain involves a multi-modal, interdisciplinary approach.[2] Opioids play a role in that approach as a later stage option, but require evaluation of individual risks and benefits. While opioid therapy is associated with modest short-term reductions in pain and improvements in functioning, opioid use is often accompanied by significant side effects.[3–5]

In recent years, the Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain and other guidelines have been released in the United States (US) to manage opioid prescribing practices. Recommendations include reducing overdose risk by limiting daily dosage morphine milligram equivalents (MME) to below 90 mg and avoiding co-prescription with benzodiazepines.[6] Such strategies to address opioid prescribing patterns

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should include comprehensive efforts to supply alternative methods of pain management. For well-selected patient populations, neuromodulation is a potential strategy to reduce long-term opioid dependence and enjoys a well-established role in treating chronic neuropathic pain. In randomized controlled trials (RCTs), the use of spinal cord stimulation (SCS) has shown promise to reduce pain and decrease opioid use.[7,8] Additionally, while SCS is associated with an initial procedural cost, the therapy appears cost-effective over the long term.[9] Most published SCS studies have only one to two years of follow-up. This study evaluated long-term opioid usage (specifically dose reduction and discontinuation) and non-opioid pain medication usage after the start of SCS therapy among patients with at least three years of follow-up.

Materials and Methods

A retrospective claims analysis was conducted using the Merative™ MarketScan® Commercial Database (MarketScan). The Merative MarketScan Commercial Database contains deidentified, longitudinal, patient-level claims data for several million individuals annually covered by employer-sponsored private health insurance in the United States, encompassing employees, their spouses, and dependents. The database includes information on medical claims (services rendered in an inpatient or outpatient setting), pharmacy claims, basic patient demographics, and health plan enrollment information. 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 claims data are linked to encounter data across sites and types of practitioners, the database reflects actual medication prescribing patterns.

Patients aged 18 and older who initiated SCS between 1/1/2010 and 3/31/2021 with ≥1 year of baseline data and ≥3 years of follow-up data were included. This analysis was restricted to patients without prior history of permanent SCS implantation, without SCS removal in the 3-year follow-up (defined as the presence of a procedure code for both generator and lead removal during the same visit), and without a procedure for an intrathecal drug delivery system or a cancer diagnosis at any time during the study period (Figure 1). We considered patients with cancer to be a clinically dissimilar group to those initiating SCS treatment for chronic, non-cancer pain; therefore patients with a cancer diagnosis were excluded. Patients with an intrathecal drug delivery system were excluded to ensure opioid use was not associated with the drug delivery system.

Patient demographics included age and sex (race is not available in the MarketScan Database). Clinically relevant conditions present at baseline (smoking status, alcohol abuse, non-alcohol substance use disorder, depression, psychosis, anxiety, obesity) were identified using Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), and International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes (see Supplemental Table 1). Comorbidity burden during baseline was evaluated using the Charlson Comorbidity Index.[10] Pain diagnosis type was also collected and included arachnoiditis, chronic pain disorder, complex regional pain syndrome (CRPS) I or II, epidural fibrosis, peripheral neuropathy of the extremities, post laminectomy syndrome, radiculopathy, back pain, limb pain, and degenerative disc disease. Baseline average opioid MME daily dose (DD) was determined (see Supplemental Table 2). MME DD was defined as (metric quantity x dose strength)/day supply. Thus, patients with invalid opioid records (eg, <1 day of supply or metric quantity or missing dose strengths) were excluded. The MarketScan Commercial database is a de-identified, HIPAA compliant, closed system of administrative claims; therefore, this study did not require institutional review board approval. Further, our study complies with the ethnical standards of the Declaration of Helsinki.

Measures and Outcomes

Opioid discontinuation, dose reduction, co-medication with benzodiazepines and/or gabapentinoids, and polypharmacy (co-medication with at least four of benzodiazepines, gabapentinoids, antidepressants, and skeletal muscle relaxants) were evaluated during baseline and follow-up. The primary endpoint was opioid discontinuation or a clinically significant reduction in opioid dose. Patients were considered to discontinue opioid therapy if they either stopped opioid use completely,[11] had less than 90 days supply of all opioid prescriptions during the 3-year follow-up (ie, sum of day supply

