ORIGINAL ARTICLE

Differences in Healthcare Utilization and Associated Costs Between Patients Prescribed vs. Nonprescribed Opioids During an Inpatient or Emergency Department Visit

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■ **Abstract**

Objectives: Compare healthcare resource utilization (HCRU) and costs between patients prescribed opioids (RxOP) and those who were not (NoRxOP) during an emergency department (ED) or inpatient visit.

Methods: Retrospective cohort analysis was performed (January 2006 to September 2010). Continuously eligible RxOP patients in ED/inpatient settings (January 2007 to September 2009) were included if age was ≥ 12 years by initial prescription date (or random date between first ED/inpatient admission and September 30, 2009 [NoRxOP patients]).

Healthcare resource utilization and costs for 12 months after initial prescription were compared. Univariate descriptive analyses were performed for baseline and outcome variables and compared using appropriate tests. Risk adjustment compared HCRU between RxOP and NoRxOP cohorts for the postindex period.

Results: Of 27,599 eligible patients, RxOP patients (n = 18,819) were younger, less likely to be male, more likely to reside in southern United States and to have Preferred Provider Organization health plans, and had lower comorbidity index scores, compared with NoRxOP patients (n = 8,780). RxOP patients were less likely to have nonpain-related comorbidities and more frequently diagnosed with pain-related comorbidities.

Unmatched and propensity-matched RxOP patients experienced higher HCRU and costs in all subcategories (total, inpatient, outpatient ED, physician, pharmacy, other outpatient settings). Opioid abuse frequency was low in patients with common diagnoses/procedures within 3 months before initial prescription (0.48%). Average time to abuse was < 1 year (201 days).

Conclusion: Most patients were prescribed opioids initially during ED/inpatient visits and incurred higher HCRU than those not prescribed opioids. Among those with diagnosed opioid abuse after initiating opioids, time to diagnosis was rapid (range: 14 to 260 days) for patients with common diseases and procedures. ■

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INTRODUCTION

Over the past 2 decades, health professionals have been addressing the issue of undertreated pain more aggressively through the increase in prescription opioids to treat cancer-related and noncancer pain. This has resulted in a simultaneous increase in opioid abuse in the United States.[1,2] The doses at which opioid analgesics are sometimes abused can lead to respiratory depression and death.[3] In 2009, there were over 2 million opioid-dependent adults in the United States, and opioid misuse has become a leading cause of death nationwide.[4] According to the Substance Abuse and Mental Health Services Administration (SAMHSA) in 2009, there were 35 emergency department (ED) visits, 161 patient reports of drug abuse or dependence, and 461 reports of nonmedical uses of opioid analgesics for every unintentional opioid-related overdose death.[5]

Use of prescription opioids in the United States increased 402% overall from 1997 to 2007,[6] and in the medically insured population, 7 to 8 patients per 10,000 have shown evidence of diagnosed opioid abuse.[7] Additionally, diagnosed abusers with multiple comorbidities incurred healthcare expenses which were 8 times higher than those without diagnosed abuse.[8] Patients with diagnosed opioid abuse were 6.7 times more likely to be hospitalized and 2.3 times more likely to have ED visits.[9]

Researchers are becoming increasingly aware of the instrumental role that ED settings play in the prescription of opioid medications. EDs prescribe 29% of all opioid medications administered and are the largest ambulatory source for opioids.[10] Inappropriate prescribing of opioid medications in the ED setting can occur and includes the prescription of long-acting opioids to treatment-naive individuals.[11] EDs also often handle the consequences of inappropriate prescription opioid use. An estimated 305,900 ED visits were related to the nonmedical use of opioid analgesics in 2008, a 111% increase from the 144,600 visits in 2004.[12]

However, while EDs have been well studied in the distribution of American opioid medications,[8–10] few studies differentiate between inpatient and ED settings. Research focused on the factors associated with prescribing opioid medications in United States inpatient hospital settings has revealed variation in demography and hospital location. According to a retrospective study conducted by Olsen et al.[13], those living in the northeast (OR = 0.60; 95% CI [0.52 to 0.69]) or Midwest (OR = 0.75; 95% CI [0.66 to 0.85]), as well as Hispanic patients (OR = 0.67; 95% CI [0.56 to 0.81]) and those of other races (OR = 0.68; 95% CI [0.52 to 0.90]), had lower odds of receiving a prescription opioid. The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) asserted that opioid use is generally safe for most patients, but the risk of problems like abuse warranted suggested actions for inpatient hospital settings, such as monitoring patients properly, tracking and analyzing opioid-related incidents, screening patients for risk factors for abuse, and building electronic alert systems for opioid dosing limits in prescription systems.[14]

In this study, healthcare resource utilization (HCRU) and costs between patients who were prescribed opioids vs. those without an opioid prescription during an ED or inpatient visit were compared. Additionally, the rate of diagnosed opioid abuse by specific diseases and procedures was determined after the first opioid prescription.

METHODS

Data Source and Study Sample

A retrospective cohort analysis was performed using data from the linked MarketScan® Commercial Claims and Encounters, Medicare Supplemental, and Hospital Drug Databases (including medical and pharmacy claims) between January 2006 and September 2010, with an identification period from January 1, 2007 through September 30, 2009.

