

Opioid Analgesic–Treated Chronic Pain Patients at Risk for Problematic Use

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Opioid utilization, especially in the United States, has been increasing for several years; Americans now consume 80% of the global opioid supply despite representing only 4.6% of the world's population.¹ The rise in opioid use can be attributed to a number of factors including changes in prescribing practices, suboptimal addiction risk factor screening, an increase in the aged population, and an increased availability of opioid medications.² The opioid abuse and addiction literature indicates that the behaviors of some chronic pain patients on opioid therapy put them at greater risk of consequences often associated with addiction, including elevated use of healthcare services, crime, and death.^{3,4}

Studies based on both clinical trial data⁵ and administrative claims databases⁶ have reported the incidence of diagnosed opioid abuse and/or addiction among the opioid analgesic–treated chronic pain (OAT-CP) population to be approximately 3%. However, there is disagreement among opioid prescribers on what constitutes aberrant drug-related behavior,⁷ compounded by OAT-CP patients' tendency to underreport these behaviors.⁸ The evidence on the prediction and identification of potentially problematic opioid use (PPOU) among OAT-CP patients is limited due to a number of factors including poor instrumentation, disagreement of terms across studies, and methodological shortcomings,⁹ though Rice and colleagues¹⁰ recently demonstrated that exposure to buprenorphine and diagnoses of nonopioid drug abuse and mental illness were predictive of opioid abuse. One review estimated addiction rates among the OAT-CP population to be between 0% and 50% depending on criteria used to define addiction.¹¹ Taken together, these findings highlight the need to build upon existing methods for identifying potentially problematic opioid users among the OAT-CP population.

Although opioid addiction results in well-documented societal costs,¹² undertreated chronic pain and associated costs cannot be ignored. Current algorithms and instruments tend to focus on either the quality of pain management or the emergence of opioid addiction and its consequences. Health plans and providers require algorithms with greater precision than those currently available to facilitate effective treatment of chronic pain patients based on both their need for analgesia and their probability of

developing problematic use or addiction. The purpose of the present study was to use a national managed care organization's administrative medical and pharmacy claims database to characterize OAT-CP pa-

Objectives: To characterize potentially problematic opioid use (PPOU) among opioid analgesic–treated chronic pain (OAT-CP) patients and to compare their healthcare service utilization and expenditures with those of a control group of OAT-CP patients not exhibiting these behaviors.

Study Design: Cross-sectional, retrospective analysis of health claims data.

Methods: Members of a national health plan (n = 3891) with chronic pain and an opioid prescription were categorized into 3 groups: PPOU group (n = 1499), those displaying evidence of doctor shopping or rapid opioid dose escalation; buprenorphine/naloxone group (n = 199), those who filled a prescription for buprenorphine/naloxone, which served as a proxy for opioid dependence; and control group (n = 2193), those not meeting either of the above criteria. Groups were compared on 1-year healthcare service utilization and costs.

Results: The PPOU group made up more than one-third of the study sample. Compared with the control group, they incurred significantly greater 1-year adjusted mean pharmacy costs (\$6573 vs \$6160), office costs (\$5705 vs \$4479), emergency department (ED) costs (\$835 vs \$388), inpatient costs (\$15,646 vs \$7445), and total healthcare costs (\$39,048 vs \$26,171) (all $P < .05$). The buprenorphine/naloxone group incurred significantly greater 1-year pharmacy costs (\$6981 vs \$6160) and ED costs (\$1126 vs \$388) (both $P < .05$) than the control group.

Conclusions: The PPOU group had the highest healthcare service utilization and costs. Although drivers of elevated service utilization and cost among this population are not clear, health plans may want to focus on PPOU case identification and development of interventions.

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Take-Away Points

The data available in medical and pharmacy claims were used to characterize a sample of opioid analgesic-treated chronic pain patients in a national health plan.

- One-third exhibited evidence of potential problematic opioid use in the absence of a clinical diagnosis of abuse or dependence.
- The potentially problematic opioid users had significantly higher healthcare service utilization and costs compared with nonproblematic opioid-using patients.
- Health plans may be able to use these methods to identify members with chronic pain who exhibit similar problematic behaviors in order to effectively intervene and optimize resource allocation.