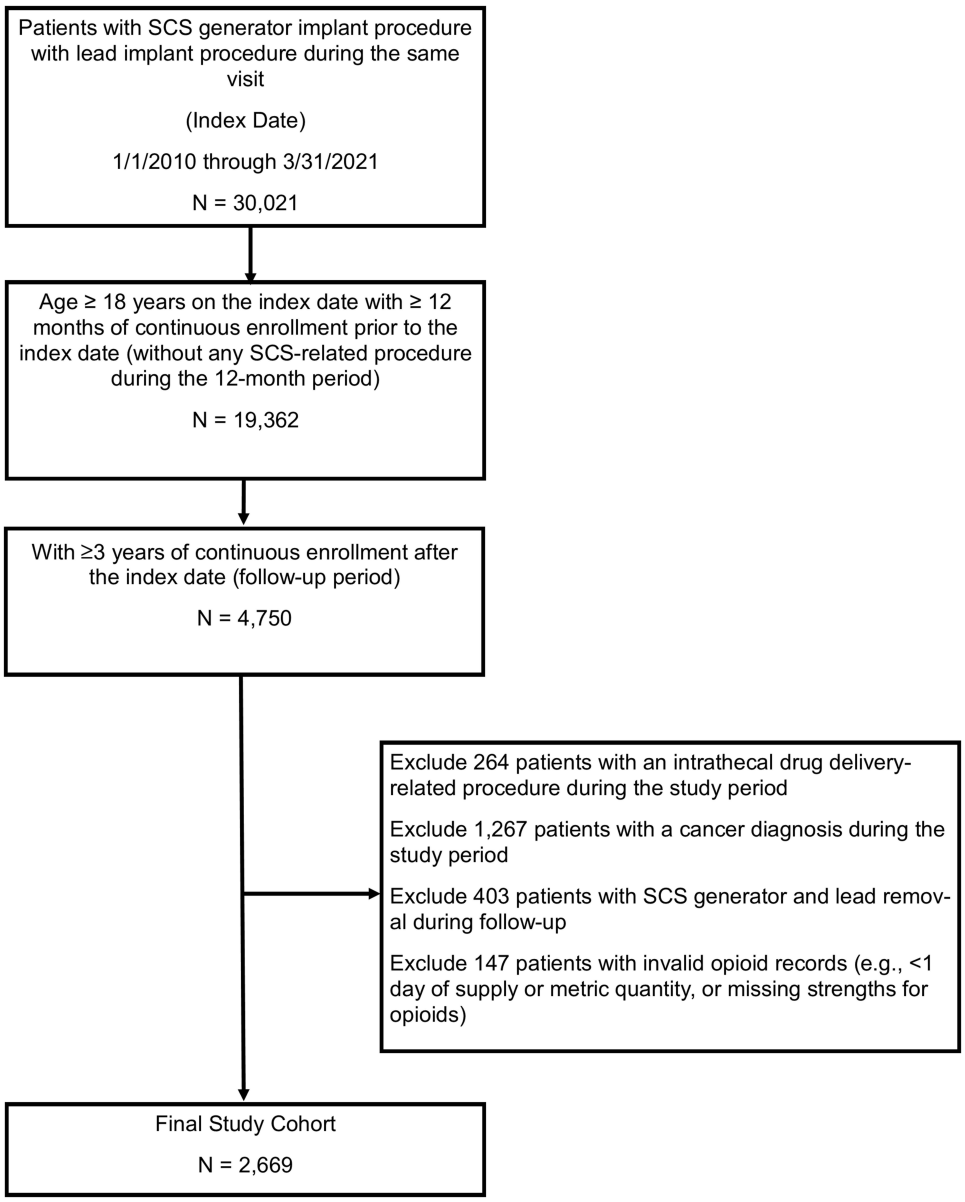

Figure 1 Flow Diagram Indicating the Number of Patients Meeting Inclusion/Exclusion Criteria.

of all opioid prescriptions),[12] or had at least a 1-year gap between consecutive opioid prescriptions during follow-up (this 1-year gap can be interpreted as a form of opioid reduction).[13] A clinically significant DD reduction was defined as a MME DD reduction of ≥20% from baseline to years 1, 2, or 3.[14,15] The proportion of days covered (PDC)[16] was calculated to estimate opioid medication adherence by looking at the proportion of days for which a patient had an opioid medication on hand during the baseline period and years 1, 2, and 3 in the follow-up period.

Statistical Analyses

Descriptive summaries include mean and standard deviations (SDs) for continuous variables and frequency and percent for categorical variables. Among patients who did not discontinue opioids, MME DD reduction during follow-up was examined by strata established using baseline MME DD. Paired *t*-test and McNemar's test were used to examine the change in mean PDC, co-medication with benzodiazepines or gabapentinoids, and polypharmacy during the baseline period and year 3 after the SCS implant. To control for type I error (family-wise error rate) due to multiple comparisons,

we applied a Bonferroni adjustment to the threshold p-value. In this study, there were 11 key hypotheses, and the number of these hypotheses were applied to the threshold p-value of 0.05, resulting in the Bonferroni adjusted p-value of 0.005. All results remained significant after the Bonferroni correction.

Adjusted logistic regression was employed to examine the association of patient demographics and clinical characteristics with three distinct outcomes: the primary endpoint, opioid discontinuation, or a DD reduction of ≥20% among only those patients who did not discontinue opioid use.