The index date was defined as the date of the initial opioid prescription for the prescription opioid user (RxOP) cohort and the random date between the first ED/inpatient admission and the end of the identification period for those not prescribed opioids in an ED/inpatient setting (NoRxOP cohort).

Baseline variables were calculated during the 12 months prior to the index date, otherwise known as the pre-index period, and outcome variables were calculated during the 12 months after the index date (ie, postindex period).

Patients who were 12 years of age or older on the index date with continuous health plan enrollment, including medical and pharmacy benefits, from the pre-index period through the postindex period were selected. Subjects were excluded from the study if they were prescribed opioid medications during the 12-month pre-index period.

Cohort Assignments

In addition to the comparison between RxOP and NoRxOP patients, the diagnosed opioid abuse after prescription cohort was created using a population of patients diagnosed with certain diseases[a] or who had certain procedures[b] during the 3 months preceding the first opioid prescription in an emergency room (ER)/inpatient setting during the identification period. Qualified participants were required to be identified as diagnosed opioid abusers if they had evidence of diagnosis of opioid abuse after the first opioid prescription date. Opioid abuse was defined as a new diagnosis for opioid type dependence (International Classification of Disease 9th Revision Clinical Modification [ICD-9-CM: 304.0X]), combinations of opioid abuse with any other [304.7X] (opioid abuse [305.5X], or poisoning by opiates and related narcotics, not including heroin [965.00, 965.02, 965.09]).

Covariates

Baseline demographic variables included age, age group (12 to 17, 18 to 25, 26 to 34, 35 to 54, 55 to 64, 65+ years), gender, geographic region (Northeast, North Central, South, West, Unknown), and insurance type (Exclusive Provider Organization, Health Maintenance Organization, Point of Service, Preferred Provider Organization, Other).

Baseline comorbidity measures included an index based on a comprehensive set of 30 ICD-9-CM comorbidity flags called the Elixhauser Index score,[15] with a cut point of at least 2. The average pre-index Quan-Charlson Comorbidity Index (CCI) score was calculated as a weighted summation of 22 comorbid conditions plus warfarin use.[16] Pre-index Chronic Disease Score (CDS)[17] values based on current medication use (ie, pharmacy claims data) were utilized as well. These 3 comorbidity indices provided an estimation of different aspects of the patients' health status, with higher index scores indicating worse health status. Pre-index pain-related comorbid conditions included low back pain, other back/neck disorders, arthritis, neuropathic pain, headache/migraine, fibromyalgia, and cancer. Pre-index nonpain-related comorbid conditions included other substance abuse, nonopioid poisoning, psychiatric disorders, human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS), endocarditis, skin infections/abscesses, gastrointestinal bleeding, cirrhosis/chronic/acute liver disease, hepatitis A, B, or C, alcoholic hepatitis, other hepatitis, pancreatitis, sexually transmitted disease, herpes simplex, burns, and trauma.

Total pre-index healthcare costs, along with inpatient, outpatient ED, physician visit, other outpatient, and pharmacy costs, were calculated and adjusted to June 2010 US dollars using the Consumer Price Index (CPI) medical care component. Pre-index HCRU measures included the number of inpatient, outpatient ED, and physician office visits as well as binary indicators of having at least one visit.

Top 10 conditions or procedures prior to opioid abuse have been grouped into different categories: cardiovascular/metabolic conditions (hypertension not otherwise specified (NOS); benign hypertension; uncontrolled type II diabetes mellitus; hyperlipidemia; coronary atherosclerosis); mental health (depressive disorder); general health/routine screening (malaise and fatigue; routine gynecologic examination, mammogram); opioid-related conditions (opioid dependence—continuous, opioid dependence—unspecified, opioid poisoning); and pain conditions (lumbago, pain in limb, abdominal pain unspecified site, chest pain). Procedures prior to opioid abuse included cardiac procedures (percutaneous transluminal coronary angioplasty or coronary atherosclerosis, left heart cardiac catheterization, coronary arteriogram-2 catheterization, left heart angiocardiogram, noncoronary angiogram), orthopedic procedures (lymphatic structure biopsy, lumbar/lumbosacral fusion lateral and posterior, total hip and knee replacements, refusion of lumbar post), gynecologic surgery (low cervical c-section, c-section, total abdominal hysterectomy, total abdominal hysterectomy NOS), general surgery (laparoscopic cholecystectomy), and other procedures (drug rehabilitation/detoxification).

Outcome Variables

Similar to pre-index costs, total, inpatient, outpatient ED, physician visit, other outpatient, and pharmacy costs were calculated during the 12-month follow-up period based upon the amount paid by the health plan on relevant claims and net cost of any patient contribution (eg, copayment). Costs were expressed in 2010 U.S. dollars and were adjusted using the medical care

[a]Cardiovascular/metabolic conditions, mental health, general health/routine screening, opioid-related conditions, pain conditions.