The *International Classification of Diseases, Ninth Revision, Clinical Modification*, (ICD-9-CM) chronic pain diagnosis code (338.xx) is underutilized; therefore, 3 specific groups of diagnoses associated with chronic pain were used in case finding: neuropathic (diabetic peripheral neuropathy), inflammatory (osteoarthritis), and functional (low back pain).^{13,14} Chronic low back pain may be categorized in any of the 3 pain

tients who may meet our definition of PPOU and to compare the healthcare service utilization and costs of these members with those of a control group of OAT-CP patients without evidence of PPOU or addiction. It was hypothesized that the identified PPOU subsample would have significantly greater healthcare service utilization and costs compared with OAT-CP patients without evidence of PPOU.

classes,¹³ but was primarily selected because a significant portion of the chronic pain population has this condition.¹⁵ A conservative rule for defining chronic pain was applied, which required 3 claims within a specific diagnosis group to appear, spanning at least a 3-month period.¹⁶ The **Figure** details the attrition of the sample at each imposition of the inclusion and exclusion criteria, resulting in the final study sample (N = 3891).

METHODS

Sample Selection

Aetna (Blue Bell, Pennsylvania) provided medical, pharmacy, and provider data for their chronic pain population during calendar years 2009 through 2011. To identify the study sample, the following inclusion and exclusion criteria were imposed:

1. Adults (aged 18-64 years) with chronic pain were defined as those with either
 - a. at least 1 medical claim with a diagnosis of chronic pain, or
 - b. during a period of at least 3 months, 3 claims with a primary diagnosis of low back pain, 3 claims with a primary diagnosis of osteoarthritis, or 3 claims with a primary diagnosis of diabetic peripheral neuropathy (first claim serving as the index event).
2. 6 months “chronic pain naïve” prior to the index date.
3. >90 days of supply of any opioids prescribed within a 180-day window around the index date (90 days pre-index, 90 days postindex), including both long- and short-acting formulations, as well as combination products.
4. Continuous eligibility for 18 months around the index date (6 months pre-index, 12 months postindex).
5. Absence of mood disorder or drug dependence diagnoses. (In the current sample, 5 patients had a diagnosis of opioid dependence while meeting no other group assignment criteria.)

Placement Into Opioid Use Groups

Each member of the study sample was assigned hierarchically to 1 of 3 mutually exclusive groups based on their 1-year postindex claims. Members who qualified for multiple groups were placed in the highest ranking group.

1. **Buprenorphine/naloxone group.** Members of this group had at least 1 fill for buprenorphine/naloxone.
2. **PPOU group.** Members of this group had a pattern of opioid prescription fills that reflected either doctor shopping, defined as receiving opioid fills from 5 or more different prescribers within 1 year,¹⁷ or rapid dose escalation, defined as either a 50% increase in opioid dose (combined standard morphine units across any long- or short-acting opioids prescriptions¹⁸) during the first 3 months or a 100% increase in dose at any time during the course of the follow-up period. Both short- and long-acting opioids were used in the dose escalation calculation, and methods were implemented to prevent double counting of day.
3. **Control group.** Members of this group did not meet any of the above criteria.

The buprenorphine/naloxone group was created as a proxy for opioid abuse or dependence.¹⁰ The PPOU group served as the main study group of interest, as these members provided no direct evidence of opioid abuse or addiction. Both the buprenorphine/naloxone and PPOU groups were compared with the control group, which was composed of normal-functioning OAT-CP patients without any discernible signs of problematic use, abuse, or addiction.

Measures

The following health services and expenditure outcomes were measured and compared across groups:

- Total prescription fills and costs.
- Opioid fills and costs.
- Inpatient hospital admissions, days, and costs.
- Emergency department (ED) visits and costs.
- Physician office visits and costs.
- Outpatient hospital visits and costs.
- Total medical costs.
- Total healthcare costs (medical plus pharmacy costs).

