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Opioid Dependence and Associated Health Care Utilization and Cost in Traumatic Spinal Cord Injury Population: Analysis Using Marketscan Database

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Background: Postinjury pain is a well-known debilitating complication of spinal cord injury (SCI), often resulting in long-term, high-dose opioid use with the potential for dependence. There is a gap in knowledge about the risk of opioid dependence and the associated health care utilization and cost in SCI. **Objectives:** To evaluate the association of SCI with postinjury opioid use and dependence and evaluate the effect of this opioid dependence on postinjury health care utilization. **Methods:** Using the MarketScan Database, health care utilization claims data were queried to extract 7187 adults with traumatic SCI from 2000 to 2019. Factors associated with post-SCI opioid use and dependence, postinjury health care utilization, and payments were analyzed with generalized linear regression models. **Results:** After SCI, individuals were more likely to become opioid users or transition from nondependent to dependent users (negative change: 31%) than become nonusers or transition from dependent to nondependent users (positive change: 14%, $p < .0001$). Individuals who were opioid-dependent users pre-SCI had more than 30 times greater odds of becoming dependent after versus not (OR 34; 95% CI, 26-43). Dependent users after injury (regardless of prior use status) had 2 times higher utilization payments and 1.2 to 6 times more health care utilization than nonusers. **Conclusion:** Opioid use and dependence were associated with high health care utilization and cost after SCI. Pre-SCI opioid users were more likely to remain users post-SCI and were heavier consumers of health care. Pre- and postopioid use history should be considered for treatment decision-making in all individuals with SCI. **Key words:** *cost, health care utilization, opioid dependence, opioid use, traumatic spinal cord injury*

Introduction

One of the most prevalent secondary complications of spinal cord injury (SCI) is pain. While the exact prevalence of pain in SCI populations remains under debate, it is estimated to affect anywhere from 33% to 80% of individuals with SCI[1,2] compared to only approximately 20.4% of people in the general population.[3] Of those experiencing pain, about half will have musculoskeletal pain, half will have neuropathic pain, and a small number will experience visceral pain.[4] Neuropathic pain, described as shocklike, sharp, and burning,[5] is challenging to treat and greatly impacts health-related quality of life.[6]

Despite gains in managing other secondary complications of SCI, pain has been documented to be one of the complications refractory to methods of management.[7] Pharmacological management of pain post-SCI includes analgesics, nonsteroidal anti-inflammatory drugs, anticonvulsants, antidepressants, opioids, and intrathecal morphine.[5] Previous studies have argued that long-term pain of any kind does not respond well to opioids.[8] Despite this, Hand and colleagues[9] have found that,

Supplementary material: This article contains supplementary digital material (eTables 1 and 2).

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compared to matched non-SCI controls, individuals with SCI are more likely to be long-term users of short-acting opioids and to be taking higher doses of long-acting opioids. Because preoperative opioid use is consistently a great predictor of long-term postoperative use, it is reasonable to assume that the increased use of opioids in the SCI population may lead to opioid dependence and overdose.[10] Additionally, persons with SCI may be at greater baseline risk for substance use disorders compared with non-SCI individuals,[9,11] potentially due to the fact that, in SCI, most medications do not work and opioids provide relief, albeit temporary.[7]

Given the declaration of a public health emergency in response to the opioid crisis in the United States, discussions have evolved in the ambulatory pain population regarding opioids. However, even though there continues to be a scarcity of debate over the use of opioids in SCI, there is an increasing body of research advocating minimizing the use of opioids in SCI due to their lack of efficacy and the associated risks linked to the worsening of already known issues affecting individuals with SCI, including constipation, urinary retention, decreased recovery, and respiratory depression with the risk of death.[2,4] Current guidelines of pain management do not recommend opioids as a first-line treatment.[12] In the present study, we aim to contribute to this conversation by evaluating the association of SCI with postinjury opioid use and predictors of opioid dependence following SCI. Thus, we hypothesized that injury is more likely to be associated with opioid use than not (Hypothesis 1) and that those who are opioid users prior to injury are more likely to remain users postinjury (Hypothesis 2). We also evaluated the effect of opioid dependence on postinjury health care utilization and costs. We hypothesized that opioid users have higher health care utilization and costs (Hypothesis 3).

Materials and Methods

Data source

IBM MarketScan Research Database was used for this study. MarketScan is a de-identified health care research claims database with medical, drug, and dental claims for more than 265 million individuals. It includes demographics, insurer, diagnosis, and procedures as well as payments of health care services including but not limited to inpatient, outpatient, and outpatient drugs.[13] Data represent the private sector sponsored insurance enrollees' trajectories through the health care system; for each person, a unique identifier links different files. Therefore, it is suitable for studying patients' health care utilization longitudinally. The data represent people with private sector insurance (private/commercial insurance, Medicare supplemental plans, Medicaid plans run by private insurance). These data have been used in studies evaluating SCI outcomes.[9,14-18] In this study, we used data spanning the years 2000-2019.

Patient selection and follow-up

We analyzed opioid dependence and health care utilization for the traumatic SCI population. International Classification of Diseases, Ninth Revision (ICD-9) code 806.0-806.3 and Tenth Revision (ICD-10) (S14.0, S14.1) + S12, (S24.0, S24.1) + S22.0 were used for traumatic SCI with cervical or thoracic injury. The first occurrence in inpatient files was taken as the index hospitalization.

We included adult patients 18 years old and older with at least 12 months of look-back and 15 months of follow-up ($N = 7187$). Pre-SCI look-back time was calculated as the difference between the enrollment start date and the index hospitalization admission date; post-SCI follow-up time was calculated as the difference between the index hospitalization discharge date and the enrollment end date. If the start and end enrollment dates were missing, the dataset's first and last claim dates were used instead. To ensure an injury incident cohort, those with any claim of SCI or paralysis in the look-back period were excluded.