Results

A total of 2,669 patients met the study criteria with a mean (SD) age of 48.8 (8.5) years (Figure 1). Of these patients, 60.2% were female (Table 1). Almost half were located in the South region of the United States, and 28% in the Midwest. The most prevalent baseline pain diagnoses were back pain (86%), degenerative disc disease (83%), and

Table 1 Patient Demographics and Baseline Characteristics

Characteristic	N or Mean	% or SD
Age at index (years), Mean, SD	48.8	8.5
Age group (years), N, %		
18–29	63	2.4%
30–39	333	12.5%
40–49	869	32.6%
50–59	1,198	44.9%
≥60	206	7.7%
Sex, N, %		
Female	1,606	60.2%
Male	1,063	39.8%
Region, N, %		
Midwest	742	27.8%
Northeast	243	9.1%
South	1,328	49.8%
West	312	11.7%
Charlson Comorbidity Score, Mean, SD	0.5	0.9
Clinical conditions during baseline, N, %		
Smoking status	448	16.8%
Alcohol abuse	33	1.2%
Non-alcohol substance use disorder	373	14.0%
Depression	1,377	51.6%
Psychosis	85	3.2%
Anxiety	625	23.4%
Obesity	410	15.4%

(*Continued*)

Table 1 (Continued).

Characteristic	N or Mean	% or SD
Pain diagnosis type, N, %		
Arachnoiditis	30	1.1%
Chronic pain disorder	1,715	64.3%
CRPS I	313	11.7%
CRPS II	342	12.8%
Epidural fibrosis	25	0.9%
Peripheral neuropathy of the extremities	54	2.0%
Post laminectomy syndrome	1,396	52.3%
Radiculopathy	2,196	82.3%
Back pain	2,288	85.7%
Limb pain	829	31.1%
Degenerative disc disease	2,210	82.8%
Baseline opioid dose*, N, %	2,479	92.9%
Average daily MME (mg), Mean, SD	75.7	72.3
Median, IQR	49.4	30–93.35
Baseline average daily MME group (mg), N, %	2,479	92.9%
<20	286	11.5%
20–49	979	39.5%
50–90	568	22.9%
91–199	466	18.8%
≥200	180	7.3%

Note: *Among patients with at least 1 opioid prescription during baseline.
Abbreviations: CRPS, complex regional pain syndrome; IQR, interquartile range; MME, morphine milligram equivalents; SD, standard deviation.

radiculopathy (82%). At baseline, 11.5% of patients had an MME DD of 20–49 mg, 39.5% with 20–50 mg, 22.9% with 51–90 mg, 18.8% with 91–199 mg, and 7.3% with ≥200 mg. Greater than 50% of patients were diagnosed with depression, followed by anxiety (23.4%), smoking (16.8%), obesity (15.4%), and non-alcohol substance abuse (14.0%). At baseline, 47.9% of patients had benzodiazepine co-medication, 58.6% had gabapentinoid co-medication, and 15.6% had polypharmacy.

During follow-up, 60% of patients met the primary outcome (discontinuation of opioid use or reduction of MME DD by at least 20% from baseline (Table 2). In total, 885 patients (33.2%) discontinued opioid use, 304 (11.4%) reduced MME DD by ≥50%, 412 (15.4%) reduced MME DD by 20–49%, and 414 patients (15.5%) reduced MME DD by 1–19%. However, 8.4% of patients maintained or increased DD by 0–20%, 15.1% increased DD by >20%, and 1.0% initiated opioid use.

Mean PDC with opioid medication started at 0.58 (210 out of 365 days) in the baseline period and decreased to 0.56, 0.53, and 0.51 (185 days) in years 1, 2, and 3, respectively ($p<0.001$ for baseline vs year 3). Among patients meeting the primary endpoint, mean PDC started at 0.49 (179 days) at baseline and decreased to 0.42, 0.36, and 0.33 (119 days) in years 1, 2, and 3, respectively ($p<0.001$). Among patients who did not meet the primary endpoint, mean PDC increased from 0.70 (257 days) at baseline to 0.78 (285 days) in year 3 ($p<0.001$).

Table 2 Opioid Prescription Pattern: Opioid Discontinuation, MME DD Reduction, or MME DD Increase

	All Patients N=2,669
Patients meeting primary endpoint (discontinuation or ≥20% MME DD reduction)	1,601 (60.0%)
Discontinuation	885 (33.2%)
MME DD reduction ≥50%	304 (11.4%)
MME DD reduction 20–49%	412 (15.4%)
Patients with MME DD reduction 1–19%	414 (15.5%)
Patients with each type of discontinuation	
Complete stop (no opioid medication in the follow-up)	32 (1.2%)
With <90 days of opioid supply in the follow-up	543 (20.3%)
With ≥1-year gap between consecutive opioid medications	310 (11.6%)
Patients with no change or increased opioid medication use in the follow-up	
Increase MME DD 0–20%	225 (8.4%)
Increase MME DD >20%	403 (15.1%)
Initiation of opioid use (without opioid medication in baseline but with opioid medication in the follow-up)	26 (1.0%)

Abbreviations: DD, daily dosage; MME, morphine milligram equivalent.