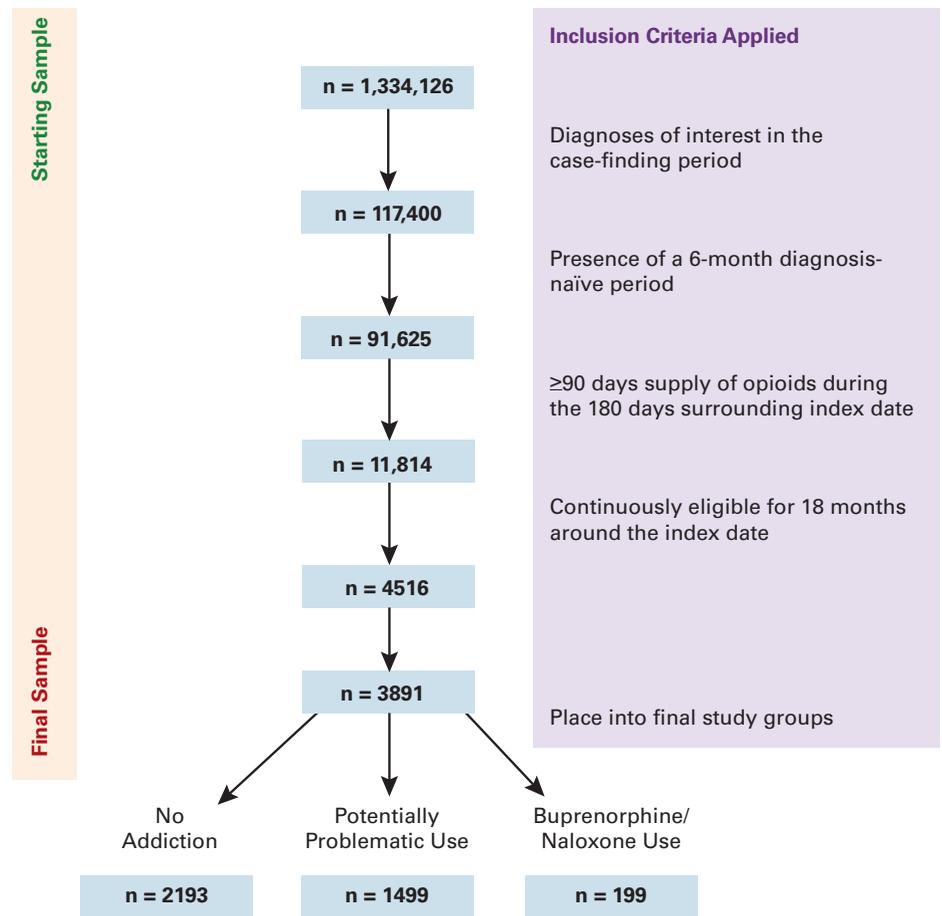
Bivariate Analyses

Study groups were compared on demographic variables including age, sex, chronic pain diagnosis, preindex Charlson Comorbidity Index score¹⁹ (a measure of overall health), and region of residence. Groups were then compared on 1-year postindex period healthcare service utilization and cost variables. Chi-square tests of equality of proportions were used for categorical variables, and 1-way analysis of variance was used for continuous variables. Tukey’s post hoc tests were conducted to examine group differences when omnibus tests were statistically significant.

Multivariate Analyses

Differences in residualized postindex period service utilization counts and costs were adjusted for sex, region of residence, age, and the Charlson Comorbidity Index score using 2-step regression models. Outpatient, inpatient, and ED measures are typically zero-inflated distributions and were therefore dichotomized into no/any utilization or spending and served as dependent variables in logistic regression models. Next, the subset of cases with any utilization/expenditure on these measures was selected and entered into generalized linear models. For service utilization counts, Poisson log-linear models were estimated. For cost variables, gamma models with a log link were estimated. Pharmacy utilization

Figure. Sample Attrition



and costs, office utilization and costs, and total costs did not present zero-inflated distributions and were directly regressed onto the predictors via generalized linear models. All data management and analyses were conducted using SPSS version 20 (IBM Corp, Armonk, New York).

RESULTS

A total of 3891 OAT-CP patients were included in the analyses. Of them, 199 (5.1%) had a fill for buprenorphine/naloxone during the postindex period. Evidence of PPOU was found in 38.5% (n = 1499) of the sample, with 25.4% (n = 989) having rapid dose escalation, 21.3% (n = 827) engaging in doctor shopping, and 8.1% (n = 317) exhibiting both behaviors. The remaining 56.4% of members (n = 2193) comprised the control group, with no evidence of PPOU, abuse, or addiction.