We evaluated opioid use and dependence for both pre- and post-SCI. Pre-SCI opioid dependence was defined 12 months before index admission. Post-SCI opioid dependence was defined from the beginning of month 4 to the end of month 15 after index discharge. The first 3 months directly following injury discharge were skipped as opioids are expected to be used in this acute phase. We classified individuals with SCI into three opioid dependence groups: none, nondependent user, and dependent user. An individual was classified as a "dependent user" if there was a claim code

of opioid use disorder (ICD-9 304.00-304.02, 304.70-304.72, 305.40-305.52, ICD-10 F11), a prescription drug for opioid use disorder (buprenorphine or naltrexone), being counseled about psychological and pharmacologic treatment options for opioid addiction (CPT-4 4306F),[19] or at least 11 or prescription refills[20,21] of opioid drugs (butorphanol, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine, nalbuphine, opium, oxycodone, oxymorphone, pentazocine, propoxyphene, tapentadol, tramadol). If there was no claim for opioid use disorder, but the individual had one to ten opioid prescription drug refills, they were classified as "nondependent user." The rest were classified in the "none" group. Depending on the use pre- and post-SCI, we obtained nine groups of opioid use and dependence transition: (1) prior nonusers who remained nonusers (N-N), (2) prior nonusers who became nondependent users (N-ND), (3) prior nonusers who became dependent users (N-D), (4) prior nondependent users who became nonusers (ND-N), (5) prior nondependent users who remained nondependent users (ND-ND), (6) prior nondependent users who became dependent users (ND-D), (7) prior dependent users who became nonusers (D-N), (8) prior dependent users who became nondependent users (D-ND), and (9) prior dependent users who remained dependent (D-D).[22,23]

Individual characteristics

Individuals' demographics, in MarketScan data, include age, gender, and insurance type (commercial, Medicaid, or Medicare supplemental). The individual burden of comorbidities was captured in the index hospitalization with the Elixhauser score[24] using Quan et al.'s adaptation to ICD-9 and ICD-10 codes.[25] We also listed eight common comorbidities individually: tobacco use, osteoporosis, hypertension, congestive heart failure, chronic obstructive pulmonary disease (COPD), myocardial infarction, diabetes, and obesity. The level of injury and whether decompression was performed or not were also noted. Post-SCI, data were screened for pain within 3 months of index hospitalization discharge and 3 to 15 months after the study period. ICD-9 729.2 and ICD-10 M54.10, M79.2 were used to identify the presence of neuropathic pain; ICD-9 729.1 and ICD-10 M60.9, M79.1, M79.7 were used for musculoskeletal pain; and ICD-9 789.00 and ICD-10 R10.9 were used for visceral pain.

Opioid use transition pre- and post-SCI

The transition to new use or higher opioid use (negative change) versus transition to lower use or no use (positive change) following injury was evaluated by comparing the probabilities of both transitions.

Risk of post-SCI opioid use and dependence

The association of pre-SCI opioid use and dependence with post-SCI opioid use and dependence was evaluated. The association of the individuals' characteristics described previously with post-opioid use and dependence was also explored.

Health care utilization and cost outcomes

We looked at health care utilization outcomes, including length of stay (LOS), associated hospital payment, and home discharge. We also looked at all-type hospital readmission, outpatient services, outpatient medication refills, and associated payments within 3 months of injury hospitalization discharge and 4 to 15 months of follow-up. Inflation adjustments to 2019 US dollars were made for payments using the medical component of the consumer price index (accessible through the United States Bureau of Labor Statistics website).[26]

Statistical analysis

Continuous variables were summarized with means and standard deviations, median and interquartile ranges, and the full range (minimum to maximum) and compared across groups using Kruskal-Wallis tests because they were all found not to be normally distributed per the Kolmogorov-Smirnov test. Categorical variables were summarized with counts and percentages and compared across groups using chi-square tests.

The pre- to post-SCI opioid use transitions (Hypothesis 1) were evaluated with a generalized McNemar test. The effect of pre-SCI opioid use

dependence and individuals' characteristics on post-SCI opioid use and dependence (Hypothesis 2) was evaluated with multinomial logistic regression. Health care utilization and cost outcomes were further compared between opioid use groups (Hypothesis 3) with multivariable generalized linear models, including all individual baseline characteristics as fixed factors in addition to the opioid analysis group. For the LOS and payments, the models were linear regressions on log-transformed values. For the number of admissions, services, and medication refills, negative binomial regression models were used. For hospital readmission (yes/no) and emergency room visit (yes/no), logistic regression models were used. These models' linear contrasts, representing different 2-by-2 group comparisons, were built on the treatment variable. Comparison estimates were presented in terms of estimate ratio (ER) for continuous, relative risk (RR) for the count, and odds ratio (OR) as appropriate, with associated 95% confidence intervals (CI) as a measure of precision. Model assumptions (residuals' independence, homoscedasticity, and normality) were evaluated.

All tests were two-sided with a significance level of .02 (=.05/25, Bonferonni family rate adjustment[27] of 25 tests and models, 1 test in Hypothesis 1, 1 model in Hypothesis 2, and 23 models in Hypothesis 3). SAS 9.4 (SAS Institute, Inc, Cary, NC) was used for data preprocessing and statistical analysis.

Results

Demographics, medical conditions, injury characteristics, and preinjury opioid use

The study cohort was comprised of 54% males with an average age of 54 (*SD* 21 years), mostly with commercial insurance (50%). At the time of injury, 31% had no comorbidities. The majority suffered a cervical injury (56%), and one-third of the cases underwent decompression. Within 3 months of injury hospitalization discharge, 10% had a pain claim, and 22% had a pain claim by 15 months. Cohort characteristics are in **Table 1**.