Results from logistic regression analysis showed several demographic and clinical factors correlated with meeting the primary endpoint. Patients in the youngest (18–29 years) and oldest (60+ years) age groups were more likely to meet the primary endpoint compared to patients between 50 and 59 years old. Patients whose SCS implantation occurred in 2016 or later were more likely to meet the primary endpoint. History of spine surgeries, being diagnosed with substance abuse, and baseline use of a prescription-level NSAID were also associated with higher odds of meeting the primary endpoint (Table 3). Furthermore, having a diagnosis of degenerative disc disease was associated with reduced likelihood of discontinuation, while limb pain diagnosis was marginally associated with increased likelihood of discontinuation.

Table 3 Adjusted Logistic Regression Results

	Primary Endpoint		**Discontinuation**		**MME Reduction ≥20%***	
	OR (LCL, UCL)	**p-value**	**OR (LCL, UCL)**	**p-value**	**OR (LCL, UCL)**	**p-value**
Age group (vs 50–59)						
18–29	2.73 (1.40, 5.31)	0.0031	1.91 (0.88, 4.17)	0.1020	3.60 (1.71, 7.58)	0.0008
30–39	1.05 (0.81, 1.35)	0.7270	1.21 (0.89, 1.64)	0.2234	0.89 (0.64, 1.24)	0.4940
40–49	0.93 (0.77, 1.13)	0.4682	0.81 (0.64, 1.02)	0.0743	1.03 (0.82, 1.30)	0.7909
60+	1.82 (1.31, 2.55)	0.0004	1.68 (1.13, 2.49)	0.0104	1.99 (1.34, 2.97)	0.0007
Male (vs Female)	1.02 (0.87, 1.21)	0.7816	1.07 (0.87, 1.31)	0.5086	0.98 (0.80, 1.21)	0.8818
Region (vs South)						
Midwest	1.20 (0.98, 1.46)	0.0717	1.26 (0.99, 1.59)	0.0567	1.13 (0.88, 1.44)	0.3380
Northeast	1.02 (0.76, 1.38)	0.8818	1.29 (0.90, 1.84)	0.1645	0.75 (0.51, 1.09)	0.1315
West	0.93 (0.71, 1.21)	0.5728	0.96 (0.69, 1.33)	0.7867	0.87 (0.63, 1.20)	0.4026
Missing	1.37 (0.68, 2.76)	0.3857	1.48 (0.66, 3.33)	0.3416	1.32 (0.56, 3.10)	0.5283

(*Continued*)

Table 3 (Continued).