Table 1 displays demographic characteristics and postindex service utilization and cost measures for the total sample as well as the study groups. Regarding demographics, the

■ **Table 1.** Demographics and Postindex Period Healthcare Service Utilization and Expenditure

Variable	Total (n = 3891)		Control Group (n = 2193)		Suboxone Group (n = 199)		Potentially Problematic Use Group (n = 1499)		P	Post hoc ^a
	Mean or f	SD or %	Mean or f	SD or %	Mean or f	SD or %	Mean or f	SD or %		
Demographic characteristics										
Age, y	47.6	9.6	48.6	9.3	41.9	10.9	46.8	9.6	<.001	A, B, C
Male	1754	45.1%	968	44.1%	119	59.8%	667	44.5%	<.001	A, C
Pain diagnosis										
Chronic pain	442	11.4%	247	11.3%	26	13.1%	169	11.3%	.739	—
Low back pain	2306	59.3%	1310	59.7%	125	62.8%	871	58.1%	.354	—
Osteoarthritis	1137	29.2%	633	28.9%	48	24.1%	456	30.4%	.159	—
Diabetic peripheral neuropathy	6	0.2%	3	0.1%	0	0.0%	3	0.2%	.757	—
Region										
Midwest	915	23.5%	545	24.9%	36	18.1%	334	22.3%	.033	A
Northeast	1007	25.9%	549	25.0%	71	35.7%	387	25.8%	.005	A, C
Southeast	1145	29.4%	638	29.1%	48	24.1%	459	30.6%	.150	—
West	805	20.7%	449	20.5%	43	21.6%	313	20.9%	.911	—
Unknown	19	0.5%	12	0.5%	1	0.5%	6	0.4%	.820	—
Charlson Comorbidity Index score (preindex)	0.03	0.24	0.03	0.19	0.02	0.12	0.04	0.31	.163	—
Healthcare service utilization										
Opioid fills	18.7	9.7	17.0	8.6	21.5	12.9	20.8	10.2	<.001	A, B
Total prescription fills	61.4	36.0	59.3	36.2	60.1	33.3	64.6	36.0	<.001	B
Office visits	10.1	8.6	9.3	8.2	11.7	9.8	11.0	8.8	<.001	A, B
Outpatient visits	2.9	5.2	2.4	4.5	2.8	5.1	3.7	6.1	<.001	B
ED visits	0.3	1.3	0.2	0.7	0.7	3.1	0.5	1.5	<.001	A, B, C
Inpatient admissions	0.6	2.8	0.4	1.9	0.6	2.0	0.9	3.7	<.001	B
Inpatient days	0.9	3.9	0.7	3.4	0.8	2.9	1.3	4.7	<.001	B
Healthcare expenditures										
Opioid costs	\$2514	\$5177	\$2396	\$5249	\$4160	\$4220	\$2468	\$5153	<.001	A, C
Total prescription costs	\$6337	\$8597	\$6266	\$8458	\$7181	\$5489	\$6330	\$9118	.355	—
Office costs	\$5036	\$8324	\$4449	\$8304	\$5667	\$7131	\$5812	\$8435	<.001	B
Outpatient costs	\$8385	\$27,754	\$7358	\$28,988	\$7117	\$18,480	\$10,055	\$26,852	.012	B
ED costs	\$610	\$2847	\$324	\$1780	\$1594	\$6165	\$897	\$3324	<.001	A, B, C
Inpatient costs	\$10,430	\$46,797	\$7530	\$40,796	\$6584	\$32,187	\$15,182	\$55,477	<.001	B, C
Total medical costs	\$24,740	\$57,652	\$19,928	\$53,481	\$21,402	\$41,031	\$32,223	\$64,278	<.001	B, C
Total healthcare costs	\$31,077	\$58,341	\$26,193	\$54,397	\$28,583	\$41,425	\$38,553	\$64,732	<.001	B

ED indicates emergency department; f, frequency.

^aPost hoc test results. A, Suboxone significantly different from control; B, problematic use significantly different from control; C, Suboxone significantly different from problematic use.