Opioid dependence transition pre- to postinjury and risk of postinjury dependence

Twelve months before SCI hospitalization, 14% were opioid-dependent users (**Figure 1A**). After the acute treatment of SCI (3 months), the rate of opioid-dependent users had almost doubled (26%). More individuals transitioned into a more dependent group than a less dependent group (31% vs. 14%, p <.0001). Prior dependent users had 34 times greater odds of remaining opioid dependent and 4.5 times greater odds of becoming nondependent opioid users versus nonopioid users (**Table 2**). Factors associated with higher odds of opioid dependence and nondependence use were prior opioid use (1.4-34 times higher odds; **Table 2, Figure 1B**), younger age (1% lower odds of each year older), type of insurance (higher odds for Medicaid/Medicare vs. commercial), injury level (1.1-1.4 higher odds for thoracic vs. cervical), surgery (1.21-1.32 higher odds for those who underwent decompression), and presence of pain (1.7-3.1 higher odds diagnosis of pain vs. not).

Pre- to postinjury opioid use and dependence groups

Nonusers who remained nonusers comprised 34% of the cohort. Ten percent were prior dependent users who remained dependent users. A total of 24% were nonusers and became users (15% dependent or 9% nondependent). Additionally, 1% of dependent users and 10% of nondependent users became nonusers. The distribution of pre- to postinjury opioid use is shown in **Figure 2A**. Individuals in different pre- to postinjury opioid use groups were statistically different in demographics, number of comorbidities, injury characteristics, and postinjury pain (eTable 1).

Health care utilization and payment associated with opioid use and dependence

The median LOS during the index hospitalization was 6 days, with a median payment of $42,282. The hospital readmission rate for the general cohort was 21%. Within 3 months of index hospital discharge, emergency room visit rate was 30%, with a median of six visits for admitted patients. The median number of outpatient services was 32 and that of prescribed medications was eight. Overall payments per individual in those 3 months had a median payment of $6733. The median cumulative payments over months 3 to 15 after injury was $15,521. Outcomes are presented in eTable 2.

Table 1. Demographics for prior and post-SCI opioid use

				Post-SCI opioid							
			Combined total = 7187	None [1] 3299 (46%)	Opioid user [2] 3888 (54%)	p-value [1] vs [2]	Non-dependent user [3] 1993 (28%)	Dependent user [4] 1895 (26%)	p-value [4] vs [3]	p-value [3] vs [1]	p-value [4] vs [1]
Demographics	Age	Mean (SD)	54 (21)	55 (22)	52 (21)		54 (22)	51 (20)			
		Median (IQR)	54 (37, 71)	56 (39, 74)	53 (36, 68)	<.0001	55 (36, 71)	52 (36, 63)	0.0002	0.0209	<.0001
		Range, min-max	18 to 100	18 to 100	18 to 98		18 to 98	18 to 97			
	Sex	Male, n (%)	3849 (54%)	1850 (56%)	1999 (51%)	<.0001	1026 (51%)	973 (51%)	0.9331	0.0011	0.001
		Female, n (%)	3338 (46%)	1449 (44%)	1889 (49%)		967 (49%)	922 (49%)			
	Insurance	Commercial, n (%)	3623 (50%)	1791 (54%)	1832 (47%)		1015 (51%)	817 (43%)			
		Medicaid, n (%)	1571 (22%)	548 (17%)	1023 (26%)	<.0001	366 (18%)	657 (35%)	<.0001	0.0513	<.0001
		Medicare, n (%)	1993 (28%)	960 (29%)	1033 (27%)		612 (31%)	421 (22%)			
	Elixhauser Index	0, n (%)	2256 (31%)	1068 (32%)	1188 (31%)		685 (34%)	503 (27%)			
		1, n (%)	2158 (30%)	993 (30%)	1165 (30%)	0.2331	583 (29%)	582 (31%)	<.0001	0.4002	<.0001
		2, n (%)	1441 (20%)	633 (19%)	808 (21%)		385 (19%)	423 (22%)			
		3+, n (%)	1332 (19%)	605 (18%)	727 (19%)		340 (17%)	387 (20%)			
	Comorbidities	Tobacco use, n (%)	813 (11%)	317 (10%)	496 (13%)	<.0001	194 (10%)	302 (16%)	<.0001	0.8813	<.0001
		Osteoporosis, n (%)	511 (7%)	239 (7%)	272 (7%)	0.6826	142 (7%)	130 (7%)	0.7463	0.8704	0.6036
		Hypertension, n (%)	2465 (34%)	1150 (35%)	1315 (34%)	0.3561	648 (33%)	667 (35%)	0.077	0.0809	0.8053
		Congestive Heart Failure, n (%)	507 (7%)	215 (7%)	292 (8%)	0.1013	156 (8%)	136 (7%)	0.4417	0.0705	0.3619
		COPD, n (%)	997 (14%)	411 (12%)	586 (15%)	0.0014	260 (13%)	326 (17%)	0.0003	0.5338	<.0001
		Myocardial Infarction, n (%)	233 (3%)	103 (3%)	130 (3%)	0.5973	64 (3%)	66 (3%)	0.6377	0.8575	0.4806
		Diabetes, n (%)	967 (13%)	424 (13%)	543 (14%)	0.168	276 (14%)	267 (14%)	0.8283	0.3	0.2062
		Obesity, n (%)	243 (3%)	94 (3%)	149 (4%)	0.0216	65 (3%)	84 (4%)	0.0572	0.3949	0.0025
		At least one of the above, n (%)	4001 (56%)	1791 (54%)	2210 (57%)	0.03	1074 (54%)	1136 (60%)	0.0001	0.7769	<.0001
Injury & Surgery	Injury Level	Cervical, n (%)	4031 (56%)	1973 (60%)	2058 (53%)	<.0001	1079 (54%)	979 (52%)	0.1219	<.0001	<.0001
		Thoracic, n (%)	3156 (44%)	1326 (40%)	1830 (47%)		914 (46%)	916 (48%)			
	Decompression	No, n (%)	4772 (66%)	2224 (67%)	2548 (66%)	0.0928	1383 (69%)	1165 (61%)	<.0001	0.1344	<.0001
		Yes, n (%)	2415 (34%)	1075 (33%)	1340 (34%)		610 (31%)	730 (39%)			
Post SCI pain	Within 3 months of injury	Neuropathic pain, n (%)	145 (2%)	56 (2%)	89 (2%)	0.0755	31 (2%)	58 (3%)	0.0017	0.6938	0.0012
		Myopathic pain, n (%)	162 (2%)	38 (1%)	124 (3%)	<.0001	47 (2%)	77 (4%)	0.0025	0.0007	<.0001
		Visceral pain, n (%)	458 (6%)	145 (4%)	313 (8%)	<.0001	127 (6%)	186 (10%)	<.0001	0.0016	<.0001
		At least one of the above, n (%)	728 (10%)	230 (7%)	498 (13%)	<.0001	195 (10%)	303 (16%)	<.0001	0.0003	<.0001
	Within 3-15 months after injury	Neuropathic pain, n (%)	320 (4%)	101 (3%)	219 (6%)	<.0001	84 (4%)	135 (7%)	<.0001	0.0269	<.0001
		Myopathic pain, n (%)	424 (6%)	102 (3%)	322 (8%)	<.0001	110 (6%)	212 (11%)	<.0001	<.0001	<.0001
		Visceral pain, n (%)	1054 (15%)	305 (9%)	749 (19%)	<.0001	284 (14%)	465 (25%)	<.0001	<.0001	<.0001
		At least one of the above, n (%)	1597 (22%)	456 (14%)	1141 (29%)	<.0001	440 (22%)	701 (37%)	<.0001	<.0001	<.0001