[b]Cardiac procedure, orthopedic procedures, gynecologic surgery, general surgery, others.

component of the U.S. CPI. Postindex HCRU included the number of inpatient, outpatient ED, and physician office visits, plus binary indicators of having at least one visit.

The frequency of diagnosed opioid abuse was defined as the number of patients detected with certain diseases[c] or procedures (Table 4) in the 3 months prior to the index date (first opioid prescription date in ED/inpatient), number of diagnosed opioid abusers after index date, and number of days from first opioid prescription to first opioid abuse diagnosis.

Statistical Analysis

Univariate descriptive analyses were performed for all baseline and outcome variables. Percentages and standard deviations were calculated for dichotomous variables, and *P* values were calculated using the chi-squared test. Means and standard deviations were calculated for continuous variables, and *P* values were calculated using the student's *t*-test.

To adjust the baseline differences in demographic and clinical characteristics between the 2 cohorts, risk adjustment was performed using 1:1 propensity score matching (PSM) to compare all postindex healthcare costs and utilization between the RxOP and NoRxOP cohorts. Variables incorporated in matching were patients' age, gender, geographic region, health plan type, comorbidities, HCRUs, and costs in the pre-index period. The PSM method created very closely balanced study cohorts that appeared similar on a large number of measures. In essence, the PSM methodology sought to mimic a randomized experiment by constructing a control group under the assumption of the ignorable treatment assignment, that is, individuals were randomly assigned to treatment and control groups, given a set of observed covariates. The propensity score modeled the clinical decision-making process; patients were matched if their propensity scores were within ±0.01 units of each other.

Multivariate analysis was performed by using generalized linear models, where log link and gamma distributions were used for cost outcomes, negative binomial distribution was used for count variables such as number of healthcare utilization visits, and logistic link was used for binary outcomes such as having at least one visit.

[c]Cardiovascular/metabolic conditions, mental health, general health/routine screening, opioid-related conditions, pain conditions.

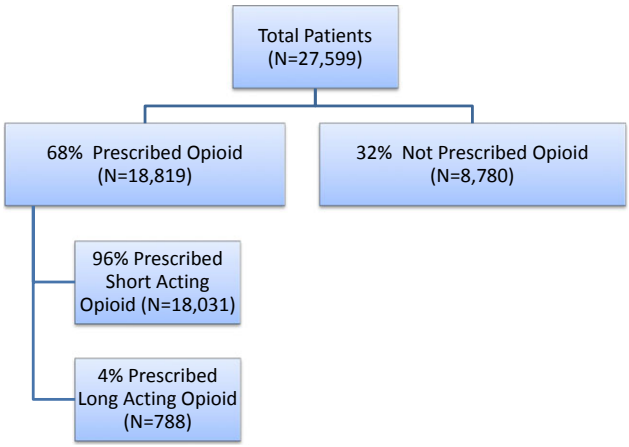

Figure 1. Patient selection.

RESULTS

Study Sample

After applying inclusion and exclusion criteria, a total of 27,599 patients were eligible for the study (Figure 1). Sixty-eight percent of the patients (RxOP; n = 18,819) were prescribed opioids (mean age = 54.5 years), and 32% (NoRxOP; n = 8,780) were not (mean age = 55.1 years). Among RxOP patients (n = 18,819), 17% (n = 3,226) were prescribed opioids in the ED setting, and 83% (n = 15,593) were prescribed opioids in inpatient settings. However, among all patients observed in the sample with an ER visit, 56% were prescribed opioids. Among all observed patients with an inpatient admission, 71% were prescribed opioids.

Among patients in the RxOP cohort, the majority of patients (96%, n = 18,031) were prescribed immediate-release opioids, and 4% (n = 788) were prescribed extended-release opioids. Among all patients who were prescribed an opioid (N = 18,819), the long-acting opioid prescription rate was slightly higher in the ED (6.5%) vs. inpatient setting (3.7%).

Demographics and Clinical Characteristics

RxOP patients were younger (54.5 vs. 55.1; P = 0.0293), less likely to be male (35.6% vs. 43.0%; P < 0.0001), more likely to reside in the southern region of the United States (86.6% vs. 78.2%; P < 0.0001), and more likely to have a PPO health plan (55.1% vs. 49.8%; P < 0.0001) compared with NoRxOP patients (Table 1).

Additionally, RxOP patients were less likely to have Elixhauser Index scores of at least 2% (18.5% vs.

Table 1. Demographic and Clinical Characteristics of Patients Prescribed and Not Prescribed Opioid Medications