sample was predominantly female (54.9%), with a mean age of 47.6 years (± 9.6 years), and was equally dispersed across the 4 regions of the United States (Midwest 23.5%; Northeast 25.9%; Southeast 29.4%; West 20.7%). The mean pre-index period Charlson Comorbidity Index score was 0.03 ± 0.24 . There was a statistically significant main effect for age ($F_{[2, 3890]} = 51.8; P < .001$), with the control group being significantly older than both the buprenorphine/naloxone and PPOU groups and with the PPOU group being significantly older than the buprenorphine/naloxone group ($P < .001$). There was also a statistically significant difference between groups on sex ($\chi^2_{[1, n = 3891]} = 18.4; P < .001$), with the buprenorphine/naloxone group being significantly more likely to be male than both the control and the PPOU groups ($P < .001$). There were no statistically significant differences between groups on the Charlson Comorbidity Index score ($F_{[2, 3890]} = 1.8; P = .163$), nor on the distribution of chronic pain diagnoses ($\chi^2_{[6, n = 3891]} = 4.5; P = .604$). Regarding postindex period service utilization and cost measures, significant group differences were found on all measures excluding total prescription costs. Compared with the control group, both the PPOU group and buprenorphine/naloxone group had significantly more mean ED visits (0.5 and 0.7 vs 0.2) and higher costs (\$897 and \$1594 vs \$324), while the buprenorphine/naloxone group had significantly more ED visits and higher costs than the PPOU group. Both the PPOU and buprenorphine/naloxone groups had significantly more mean office visits (11.0 and 11.7 vs 9.3) and opioid fills (20.8 and 21.5 vs 17.0) compared with controls. The buprenorphine/naloxone group had significantly higher opioid costs than both the PPOU and control groups (\$4160 vs \$2468 and \$2396). Compared with both the buprenorphine/naloxone and control groups, the PPOU group had significantly higher mean inpatient costs (\$15,182 vs \$6584 and \$7530) and total medical costs (\$32,223 vs \$21,402 and \$19,928). Finally, compared with the control group, the PPOU group had significantly more mean prescription fills (64.6 vs 59.3), outpatient visits (3.7 vs 2.4), inpatient admissions (0.9 vs 0.4), and inpatient days (1.3 vs 0.7), and higher office costs (\$5812 vs \$4449), outpatient costs (\$10,055 vs \$7358), and total healthcare costs (\$38,553 vs \$26,193).

Tables 2A, 2B, and 2C and **Tables 3A, 3B, and 3C** display parameter estimates from regression models for health service utilization and costs during the postindex period. Logistic models were constructed for outpatient, inpatient, and ED indicators due to zero-inflated distributions. Subsequent Poisson and gamma models are presented for these outcomes in the subsample with non-zero cost values. With regard to prescription fills/costs and total healthcare costs, the entire sample was utilized, as true zero values were absent

from these distributions. Three percent of cases ($n = 125$) had true zero office visits and costs, which although they did not qualify as a zero inflation problem, were required to be dropped from the final office models. Regardless, there were no statistically significant differences between groups on the proportion of members with zero office visits ($\chi^2_{[2, n = 3891]} = 1.5; P = .468$).

Logistic models revealed that males were significantly less likely than females to utilize any outpatient or ED services and costs ($P < .05$). Older members were more likely to have any outpatient and inpatient hospital visits and costs, but were less likely to incur any ED services or costs ($P < .001$). Compared with control members, PPOU group members were more than 1.85 times as likely to receive outpatient services and more than twice as likely to receive inpatient and ED services ($P < .001$). The buprenorphine/naloxone group members were 1.7 times as likely to receive inpatient services as control members and were more than twice as likely to visit the ED ($P < .01$).

Poisson models of non-zero health service utilization rates revealed that males had significantly fewer prescription fills, office visits, and outpatient visits than females, while age was positively associated with prescription fills, outpatient visits, and inpatient admissions ($P < .01$). Poorer health was associated with increased pharmacy fills but decreased office visits ($P < .05$). Compared with the control group, the PPOU group had 9% more prescription fills, 15% more office visits, 17% more outpatient visits, 13% more inpatient admissions, and 34% more ED visits ($P < .01$). Additionally, the buprenorphine/naloxone group had 9% more prescription fills, 22% more office visits, 18% more outpatient visits, 13% more inpatient admissions, and 37% more ED visits than controls ($P < .01$).

Gamma models of non-zero healthcare expenditure revealed that males had significantly lower pharmacy and office costs than females, while age was inversely associated with outpatient costs ($P < .05$). Poorer health was positively associated with office and total healthcare costs ($P < .05$). Compared with the control group, the PPOU group incurred 12% greater pharmacy costs, 35% greater office costs, 14% greater outpatient costs, and 54% greater total healthcare costs ($P < .01$). Additionally, the buprenorphine/naloxone group incurred 52% greater pharmacy costs, 26% greater office costs, and 24% greater total healthcare costs than controls ($P < .01$).