Note: Nondependent user group includes individuals with one to nine prescriptions in 12 months. Dependent users are those with 10 or more prescriptions or prescriptions of opioid disorder or psychological counseling for opioid addiction in 12 months. COPD = chronic obstructive pulmonary disease.

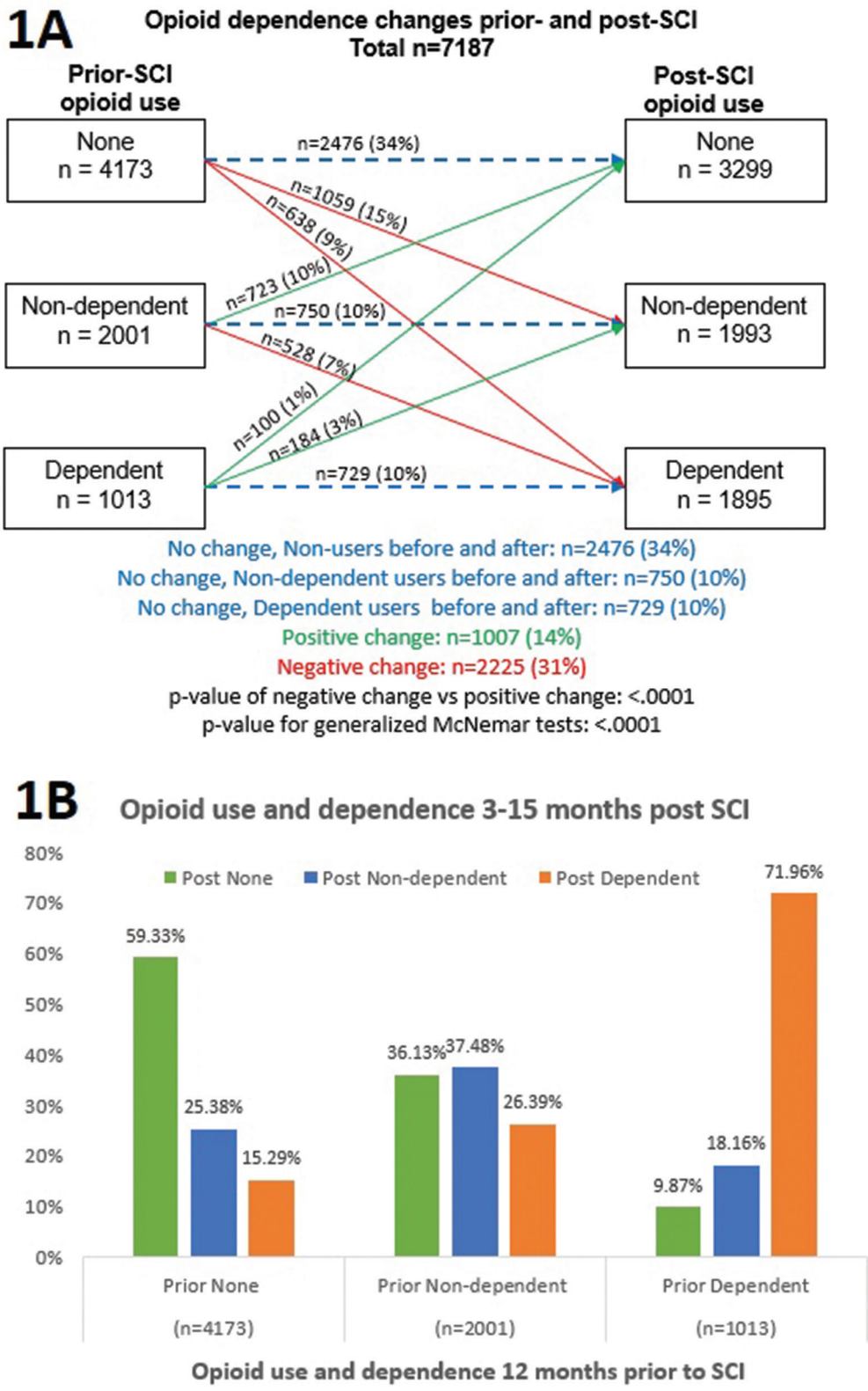

Figure 1. (A) Transition chart between opioid use 12 months preinjury to months 3 to 15 postinjury. (B) Postinjury opioid use and dependence relative to preinjury opioid use and dependence.