	Prescription Opioid Patients (*N* = 18,819)		Patients Not Prescribed Opioids (*N* = 8,780)			
Baseline Demographic Conditions	*N*/Mean	%/STD	*N*/Mean	%/STD	*P* Value	Effect Size
Age (mean)	54.54	17.62	55.08	19.69	0.0293	2.87
12 to 17	257	1.37%	241	2.74%	< 0.0001	9.73
18 to 25	582	3.09%	370	4.21%	< 0.0001	5.98
26 to 34	2,306	12.25%	1,143	13.02%	0.0736	2.30
35 to 54	5,616	29.84%	2,242	25.54%	< 0.0001	9.64
55 to 64	4,575	24.31%	1,900	21.64%	< 0.0001	6.35
65+	5,483	29.14%	2,884	32.85%	< 0.0001	8.03
Gender (male)	6,690	35.55%	3,779	43.04%	< 0.0001	15.38
Geographic region						
Northeast	396	2.10%	224	2.55%	0.0196	2.96
North Central	1,752	9.31%	1,468	16.72%	< 0.0001	22.16
South	16,287	86.55%	6,867	78.21%	< 0.0001	22.00
West	346	1.84%	209	2.38%	0.0028	3.77
Insurance plan type						
HMO	2,358	12.53%	1,215	13.84%	0.0026	3.87
PPO	10,375	55.13%	4,372	49.79%	< 0.0001	10.70
Other	3,388	18.00%	1,876	21.37%	< 0.0001	8.47
Baseline comorbid conditions						
Elixhauser Index (≥ 2%)	3,473	18.45%	1,710	19.48%	0.0430	2.61
Charlson Comorbidity Index (CCI) score	1.10	1.73	1.31	1.88	< 0.0001	11.63
Chronic disease score	4.54	3.96	4.88	4.06	< 0.0001	8.43
Nonpain-related comorbid condition						
Other substance abuse	490	2.60%	385	4.38%	< 0.0001	9.71
Nonopioid poisoning	159	0.84%	145	1.65%	< 0.0001	7.27
Psychiatric disorders	2,596	13.79%	1,547	17.62%	< 0.0001	10.53
Endocarditis	45	0.24%	39	0.44%	0.0040	3.51
Gastrointestinal bleed	2,217	11.78%	1,140	12.98%	0.0044	3.65
Cirrhosis/chronic or acute liver disease	548	2.91%	326	3.71%	0.0004	4.48
Alcoholic hepatitis	9	0.05%	15	0.17%	0.0012	3.72
Pancreatitis	166	0.88%	143	1.63%	< 0.0001	6.71
Sexually transmitted disease	1,277	6.79%	496	5.65%	0.0003	4.71
Trauma	4,217	22.41%	1,866	21.25%	0.0310	2.80
Pain-related Comorbid Conditions						
Cancer	2,275	12.09%	945	10.76%	0.0014	4.17
Low back pain	4,467	23.74%	1,525	17.37%	< 0.0001	15.81
Other back/neck disorders	4,102	21.80%	1,426	16.24%	< 0.0001	14.19
Arthritis	8,011	42.57%	3,123	35.57%	< 0.0001	14.38
Neuropathic pain	2,005	10.65%	846	9.64%	0.0096	3.37
Fibromyalgia	601	3.19%	193	2.20%	< 0.0001	6.15
Baseline healthcare utilization						
Patients with inpatient visits	3,440	18.28%	6,866	78.20%	< 0.0001	149.83
Patients with outpatient ED visits	6,798	36.12%	4,153	47.30%	< 0.0001	22.81
Patients with outpatient physician visits	17,931	95.28%	8,240	93.85%	< 0.0001	6.32
Number of inpatient visits	0.26	0.70	0.98	0.82	< 0.0001	94.07
Number of outpatient ED visits	0.68	1.55	0.84	1.39	< 0.0001	10.41
Number of outpatient Physician visits	9.03	7.40	8.44	7.26	< 0.0001	8.01
Baseline healthcare costs						
Total costs	$17,120	$36,837	$25,569	$41,535	< 0.0001	21.52
Inpatient costs	$4,462	$21,813	$13,131	$28,211	< 0.0001	34.38
Outpatient physician visit costs	$832	$749	$760	$704	< 0.0001	9.87

STD, standard deviation; EPO, exclusive provider organization; HMO, health maintenance organization; POS, point of service; PPO, preferred provider organization; ED, emergency department.

19.5%; $P = 0.0430$) and had lower CCI (1.10 vs. 1.31; $P < 0.0001$) and CDS scores (4.54 vs. 4.88; $P < 0.0001$) than NoRxOP patients.

RxOP patients were less likely to have many of the nonpain-related comorbid conditions studied, including other substance abuse (2.6% vs. 4.4%; $P < 0.0001$), nonopioid poisoning (0.8% vs. 1.7%; $P < 0.0001$), psychiatric disorders (13.8% vs. 17.6%; $P < 0.0001$), endocarditis (0.2% vs. 0.4%; $P = 0.0040$), gastrointestinal bleeding (11.8% vs. 13.0%; $P = 0.0044$), cirrhosis/chronic or acute liver disease (2.9% vs. 3.7%, $P = 0.0004$), alcoholic hepatitis (0.1% vs. 0.2%; $P = 0.0012$), and pancreatitis (0.9% vs. 1.6%, $P < 0.0001$). Exceptions included sexually transmitted diseases (6.8% vs. 5.7%;

$P = 0.0003$) and trauma (22.4% vs. 21.3%; $P = 0.0310$).

While RxOP patients were generally less likely to have nonpain-related comorbid conditions, they were more often found with every pain-related comorbid condition studied (Table 1). Common conditions included arthritis (42.6% vs. 35.6%; $P < 0.0001$), low back pain (23.7% vs. 17.4%; $P < 0.0001$), other back/neck disorders (21.8% vs. 16.2%; $P < 0.0001$), and cancer (12.1% vs. 10.8%; $P = 0.0014$).