	Primary Endpoint		Discontinuation		MME Reduction ≥20%*	
	OR (LCL, UCL)	p-value	OR (LCL, UCL)	p-value	OR (LCL, UCL)	p-value
Charlson Comorbidity Score	0.96 (0.87, 1.05)	0.3784	0.94 (0.84, 1.05)	0.2555	0.99 (0.88, 1.11)	0.8521
Index year ≥ 2016 (vs <2016)	1.67 (1.34, 2.09)	<0.0001	1.96 (1.51, 2.54)	<0.0001	1.46 (1.10, 1.93)	0.0085
Baseline daily dosage (vs <20 mg)						
20 to 50 mg	0.92 (0.70, 1.21)	0.5410	0.63 (0.46, 0.84)	0.0019	2.88 (1.76, 4.73)	<0.0001
51 to 90 mg	1.08 (0.80, 1.46)	0.6127	0.58 (0.42, 0.82)	0.0017	4.37 (2.62, 7.29)	<0.0001
91–199 mg	1.26 (0.92, 1.72)	0.1520	0.42 (0.29, 0.62)	<0.0001	6.82 (4.07, 11.43)	<0.0001
≥200 mg	1.19 (0.80, 1.78)	0.3825	0.31 (0.18, 0.54)	<0.0001	7.14 (4.00, 12.73)	<0.0001
Missing	4.52 (2.78, 7.37)	<0.0001	4.91 (2.98, 8.07)	<0.0001	N/A	N/A
Pain diagnosis type						
Arachnoiditis	1.31 (0.60, 2.86)	0.5028	1.77 (0.72, 4.35)	0.2136	0.87 (0.32, 2.36)	0.7828
Back pain	0.98 (0.76, 1.27)	0.9002	0.97 (0.72, 1.31)	0.8518	0.99 (0.71, 1.39)	0.9750
CRPS I	1.15 (0.87, 1.54)	0.3282	1.21 (0.86, 1.71)	0.2823	1.02 (0.70, 1.47)	0.9320
CRPS II	0.83 (0.64, 1.07)	0.1574	0.82 (0.60, 1.12)	0.2151	0.84 (0.61, 1.16)	0.2978
Chronic pain disorder	1.09 (0.91, 1.30)	0.3468	1.06 (0.86, 1.32)	0.5827	1.13 (0.90, 1.41)	0.2954
Degenerative disc disease	0.78 (0.60, 1.00)	0.0473	0.69 (0.51, 0.92)	0.0124	1.00 (0.72, 1.38)	0.9888
Epidural fibrosis	0.75 (0.33, 1.70)	0.4881	0.58 (0.20, 1.74)	0.3342	1.01 (0.38, 2.64)	0.9913
Limb pain	1.17 (0.97, 1.41)	0.0910	1.24 (0.98, 1.55)	0.0677	1.12 (0.88, 1.41)	0.3558
Post laminectomy syndrome	0.98 (0.82, 1.16)	0.7880	0.91 (0.74, 1.12)	0.3703	1.08 (0.87, 1.34)	0.4689
Peripheral neuropathy of extremities	1.32 (0.68, 2.58)	0.4130	1.31 (0.62, 2.77)	0.4850	1.46 (0.63, 3.39)	0.3737
Radiculopathy	1.20 (0.95, 1.53)	0.1312	1.20 (0.90, 1.61)	0.2070	1.15 (0.85, 1.56)	0.3576
History of spine surgeries	1.59 (1.15, 2.19)	0.0049	1.95 (1.32, 2.88)	0.0007	1.30 (0.88, 1.92)	0.1831
Other clinical conditions						
Alcohol abuse	2.32 (0.97, 5.57)	0.0585	3.92 (1.54, 9.94)	0.0041	1.39 (0.42, 4.65)	0.5937
Non-alcohol abuse (including opioid abuse)	1.41 (1.09, 1.81)	0.0077	1.19 (0.87, 1.62)	0.2800	1.63 (1.22, 2.19)	0.0011
Anxiety	1.13 (0.92, 1.38)	0.2512	1.20 (0.93, 1.54)	0.1539	1.06 (0.82, 1.36)	0.6722
Depression	0.98 (0.83, 1.16)	0.8262	0.83 (0.68, 1.02)	0.0812	1.14 (0.93, 1.41)	0.2076
Obesity	0.86 (0.68, 1.08)	0.1905	0.90 (0.68, 1.18)	0.4492	0.78 (0.58, 1.05)	0.0986
Psychosis	1.39 (0.87, 2.23)	0.1687	1.27 (0.70, 2.31)	0.4280	1.47 (0.84, 2.56)	0.1729
Smoking status	0.96 (0.77, 1.21)	0.7419	1.07 (0.81, 1.41)	0.6271	0.85 (0.64, 1.13)	0.2683
Baseline non-opioid medication						
Gabapentinoids	1.00 (0.84, 1.18)	0.9964	1.00 (0.81, 1.22)	0.9688	0.99 (0.80, 1.22)	0.9217
Benzodiazepines	0.84 (0.70, 1.02)	0.0718	0.77 (0.61, 0.96)	0.0195	0.94 (0.74, 1.19)	0.6089
Antidepressants	0.95 (0.79, 1.15)	0.6147	0.98 (0.78, 1.23)	0.8728	0.93 (0.73, 1.18)	0.5368
Skeletal muscle relaxants	0.88 (0.73, 1.06)	0.1693	0.78 (0.63, 0.98)	0.0296	0.97 (0.76, 1.22)	0.7740
Prescription level NSAID	1.23 (1.04, 1.46)	0.0131	1.18 (0.96, 1.44)	0.1112	1.36 (1.11, 1.67)	0.0036
Polypharmacy	0.88 (0.66, 1.19)	0.4188	0.81 (0.56, 1.18)	0.2796	0.89 (0.62, 1.28)	0.5335
Constant	1.08 (0.70, 1.67)	0.7187	1.20 (0.73, 1.98)	0.4781	0.10 (0.05, 0.19)	<0.0001

Note: *Among patients who did not discontinue opioids.
Abbreviations: OR, odds ratio; LCL, lower confidence limit; UCL, upper confidence limit; MME, morphine milligram equivalent.

Logistic regression on opioid discontinuation produced estimated odds ratios of discontinuation that decreased across increasing baseline MME DD categories (Table 3). Among patients with an MME DD of less than 20 mg at baseline, 37.1% reduced their dosage during follow up, versus 59.3% among those with a DD of 20–50 mg at baseline, 65.3% with a DD of 51–90 mg at baseline, 76.9% with a DD of 91–199 mg at baseline, and 76.5% with a DD of ≥200mg at baseline (Figure 2). Adjusting for confounders, logistic regression confirmed that patients with a higher baseline opioid MME DD