Table 2. The risk of postinjury opioid dependence relative to pre-injury opioid use, demographics, medical conditions, injury level, treatment, and diagnosis of postinjury pain

Variables		Post-SCI Opioid non-dependent vs None Odds Ratio (95% CI)	Post-SCI Opioid dependent vs None Odds Ratio (95% CI)	Post-SCI Opioid dependent vs non-dependent Odds Ratio (95% CI)
Prior opioid	Non-dependent user vs None	2.511 (2.207, 2.857)	3.432 (2.947, 3.998)	1.367 (1.17, 1.597)
	Dependent user vs None	4.518 (3.49, 5.849)	33.699 (26.516, 42.827)	7.459 (6.093, 9.131)
	Dependent user vs Non-dependent	1.799 (1.379, 2.347)	9.804 (7.692, 12.5)	5.464 (4.464, 6.667)
Age	1-year increment	0.987 (0.983, 0.992)	0.985 (0.98, 0.989)	0.997 (0.992, 1.002)
Gender	female vs male	1.08 (0.957, 1.219)	0.891 (0.775, 1.024)	0.825 (0.715, 0.951)
Insurance	Medicaid vs commercial	1.127 (0.958, 1.326)	2.193 (1.854, 2.594)	1.945 (1.634, 2.316)
	Medicare vs commercial	1.443 (1.19, 1.75)	1.147 (0.917, 1.435)	0.795 (0.63, 1.002)
Elixhauser index	1 vs 0	0.909 (0.783, 1.055)	1.113 (0.936, 1.324)	1.225 (1.025, 1.464)
	2 vs 0	0.971 (0.815, 1.157)	1.214 (0.994, 1.483)	1.25 (1.019, 1.535)
	3+ vs 0	0.89 (0.737, 1.075)	1.018 (0.819, 1.264)	1.144 (0.916, 1.429)
Comorbidities	yes vs no	0.954 (0.831, 1.094)	0.933 (0.797, 1.093)	0.979 (0.832, 1.152)
Injury Level	Thoracic vs Cervical	1.145 (1.019, 1.288)	1.379 (1.205, 1.577)	1.204 (1.048, 1.382)
Decompression	yes vs no	0.917 (0.807, 1.043)	1.209 (1.048, 1.394)	1.318 (1.136, 1.529)
Post SCI pain	yes vs no	1.736 (1.495, 2.016)	3.124 (2.675, 3.648)	1.8 (1.545, 2.096)

All outcomes considered, home discharge, postdischarge health care utilization, and payments were statistically different in unadjusted comparisons across the different pre-post opioid use groups (eTable 2). Postinjury health care utilization payments were highest among those who became dependent users. Towards month 15, payments were comparable for dependent users regardless of prior history (**Figure 2B**). In adjusted comparisons (**Table 3**), nonusers who became users had lower odds of home discharge from index hospitalization and higher utilization and payments throughout compared to nonusers before and after. Dependent users after injury (N-D, ND-D, D-D) had about two times the utilization payments than those whose who were nonusers pre and post (N-N). Dependent users before and after (D-D) had 1.2 to 6 times more health care utilization than nonusers before and after (N-N).

Discussion

It is common practice to prescribe opioids to alleviate pain after SCI. However, an increasing body of research advocates for the avoidance of prescribing these powerful medications for pain management after SCI.[4] The findings of our study indicate that patients with SCI are more likely to transition toward opioid use and dependence than toward less and no use. More importantly, individuals who used opioids before SCI were more likely to remain opioid users after the injury. Factors associated with postinjury opioid-dependent or nondependent use were young age, commercial insurance type, diagnosis of postinjury pain, and surgical treatment. Post-SCI opioid-dependent users had the highest health care utilization and expenditures, followed by opioid nondependent users.

In our study, 42% were opioid users (28% nondependent, 14% dependent) within 12 months before SCI, and 54% were opioid users (28% nondependent, 26% dependent) within 3 to 15 months after the injury. Using two state databases in South Carolina (n = 503), DiPiro et al.[28] reported an opioid use incidence of 53.5% in years 2 and 3 after injury; we found the same incidence. Another study, using population-level administrative data in Canada, reported that 35% of 1842 individuals with traumatic SCI had at least one opioid prescription.[29] The discordance of this study with our data might be due to the differences in the samples; our study only included cervical and thoracic injuries whereas theirs included all injury levels.

We found that, after SCI, individuals were more likely to make a negative change (i.e., from nonuser to nondependent/dependent user or from