Baseline Costs and Utilization

RxOP patients were less likely to have inpatient (18.3% vs. 78.2%; $P < 0.0001$) and ED visits (36.1% vs. 47.3%; $P < 0.0001$), but more likely to have physician visits (95.3% vs. 93.9%; $P < 0.0001$) in the pre-index period. Correspondingly, RxOP patients had a lower number of average inpatient (0.26 vs. 0.98; $P < 0.0001$) and ED visits (0.68 vs. 0.84; $P < 0.0001$) but greater physician visits (9.03 vs. 8.44; $P < 0.0001$).

RxOP patients had lower total ($17,120 vs. $25,569; $P < 0.0001$) and inpatient costs ($4,462 vs. $13,131; $P < 0.0001$) but higher outpatient physician visit costs than NoRxOP patients ($832 vs. $760; $P < 0.0001$).

Postindex Descriptive Outcomes

In the unmatched cohorts, it was more common for RxOP patients to have inpatient (100% vs. 23.1%, $P < 0.0001$), outpatient ED (45.2% vs. 29.8%; $P < 0.0001$), and physician visits (93.4% vs. 90.2%; $P < 0.0001$), and RxOP patients utilized more of these 2 types of visits compared with NoRxOP patients (Table 2). RxOP patients also had higher average healthcare costs in all subcategories, including total ($42,829 vs. $16,861; $P < 0.0001$), inpatient ($26,484 vs. $5,199; $P < 0.0001$), outpatient ED ($520 vs. $360; $P < 0.0001$), and physician visit costs ($833 vs. $682; $P < 0.0001$), pharmacy ($3,042 vs. $2,898; $P = 0.0406$), and other outpatient costs ($11,954 vs. $7,722; $P < 0.0001$).

Postindex-Adjusted Outcomes

After PS matching and controlling for baseline demographic and clinical differences using the generalized linear model, results were slightly different in magnitude from the unadjusted values but did not change the postindex descriptive healthcare cost and utilization pattern, as illustrated in Figure 2. Demographic and clinical results of RxOP and NoRxOP cohorts after PSM are outlined in Table 3. After matching, no demographic or clinical variable differed significantly between the 2 cohorts. Among the 5,099 matched pairs, the RxOP cohort had more inpatient (1.58 vs. 0.36; $P < 0.0001$), physician office (10.17 vs. 8.96; $P < 0.0001$), and ED visits (1.12 vs. 0.67; $P < 0.0001$) than matched NoRxOP patients in the follow-up period.

RxOP users had significantly higher healthcare costs in terms of total healthcare ($49,766 vs. $19,875; $P < 0.0001$), inpatient ($30,659 vs. $6,104; $P < 0.0001$), outpatient ED ($627 vs. $408; $P < 0.0001$), outpatient physician visit ($892 vs. $778; $P < 0.0001$), outpatient pharmacy ($3,583 vs. $3,199; $P = 0.0074$),

Table 2. Outcomes Comparison of Patients Prescribed and Not Prescribed Opioid Medications

	Prescription Opioid Patients (N = 18,819)		Not Prescribed Opioid Patients (N = 8,780)			
	N/Mean	%/STD	N/Mean	%/STD	P Value	Effect Size
Follow-up healthcare utilization						
Patients with inpatient visits	18,819	100.00%	2,024	23.05%	< 0.0001	257.29
Patients with outpatient ED visits	8,504	45.19%	2,619	29.83%	< 0.0001	32.13
Patients with outpatient physician visits	17,583	93.43%	7,919	90.19%	< 0.0001	11.83
Number of inpatient visits	1.40	0.95	0.32	0.77	< 0.0001	124.31
Number of outpatient ER visits	0.91	1.80	0.57	1.40	< 0.0001	20.61
Number of outpatient physician visits	9.45	8.41	7.89	7.80	< 0.0001	19.31
Follow-up healthcare cost						
Total costs	$42,829	$63,927	$16,861	$37,825	< 0.0001	49.44
Inpatient costs	$26,484	$45,321	$5,199	$20,955	< 0.0001	60.29
Outpatient ED costs	$520	$1,918	$360	$1,379	< 0.0001	9.56
Outpatient physician visit costs	$833	$864	$682	$711	< 0.0001	19.02
Outpatient pharmacy costs	$3,042	$6,210	$2,898	$4,994	0.0406	2.54
Outpatient other costs	$11,954	$32,276	$7,722	$23,487	< 0.0001	14.99

STD, standard deviation; ED, emergency department.