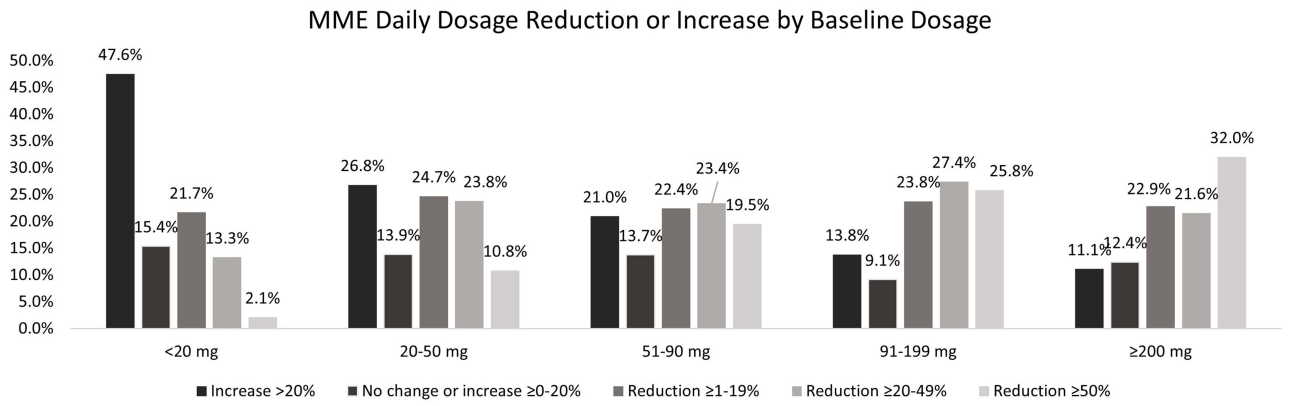

Figure 2 Morphine Milligram Equivalent (MME) Dose Reduction by Baseline MME Daily Dosage. The percent of patients experiencing changes in MME daily dose over the study period, stratified by baseline MME daily dose.

were more likely to reduce MME DD by ≥20% (p≤0.002), with estimated odds ratios increasing with baseline MME DD category (Table 3). Additionally, mean PDC decreased the most among patients with the highest baseline MME DD. Mean PDC decreased from 0.80 at baseline to 0.68 in year 3 for patients whose baseline MME DD was 91–199 mg (p<0.001) and decreased from 0.87 to 0.72 for those with a baseline DD of ≥200 mg (p<0.001) (Figure 3). A sensitivity analysis was conducted among patients whose baseline DD was >90 mg/day. Similar to the main findings, 61.3% of patients met the primary endpoint (discontinued or reduced DD by ≥20%), 19.5% reduced DD by 1–19%, 8.4% did not change or increased DD by 0–20%, and 10.8% increased DD by >20%.

Another sensitivity analysis was also conducted to assess opioid reduction among patients with ≥90 day supply of opioid prescriptions (N=2,006), which found that 51.3% of patients met the primary endpoint (discontinuation or DD reduction of ≥20%), 19.8% reduced DD by 1–19%, 10.7% increased DD by 0–20%, and 18.2% increased DD by >20%.

Non-opioid pain medication usage was observed to decline after initiating SCS therapy. Co-medication with benzodiazepines decreased from 47.9% at baseline to 30.3% at year 3 (p<0.001), co-medication with gabapentinoids reduced from 58.6% at baseline to 42.2% at year 3 (p<0.001), and polypharmacy dropped from 15.6% at baseline to 9.6% at year 3 (p<0.001) (Figure 4).