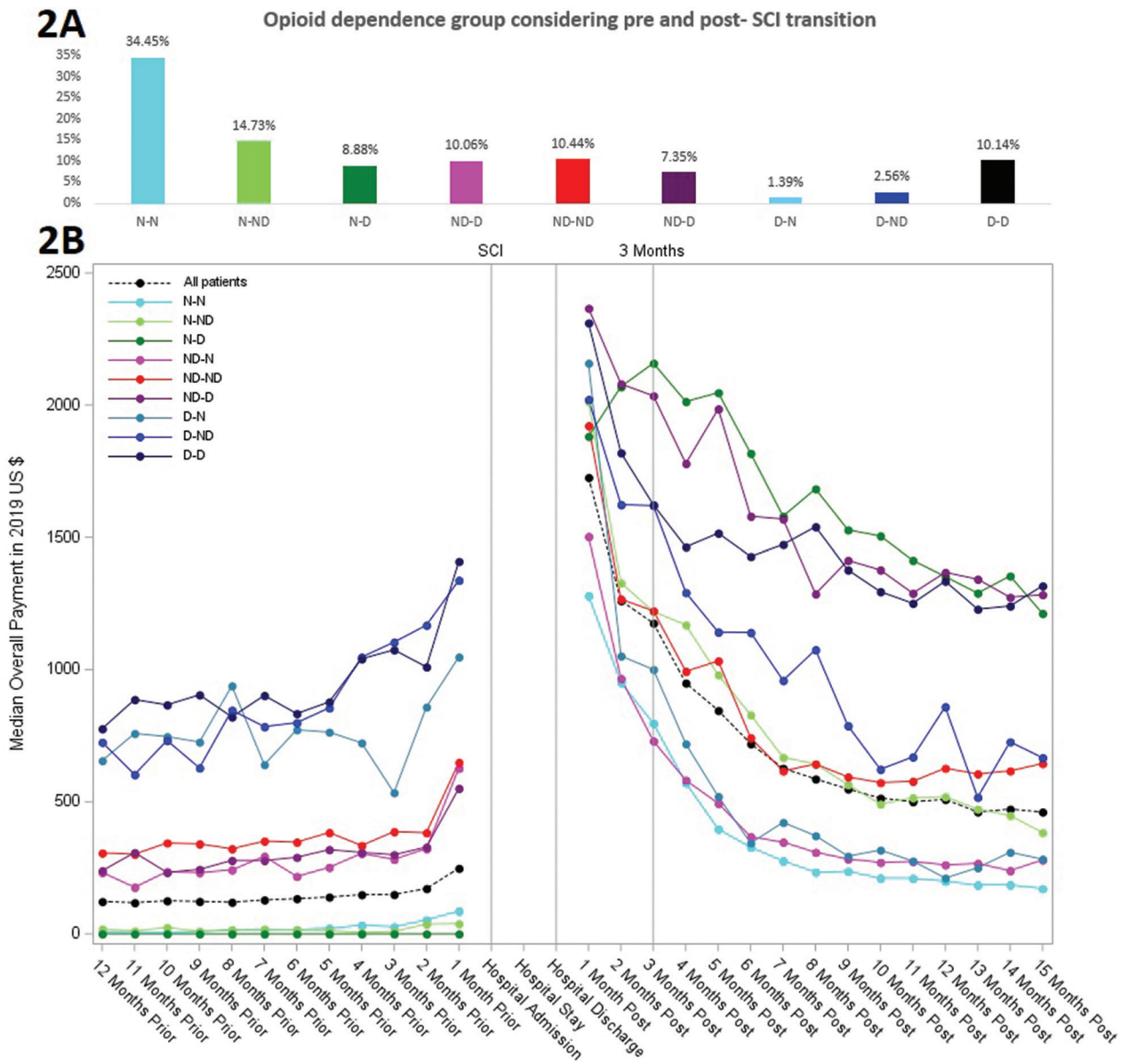

Figure 2. The pre- and post-SCI opioid dependence groups are defined as: (1) prior nonusers who remained nonusers (N-N), (2) prior nonusers who became nondependent users (N-ND), (3) prior nonusers who became dependent users (N-D), (4) prior nondependent users who became nonusers (ND-N), (5) prior nondependent users who remained nondependent users (ND-ND), (6) prior nondependent users who became dependent users (ND-D), (7) prior dependent users who became nonusers (D-N), (8) prior dependent users who became nondependent users (D-ND), and (9) prior dependent users who remained dependent (D-D). (A) Pre- and postinjury opioid use and dependence groups. (B) Health care utilization payments pre- and postinjury. Prior to SCI, those who were not opioid users had the lowest cost, followed by nondependent opioid users; dependent opioid users had the highest cost. Post-SCI, those who became users had the highest costs, especially prior nonusers.