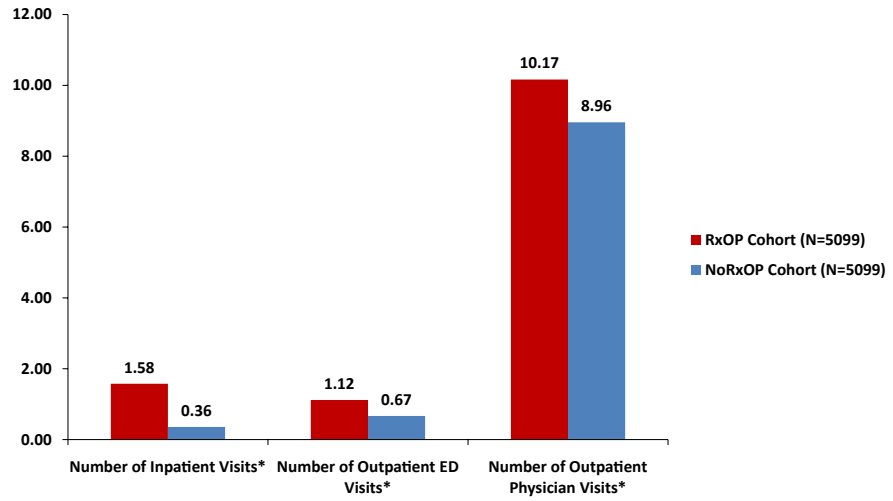

Figure 2. Adjusted utilization among RxOP and NoRxOP cohorts. RxOP, prescription opioid; NoRxOP, no prescription opioid; ED, emergency department. *P-value < 0.0001.

and other outpatient costs ($14,011 vs. $9,387; $P < 0.001$) compared with NoRxOP patients (Figure 3).

Diagnosed Opioid Abuse After Initiation of Prescription Opioids in ED/Inpatient Setting

Of the total eligible patients, 110 individuals (0.5%) were diagnosed with opioid abuse after an average of 201 days from their first opioid prescription (Table 4). By disease, the 7 of 18 patients with opioid-related conditions (38.9%) were diagnosed with opioid abuse after an average of 14 days from first opioid prescription, followed by mental health conditions (8 of 313, or 2.6%, diagnosed after 201 days), pain conditions (56 of 6,048, or 0.9%, diagnosed after 167 days), cardiovascular/metabolic conditions (43 of 8,969, or 0.5%, diagnosed after 142 days), and general health/routine screening (14 of 2,906, or 0.5% diagnosed after 260 days).

By procedure, 5 of 161 patients with cardiac procedures (3.1%) were diagnosed with opioid abuse after an average of 167 days. Of those patients with orthopedic procedures ($n = 51$), gynecologic surgery ($n = 39$), general surgery ($n = 26$), and others ($n = 0$), no diagnosed opioid abuse was detected after the first opioid prescription.

DISCUSSION

This observational study, using a linked U.S. commercial administrative claims database from 2006 to 2010, compared healthcare costs and utilization of patients who initiated prescription opioids vs. those who did not in ED and inpatient hospital settings.

Results indicated that initial opioid prescribing remains a common practice in ED and inpatient settings. In our study, a greater proportion of opioid prescriptions were made in the inpatient hospital setting (71%) than the ED (56%).

There appears to be an inverse correlation between baseline clinical characteristics and cost/utilization outcomes for RxOP and NoRxOP patients. While RxOP patients have lower comorbidity scores (Elixhauser, CDS, CCI) when compared with NoRxOP patients, their postindex healthcare utilization (higher inpatient, physician office, ED visits) and costs (adjusted total, outpatient physician visit, outpatient ED, outpatient pharmacy, other outpatient costs) were higher. However, after PSM, baseline differences between cohorts adjusted well. In the postmatch samples, patients in both cohorts had similar demographic characteristics and comorbidities. Some previous studies have demonstrated that certain comorbidities such as depression, pain, and workers' compensation status are significant risk predictors for high healthcare costs and utilizations.[18,19] In our study, trauma, gastrointestinal bleeding, and psychiatric disorder were the 3 most common nonpain-related comorbidities observed during the baseline period. Arthritis, low back pain, and other back/neck disorders were the most common pain-related baseline comorbidities. Although identifying predictors of high healthcare costs and utilizations were not one of the objectives in this study, future research will be necessary to explore the significance of these factors.

Table 3. Baseline Demographic and Clinical Conditions of Patients Prescribed and Not Prescribed Opioid Medications, After PSM