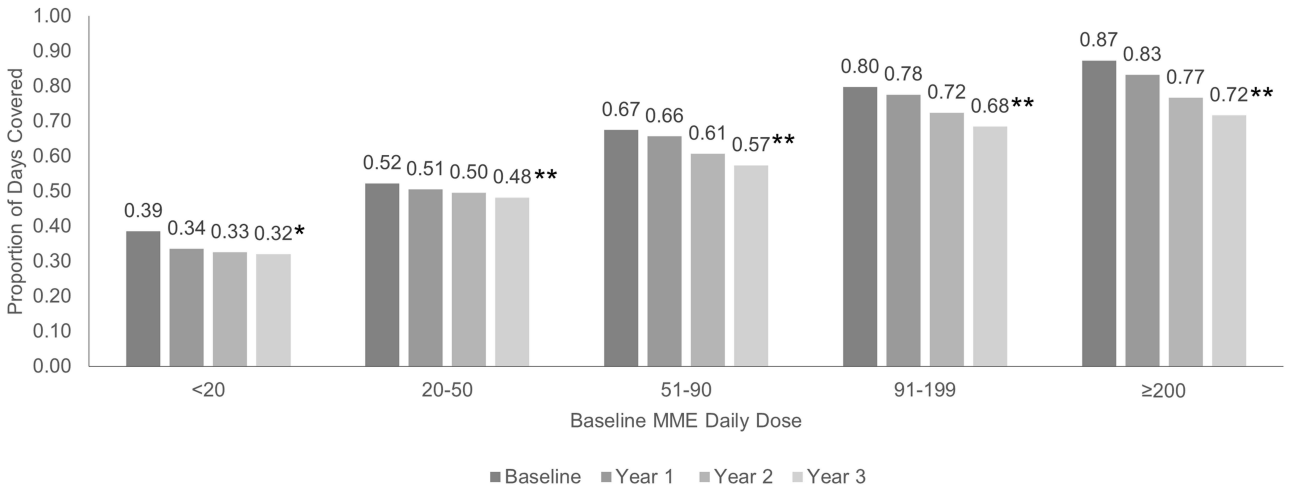

Figure 3 Proportion of Days Covered by Baseline Morphine Milligram Equivalent Daily Dosage. The proportion of days covered with statistical comparisons between baseline and year 3 (*p-value for change from baseline to year 3 = 0.001; **p-value for change from baseline to year 3 <0.001).

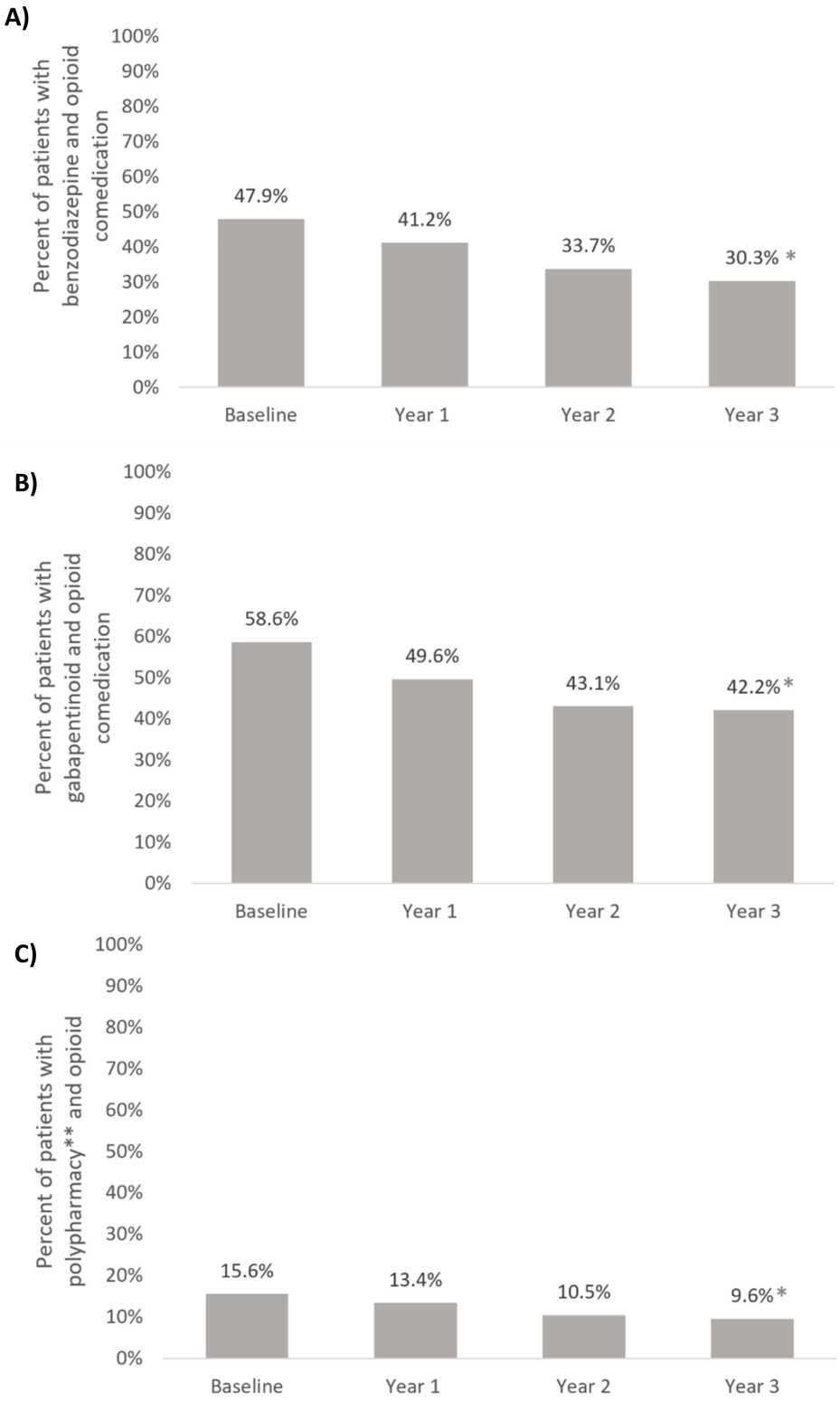

Figure 4 Co-Medication Trends. (**A**) The percent of patients with benzodiazepine co-medication with opioid. (**B**) The percent of patients with gabapentinoids co-medication with opioid. (**C**) The percent of patients with polypharmacy (defined as 4 or more medication classes in addition to an opioid). Includes statistical comparisons between baseline and year 3 (*p-value for change from baseline to year 3 <0.001).