Table 3. Outcome-adjusted comparison among opioid dependency groups

		Opioid dependency before and after SCI								
		N-N [1]	N-ND [2]	N-D [3]	ND-N [4]	ND-ND [5]	ND-D [6]	D-N [7]	D-ND [8]	D-D [9]
Outcomes		2476 (34%)	1059 (15%)	638 (9%)	723 (10%)	750 (10%)	528 (7%)	100 (1%)	184 (3%)	729 (10%)
Index hospital	Length of stay, ER (95% CI)	Reference	1.203 (1.123, 1.29)	1.662 (1.525, 1.811)	0.863 (0.796, 0.935)	0.987 (0.911, 1.068)	1.372 (1.252, 1.502)	0.986 (0.813, 1.196)	1.021 (0.883, 1.18)	1.036 (0.956, 1.124)
	Payment, ER (95% CI)	Reference	1.18 (1.076, 1.295)	1.943 (1.731, 2.18)	0.871 (0.783, 0.968)	0.986 (0.887, 1.096)	1.261 (1.117, 1.425)	0.779 (0.601, 1.008)	0.82 (0.676, 0.994)	0.95 (0.852, 1.06)
	Discharge home, OR (95% CI)	Reference	0.861 (0.743, 0.998)	0.523 (0.434, 0.63)	1.284 (1.08, 1.527)	1.131 (0.954, 1.341)	0.838 (0.691, 1.016)	1.075 (0.713, 1.618)	1.455 (1.061, 1.994)	1.203 (1.012, 1.431)
3-months post discharge	Emergency Room admissions									
	Admitted, OR (95% CI)	Reference	1.194 (0.971, 1.468)	1.911 (1.533, 2.383)	0.96 (0.729, 1.264)	1.406 (1.088, 1.819)	2.054 (1.605, 2.629)	1.347 (0.773, 2.345)	1.952 (1.283, 2.968)	2.311 (1.843, 2.898)
	#admissions (admitted), RR (95%CI)	Reference	1.165 (0.98, 1.385)	0.985 (0.834, 1.163)	0.987 (0.779, 1.249)	1.234 (1.004, 1.519)	1.271 (1.054, 1.532)	1.474 (0.959, 2.266)	0.954 (0.696, 1.308)	1.401 (1.186, 1.654)
	Payments (admitted), ER (95% CI)	Reference	1.364 (1.062, 1.75)	1.682 (1.315, 2.15)	1.369 (0.984, 1.905)	1.632 (1.203, 2.214)	1.658 (1.268, 2.168)	1.378 (0.735, 2.583)	1.198 (0.76, 1.888)	1.774 (1.39, 2.264)
	Hospital admissions									
	Admitted, OR (95% CI)	Reference	1.516 (1.261, 1.822)	2.588 (2.111, 3.173)	1.028 (0.811, 1.305)	1.37 (1.099, 1.709)	2.292 (1.836, 2.86)	1.115 (0.645, 1.928)	1.604 (1.1, 2.34)	1.796 (1.458, 2.212)
	#admissions (admitted), RR (95%CI)	Reference	0.993 (0.868, 1.136)	1.072 (0.936, 1.228)	0.915 (0.758, 1.104)	0.952 (0.805, 1.126)	1.143 (0.986, 1.324)	0.88 (0.569, 1.362)	1.016 (0.772, 1.336)	1.012 (0.872, 1.175)
	Payments (admitted), ER (95% CI)	Reference	1.068 (0.861, 1.324)	1.745 (1.394, 2.185)	1.213 (0.91, 1.617)	1.053 (0.808, 1.372)	1.346 (1.05, 1.724)	0.402 (0.207, 0.781)	0.865 (0.558, 1.342)	0.917 (0.717, 1.172)
	Outpatient services									
	# services, RR (95% CI)	Reference	1.111 (1.04, 1.187)	1.267 (1.168, 1.374)	0.955 (0.885, 1.03)	1.122 (1.041, 1.209)	1.341 (1.231, 1.462)	1.22 (1.017, 1.463)	1.136 (0.991, 1.302)	1.199 (1.111, 1.295)
	Payments, ER (95% CI)	Reference	1.398 (1.258, 1.553)	1.84 (1.615, 2.096)	0.893 (0.792, 1.007)	1.175 (1.042, 1.325)	1.859 (1.62, 2.135)	1.265 (0.946, 1.693)	1.26 (1.013, 1.566)	1.382 (1.221, 1.564)
	Medication refills									
	# refills, ER (95% CI)	Reference	2.07 (1.909, 2.244)	2.82 (2.554, 3.114)	1.827 (1.665, 2.005)	2.456 (2.242, 2.69)	3.377 (3.043, 3.747)	1.956 (1.568, 2.442)	3.149 (2.672, 3.71)	4.171 (3.802, 4.575)
	Payments, ER (95% CI)	Reference	1.482 (1.304, 1.684)	2.493 (2.131, 2.916)	1.377 (1.194, 1.589)	1.954 (1.699, 2.248)	3.307 (2.814, 3.887)	1.7 (1.171, 2.467)	2.835 (2.226, 3.611)	4.223 (3.653, 4.881)
	Overall payments, median (IQR)	Reference	1.672 (1.489, 1.877)	3.011 (2.609, 3.475)	1.067 (0.935, 1.217)	1.464 (1.283, 1.671)	2.686 (2.308, 3.126)	1.261 (0.916, 1.736)	1.815 (1.43, 2.305)	1.977 (1.725, 2.266)
3-15 months post discharge	Emergency Room admissions									
	Admitted, OR (95% CI)	Reference	1.75 (1.45, 2.112)	2.669 (2.137, 3.334)	0.877 (0.678, 1.135)	2.282 (1.802, 2.89)	3.049 (2.378, 3.908)	1.13 (0.656, 1.948)	2.754 (1.799, 4.215)	3.149 (2.5, 3.968)
	#admissions (admitted), RR (95%CI)	Reference	1.029 (0.889, 1.191)	1.387 (1.19, 1.616)	1.019 (0.814, 1.276)	1.088 (0.914, 1.295)	1.51 (1.281, 1.781)	2.186 (1.455, 3.285)	1.304 (0.993, 1.714)	1.788 (1.538, 2.079)
	Payments (admitted), ER (95% CI)	Reference	1.221 (1.013, 1.472)	1.565 (1.294, 1.893)	1.188 (0.897, 1.574)	1.329 (1.06, 1.666)	1.719 (1.396, 2.117)	1.907 (1.114, 3.266)	1.417 (1.004, 1.998)	2.189 (1.803, 2.658)
	Hospital admissions									
	Admitted, OR (95% CI)	Reference	1.873 (1.58, 2.22)	3.211 (2.633, 3.915)	0.705 (0.561, 0.887)	1.833 (1.518, 2.212)	2.442 (1.982, 3.01)	1.026 (0.633, 1.663)	2.033 (1.466, 2.819)	2.764 (2.294, 3.331)
	#admissions (admitted), RR (95%CI)	Reference	0.952 (0.853, 1.062)	1.138 (1.022, 1.267)	0.943 (0.793, 1.122)	1.054 (0.936, 1.187)	1.246 (1.113, 1.395)	1.107 (0.819, 1.498)	1.03 (0.848, 1.25)	1.169 (1.054, 1.296)
	Payments (admitted), ER (95% CI)	Reference	1.033 (0.856, 1.248)	1.223 (1, 1.494)	0.922 (0.7, 1.216)	1.07 (0.872, 1.313)	1.322 (1.066, 1.639)	0.927 (0.533, 1.613)	1.113 (0.797, 1.555)	1.104 (0.913, 1.336)
	Outpatient services									
	# services, RR (95% CI)	Reference	1.345 (1.248, 1.449)	1.893 (1.726, 2.076)	0.973 (0.893, 1.059)	1.34 (1.232, 1.458)	1.823 (1.655, 2.009)	1.482 (1.206, 1.82)	1.31 (1.123, 1.528)	1.603 (1.47, 1.748)
	Payments, ER (95% CI)	Reference	1.788 (1.608, 1.988)	3.123 (2.737, 3.563)	0.914 (0.808, 1.034)	1.655 (1.466, 1.868)	2.845 (2.475, 3.27)	1.252 (0.921, 1.701)	1.693 (1.359, 2.109)	2.107 (1.859, 2.387)
	Medication refills									
	# refills, RR (95% CI)	Reference	2.396 (2.201, 2.608)	4.886 (4.397, 5.429)	1.642 (1.489, 1.81)	2.624 (2.384, 2.888)	4.934 (4.417, 5.511)	1.607 (1.271, 2.031)	2.846 (2.39, 3.388)	5.31 (4.807, 5.866)
	Payments, ER (95% CI)	Reference	1.416 (1.241, 1.615)	4.843 (4.127, 5.684)	1.387 (1.187, 1.619)	2.183 (1.884, 2.528)	5.246 (4.438, 6.203)	0.988 (0.656, 1.488)	2.817 (2.185, 3.632)	5.855 (5.026, 6.821)
	Overall payments, ER (95% CI)	Reference	2.072 (1.855, 2.315)	4.121 (3.59, 4.729)	1.015 (0.892, 1.154)	2.051 (1.807, 2.327)	3.808 (3.292, 4.403)	1.266 (0.92, 1.742)	2.128 (1.693, 2.674)	3.133 (2.75, 3.569)