	Patients Prescribed Opioids (N = 5,099)		Patients not Prescribed Opioids (N = 5,099)			
Baseline Demographic Conditions	*N*/Mean	%/STD	*N*/Mean	%/STD	*P* Value	Effect Size
Age (mean)	56.30	18.01	56.84	18.47	0.1309	2.99
12 to 17	98	1.92%	89	1.75%	0.5065	1.32
18 to 25	159	3.12%	156	3.06%	0.8637	0.34
26 to 34	522	10.24%	518	10.16%	0.8959	0.26
35 to 54	1,352	26.52%	1,367	26.81%	0.7369	0.67
55 to 64	1,248	24.48%	1,265	24.81%	0.6961	0.77
65 or older	1,720	33.73%	1,704	33.42%	0.7373	0.66
Gender (male)	2,151	42.18%	2,135	41.87%	0.7482	0.64
Geographic region						
Northeast	114	2.24%	118	2.31%	0.7905	0.53
North Central	621	12.18%	582	11.41%	0.2312	2.37
South	4,251	83.37%	4,296	84.25%	0.2264	2.40
West	107	2.10%	94	1.84%	0.3544	1.83
Unknown	6	0.12%	9	0.18%	0.4382	1.54
Insurance plan type						
EPO	25	0.49%	16	0.31%	0.1590	2.79
HMO	644	12.63%	637	12.49%	0.8343	0.41
POS	680	13.34%	676	13.26%	0.9071	0.23
PPO	2,756	54.05%	2,758	54.09%	0.9683	0.08
Others	994	19.49%	1,012	19.85%	0.6539	0.89
Baseline comorbid conditions						
Elixhauser Index score (≥ 2%)	1,232	24.16%	1,236	24.24%	0.9263	0.18
Charlson Comorbidity Index score	1.49	2.04	1.47	2.03	0.7297	0.68
Chronic Disease score	5.32	4.19	5.28	4.12	0.6132	1.00
Nonpain-related comorbid condition						
Other substance abuse	193	3.79%	195	3.82%	0.9175	0.21
Nonopioid poisoning	64	1.26%	79	1.55%	0.2065	2.50
Psychiatric disorders	885	17.36%	874	17.14%	0.7731	0.57
HIV–AIDS	15	0.29%	14	0.27%	0.8525	0.37
Endocarditis	25	0.49%	32	0.63%	0.3525	1.84
Skin infections/abscesses	496	9.73%	468	9.18%	0.3433	1.88
Gastrointestinal bleed	757	14.85%	713	13.98%	0.2148	2.46
Cirrhosis/chronic or acute liver disease	205	4.02%	229	4.49%	0.2391	2.33
Hepatitis A, B, C	33	0.65%	29	0.57%	0.6104	1.01
Alcoholic hepatitis	4	0.08%	11	0.22%	0.0705	3.58
Other hepatitis	5	0.10%	8	0.16%	0.4051	1.65
Pancreatitis	78	1.53%	90	1.77%	0.3505	1.85
Sexually transmitted disease	287	5.63%	285	5.59%	0.9314	0.17
Herpes simplex	43	0.84%	38	0.75%	0.5770	1.10
Burns	16	0.31%	18	0.35%	0.7312	0.68
Trauma	1,278	25.06%	1,285	25.20%	0.8730	0.32
Motor vehicle accidents	8	0.16%	5	0.10%	0.4051	1.65
Pain-related comorbid condition						
Cancer	661	12.96%	664	13.02%	0.9296	0.17
Low back pain	1,140	22.36%	1,160	22.75%	0.6356	0.94
Other back/neck disorders	1,040	20.40%	1,056	20.71%	0.6950	0.78
Arthritis	2,170	42.56%	2,196	43.07%	0.6028	1.03
Neuropathic pain	653	12.81%	602	11.81%	0.1242	3.04
Fibromyalgia	157	3.08%	150	2.94%	0.6850	0.80
Headache/migraine	546	10.71%	510	10.00%	0.2420	2.32
Baseline healthcare utilization						
Patients with inpatient visits	3,163	62.03%	3,185	62.46%	0.6531	0.89
Patients with outpatient ER visits	2,483	48.70%	2,529	49.60%	0.3622	1.80
Patients with outpatient physician visits	4,810	94.33%	4,836	94.84%	0.2552	2.25
Number of inpatient visits	0.84	0.95	0.85	0.98	0.4869	1.38
Number of outpatient ER visits	0.98	1.60	0.98	1.64	0.9561	0.11
Number of outpatient physician visits	9.77	7.94	9.73	8.07	0.8480	0.38
Baseline healthcare cost						
Total costs	$28,727	$45,413	$28,219	$50,954	0.5947	1.05
Inpatient cost	$13,200	$31,029	$13,084	$34,126	0.8565	0.36
Outpatient ER cost	$561	$1,488	$567	$1,601	0.8402	0.40
Outpatient physician visit cost	$887	$754	$887	$802	0.9932	0.02
Outpatient pharmacy cost	$3,199	$5,324	$3,191	$4,834	0.9289	0.18
Outpatient other costs	$10,881	$25,466	$10,568	$29,561	0.5670	1.13

STD, standard deviation; EPO, exclusive provider organization; HMO, health maintenance organization; POS, point of service; PPO, preferred provider organization; ER, emergency room; HIV/AIDS, human immunodeficiency virus/acquired immunodeficiency syndrome; PSM, propensity score matching.