Discussion

Over a 3-year follow-up of patients receiving SCS, 60% discontinued opioid use or reduced their average MME DD relative to baseline by at least 20%. Thirty-three percent of patients discontinued opioids, while an additional 27% experienced a clinically meaningful reduction in daily dose. An additional 15% reduced their average MME DD by less than 20%, while 8% remained the same or increased DD by 0–20%, and 15% increased DD by >20%. Patterns of discontinuation and dose reduction differed by baseline dosage. Patients with higher baseline dosages were less likely to discontinue opioids but were more likely to experience dose reductions. This is especially important given that the risk of adverse events (including overdose and death) increases with higher opioid doses.[17]

Co-medication with benzodiazepines or gabapentinoids, and polypharmacy also decreased among patients that received SCS. This is relevant given co-medication with benzodiazepines is more likely among those receiving a high opioid dose[18] and has been linked to a higher risk of overdose and death.[19] It has also been linked to higher risk of fracture among older adults.[20] In opioid overdose deaths, the most common non-opioid medications involved are benzodiazepines and antidepressants.[21]

Recent studies have explored the effect of SCS on opioid usage. Adil et al (2020)[11] observed at 1-year post-implant, 60.4% of patients had reduced opioid dose, including 34.2% with a dosage group reduction and 17.0% who discontinued. The authors observed that discontinuation was more likely in groups with lower pre-SCS opioid doses. In a study by Fraifeld et al with a 2-year follow-up, 22% of patients discontinued opioids, 20% reduced their dose by at least half, and 24.0% reduced their dose between 1% and 49%.[13] They further found that higher baseline dose was not associated with discontinuation. This 3-year study provides consistent results in which more than 60% of patients either discontinued or reduced opioid daily dose, and patients with higher dosages were less likely to discontinue opioid use but more likely to reduce their daily dose. A minimum clinically important difference in opioid dose has not been standardized 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. A threshold of a 20% reduction has previously been used.[22]

Patients with an SCS implant date of 2016 or later (versus before 2016) were more likely to meet the primary endpoint, which may be related to the impact of the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain.[22] The presence of an alcohol or non-alcohol abuse diagnosis was also associated with meeting the primary endpoint. Such a diagnosis in claims (indicating it was medically attended with a confirmed diagnosis) could mean patients sought help from their physicians for substance abuse and may have been placed into medically assisted treatment (MAT). Patients receiving MAT will typically receive medications (methadone, buprenorphine, naltrexone) along with counseling and behavioral therapy.[23] In addition, patient history of spine surgeries was associated with meeting the primary endpoint, which may reflect the potential pain reductions associated with SCS in patients with pain following spine surgery.

The strengths of this study include a geographically diverse sample across the US and multi-year follow-up. This analysis was restricted to patients who did not undergo a subsequent SCS device removal within 3 years of their implant to more closely estimate the impact of SCS therapy on opioid utilization among "responders." The definition of "responders" as patients with no explanation procedure is imperfect, but given the lack of pain or functional scores in claims data, it is the best available proxy.

The limitations of this study include those inherent to all retrospective claims analyses. The validity of medical claims data depends on coding accuracy and may omit some information from health encounters including disease severity and patient-reported outcomes, such as pain scores. In addition, prescriptions that are filled and paid for by means other than commercial insurance, such as cash/self-pay, are not accounted for in claims data. Therefore, estimates of systemic opioid dose reduction are sensitive to the proportion of patients not using their commercial insurance to fill their prescriptions. Further, days' supply of medication, which was used to calculate opioid usage and dosage, may not reflect the actual number of days opioids were taken by patients, and PDC is not a "true" measure of adherence because filling a prescription is not indicative of a patient using it as prescribed. Additionally, it is important to note that due to the observational study design, the results are correlational without a direct comparison/control group. The results from this study do not claim a causal relationship between SCS and opioid reduction. The identification of a comparison/control group would be unreliable in the MarketScan database for several reasons. First, it is difficult to identify two groups of patients with similar durations of chronic pain because we can only estimate the duration of pain using insurance claims

with chronic pain diagnoses. Additionally, severity of pain is not captured in claims. Nevertheless, the association between SCS and a reduction in opioid and other medication use, especially among patients with high use of opioids, suggests SCS may be an effective treatment option for patients with chronic pain.

Conclusions

A majority of patients who continued SCS therapy for at least 3 years were able to discontinue and/or reduce usage of systemic opioid and other pain-related medications. Opioid misuse is a significant issue in the US; reducing chronic pain may help reduce the need for pain-related medications within certain populations.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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