Note: Adjusted comparisons are obtained from linear contrasts from multivariable regression models that include covariates gender, age, insurance, Elixhauser Index, and comorbidities in addition to the opioid dependency group. The pre- and post-SCI opioid dependence groups are defined as: (1) prior nonusers who remained nonusers (N-N), (2) prior nonusers who became nondependent users (N-ND), (3) prior nonusers who became dependent users (N-D), (4) prior nondependent users who became nonusers (ND-N), (5) prior nondependent users who remained nondependent users (ND-ND), (6) prior nondependent users who became dependent users (ND-D), (7) prior dependent users who became nonusers (D-N), (8) prior dependent users who became nondependent users (D-ND) and (9) prior dependent users who remained dependent (D-D).

nondependent to a dependent user; 31% total) than a positive change (i.e., from nondependent/dependent user to nonuser or from dependent to a nondependent user; 14% total). The transition of opioid use status has not yet been evaluated in the literature. However, we noted that the majority (56%) of those who are opioid users postinjury were users before. As outlined previously, prior opioid use had the highest odds of postinjury opioid use and abuse. Dependent users before injury had 34 times higher odds of becoming dependent users and more than four times higher odds of becoming nondependent users after injury compared to nonusers. Pre-SCI nondependent users had, respectively, 2.5 and 3.4 higher odds of becoming nondependent or becoming dependent users compared to nonusers.

Postinjury pain is a condition in 33% to 80% of people with SCI,[1,2,30,31] and opioids are oftentimes presented as a medical solution. However, there are several arguments against opioid use for post-SCI pain, chief among them being the debate over their global effectiveness. Many studies have been unable to support their effectiveness for pain relief, especially when compared to nonopioid analgesics.[32,33] Moreover, there is evidence that they could negatively affect SCI recovery. Recent studies have shown that administration of morphine, especially using an intrathecal route, is associated with attenuation of motor recovery, loss of neurons and glia, development of opioid-induced hyperalgesia, and an overall decrease in the subject's general health.[2,34,35] Although these studies were predominantly focused on acute administration of intrathecal morphine, the authors note that negative effects may exist with chronic administration.[2] Additional studies have shown the negative correlation of opioid intake with bowel movement frequency and increased fracture risk after SCI.[36,37] This study showed that postinjury pain was associated with a high likelihood of opioid use or abuse. The results of these studies are clinically relevant in the conversation surrounding the management of pain post-SCI, and they highlight the need to emphasize opioid stewardship after SCI. However, pain after SCI may be challenging to classify, particularly neuropathic pain.[38,39] Without a clear understanding of pain after SCI, successful management of coping with pain is less likely to occur, leading to risk for overuse of pain medications, which is concerning given the high prevalence of overdose from prescription drugs in this population.[40] As time progresses in the chronic SCI phase, there is increased use of pain medication that has been linked to increased odds of mortality.[41] Therefore, it becomes essential to establish ongoing screening for opioid use in SCI to help with pharmacological and nonpharmacological treatment plans for pain management.

The secondary medical issues associated with increased opioid use disorder among individuals with SCI may be the main contributor to the increased health care burden of prescription opioids found in our study. Opioids and opioid overdose are associated with several secondary complications already exacerbated in individuals with SCI. Arguments against the use of opioids for pain following SCI cite the increased risk of respiratory depression and death: those with SCI are particularly vulnerable to respiratory depression due to adverse effects on the autonomic nervous system and the increased risk of adverse drug events due to polypharmacy among individuals with SCI.[14] As stated previously, opioids are also known to exacerbate neurogenic bowel symptoms due to opioid-induced constipation.[42] Our results found an average 2 to 4 times increase in health care expenditures in nondependent and dependent opioid users, respectively, compared to opioid-naïve individuals. Increased utilization was observed in emergency room and hospital admissions, outpatient services, and medication refills. This increase in health care burden is also consistent with studies that have found opioid abusers had a mean excess cost of $16,508 per patient per year.[43] Societal costs were borne between health care, criminal justice, and workplace sectors, totaling some $55.7 billion in the United States annually.[43] Also observed was an increase in LOS among those previously or who became opioid users following SCI. This has been observed in non-SCI postoperative populations, pointing to a general effect of opioids regardless of diagnosis.[22]

Strengths and limitations

A strength of this study is the use of the MarketScan database, which provides a large,

geographically representative sample of the entire United States, with longitudinal and real-world use of opioids and health care utilization and payments. However, this study's notable limitation is the inability to account for the use of opioids acquired outside of insurance claims (i.e., illicit use or illegal purchasing). Also, there is no way to confirm that the prescription drugs refilled were actually consumed. The SCI population is economically in poverty[44]; therefore, there is the potential for diversion of prescribed drugs. Another notable limitation is that the American Spinal Cord Injury Association Impairment Scale (AIS), quantifying the severity of injury, is not routinely collected in claims databases. This should be kept in mind when clinically interpreting the findings of this study. Another important limitation is the inability to evaluate the impact of opioids on psychological functioning and quality of life. Finally, it is important to note that the study period post-SCI (months 4-15 after injury) is relatively short and that a longer period is needed to evaluate chronic use. Nonetheless, this study informs the greater conversation surrounding the use of opioids after SCI. Further research should investigate alternative medical management methods that can have the risk to result in opioid use and abuse.

Conclusion

Our study demonstrates that opioid users before SCI are more likely to remain nondependent or dependent opioid users after. Other significant predictors of post-SCI opioid use were young age, insurance type, postinjury pain diagnosis, and surgical treatment. In addition, we found that nondependent and dependent opioid users utilized significantly greater amounts of health care resources, most likely due to known opioid use side effects. Opioid use history before SCI should be considered in postinjury treatment decision-making.

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