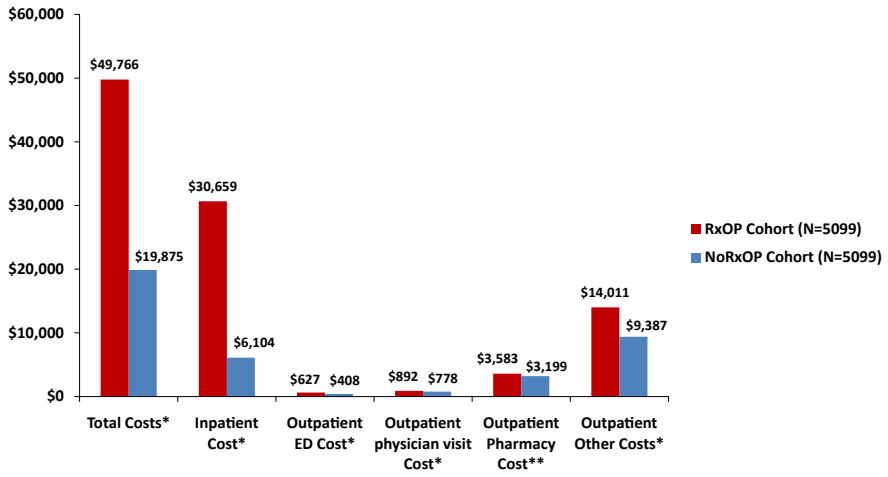

Figure 3. Adjusted cost outcomes for RxOP and NoRxOP cohorts. RxOP, prescription opioid; NoRxOP, no prescription opioid; ED, emergency department. *P value < 0.0001, **P value < 0.0010.

Table 4. Frequency of Diagnosed Opioid Abuse by Disease and Procedure

Description	Patients with ED/Inpatient Visits *N* (%)	Diagnosed Opioid Abusers *N* (%)	Days from First Opioid Prescription to Opioid Abuse Diagnosis Mean
Total patients	18,819	110	200.65
By disease*			
Cardiovascular/metabolic conditions	7,043 (37.42)	43 (39.09)	141.51
Mental health	236 (1.25)	8 (7.27)	201.38
General health/routine screening	2,302 (12.23)	14 (12.73)	260.21
Opioid-related conditions	9 (0.05)	7 (6.36)	14.14
Pain conditions	4,679 (24.86)	56 (50.91)	166.95
By procedure*			
Cardiac procedure	129 (0.69)	5 (4.55)	167.40
Orthopedic procedures	36 (0.19)	0	
Gynecologic surgery	28 (0.15)	0	
General surgery	17 (0.09)	0	
Other	0	0	

ED, emergency department.
*Within the 3 months before initial opioid prescription in inpatient/ED setting.

In our study, a lower frequency of prescription opioid users was found living in the Northeast and Midwest/North Central United States regions (2.1% and 9.3%, respectively), and most patients prescribed opioids resided in the south (86.55%). This study provides evidence supporting the consistency in geographic opioid prescribing tendencies, as reported in previous studies. Olsen et al.[13] found that U.S. physicians in the Northeast and Midwest were significantly less likely to prescribe opioids than those working in the south and west and that patients in these regions had lower odds of being prescribed an opioid medication (OR = 0.60 and 0.75).[11] In the recent study by McDonald et al.,[20] Appalachia, western, and southern states were found to have the highest opioid prescribing rates. Number of available physicians was the strongest predictor of opioid prescription patterns. Unfortunately, the number of physicians and surgeons was not available in the database used for this study; therefore, further analysis will be needed to confirm the risk factors for opioid prescribing patterns, using alternative data.

This study also examined the frequency and time to diagnosed opioid abuse by selected diagnosis and procedure designations. Overall, the frequency of diagnosed opioid abuse in patients with common diagnoses/procedures was low (0.5%); however, the average time to diagnosed abuse was < 1 year (201 days). As the use of ICD-9-CM codes could only determine diagnosed opioid abuse, the generalization of results for undiagnosed opioid abusing populations may be invalid. Rates of prescription opioid abuse in patients from pain clinics have ranged from 0% to 90%, which demonstrates

study population heterogeneity and variations in defining prescription opioid abuse.[21]

Common cardiovascular/metabolic diseases and general health screenings are unlikely causes to initiate opioid use, and correspondingly, patients in these categories had low frequencies of diagnosed opioid abuse. While 2.6% of those with a mental health condition were later diagnosed with opioid abuse in this study, the sample size of patients with mental disorders was small (n = 313), and further research would be necessary to determine any connections. Although the sample sizes were small, there was a lack of diagnosed opioid abuse related to recent clinical procedures, suggesting that patients prescribed opioid medications after common clinical procedures are less likely to become diagnosed opioid abusers.

Due to the nature of the commercial claims database, the study results only represent the patients who were continuously insured in the commercial insurance plan. Uninsured and Medicaid patients, who have been demonstrated to have a high incidence of obtaining prescription opioids and percentage of chronic opioid misuse, were not included in this study. Due to the retrospective design of the study,[22] it is difficult to be certain of causal relationships. Due to this limitation, only the association between the variables of interest and the outcomes could be calculated. Additionally, residual confounding from unmeasured variables (such as treatment patterns, socioeconomic status, or disease severity) could have affected associations between various exposure variables and resulting health outcomes. The presence of a claim for a filled opioid prescription does not indicate whether the medication was actually taken as prescribed. Diversion still exists in situations where patients obtain opioids outside of the studied healthcare settings, and claims of diagnosed abuse only capture those patients whose physicians document their abuse in the claims system. Therefore, total opioid abuse would likely be underestimated. Despite these limitations, the use of a large claims database and a 4-year observation period in this study contribute to its nationally representative implications. This study also uses recent data, which is important in a population with increasing, rather than stationary, opioid abuse rates.

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