DISCUSSION

The purpose of this study was to characterize OAT-CP patients who exhibited PPOU or elevated likelihood of opioid abuse or addiction¹⁰ and compare their healthcare service uti-

■ **Table 2A.** Binary Logistic Models of Select Healthcare Utilization

Predictor	Outpatient Visits Dichotomized			Inpatient Visits Dichotomized			ED Visits Dichotomized		
	β	Exp(B)	P	β	Exp(B)	P	β	Exp(B)	P
Suboxone	0.19	1.21	.21	0.54	1.72	.01	0.73	2.08	<.001
Potentially problematic use	0.61	1.85	<.001	0.89	2.44	<.001	0.76	2.14	<.001
Male	-0.14	0.87	.04	-0.14	0.87	.11	-0.34	0.71	<.001
Northeast region	-0.19	0.82	.04	-0.11	0.89	.37	0.06	1.06	.66
Southeast region	-0.31	0.73	<.001	-0.05	0.96	.71	0.09	1.09	.51
West region	-0.20	0.82	.05	-0.02	0.98	.90	-0.03	0.97	.84
Age	0.01	1.01	<.001	0.04	1.04	<.001	-0.02	0.98	<.001
Charlson Comorbidity Index score	0.09	1.10	.55	0.13	1.14	.39	0.12	1.13	.49
Preindex period value	0.37	1.45	<.001	0.25	1.28	<.001	1.40	4.04	<.001
Constant	-0.46	0.00	.01	-3.68	.00	<.001	-1.31	0.00	<.001

ED indicates emergency department.

■ **Table 2B.** Poisson Log Linear Models of Pharmacy Fills, Office Visits, and Outpatient Visits

Predictor	Pharmacy Fills			Office Visits			Outpatient Visits		
	β	Exp(B)	P	β	Exp(B)	P	β	Exp(B)	P
Constant	3.32	.00	<.001	2.09	.00	<.001	1.30	0.00	<.001
Potentially problematic use	0.09	1.09	<.001	0.14	1.15	<.001	0.16	1.17	<.001
Suboxone	0.09	1.09	<.001	0.20	1.22	<.001	0.16	1.18	<.001
Male	-0.07	0.93	<.001	-0.03	0.97	.01	-0.05	0.95	<.001
West region	-0.01	0.99	.05	0.07	1.08	<.001	-0.19	0.82	<.001
Southeast region	-0.01	0.99	.01	0.07	1.07	<.001	-0.06	0.94	.01
Northeast region	-0.04	0.96	<.001	0.04	1.04	.01	-0.07	0.93	<.001
Age	.000	1.00	<.001	0.00	1.00	.75	0.01	1.01	<.001
Charlson Comorbidity Index score	0.02	1.02	<.001	-0.04	0.96	.05	-0.03	0.97	.30
Preindex period value	0.02	1.02	<.001	0.05	1.05	<.001	0.05	1.06	<.001

■ **Table 2C.** Poisson Log Linear Models of Inpatient Hospital Admissions and ED Visits

Predictor	Inpatient Hospital Admissions			ED Visits		
	β	Exp(B)	P	β	Exp(B)	P
Constant	1.07	0.00	<.001	0.88	0.00	<.001
Potentially problematic use	0.12	1.13	.01	0.29	1.34	<.001
Suboxone	0.12	1.13	.24	0.31	1.37	.01
Male	0.06	1.06	.19	0.06	1.06	.32
West region	-0.43	0.65	<.001	-0.14	0.87	.16
Southeast region	-0.26	0.77	<.001	-0.08	0.92	.32
Northeast region	-0.30	0.74	<.001	0.11	1.11	.19
Age	0.01	1.01	.01	-0.01	0.99	<.001
Charlson Comorbidity Index score	-0.06	0.94	.34	-0.01	0.99	.92
Preindex period value	0.08	1.08	<.001	0.08	1.09	<.001

ED indicates emergency department.

Opioid Analgesic–Treated Chronic Pain Patients at Risk

■ **Table 3A.** Binary Logistic Models of Select Healthcare Costs

Predictor	Outpatient Costs Dichotomized			Inpatient Hospital Costs Dichotomized			ED Costs Dichotomized		
	β	Exp(B)	P	β	Exp(B)	P	β	Exp(B)	P
Suboxone	0.21	1.23	.18	0.35	1.42	.18	0.76	2.13	<.001
Potentially problematic use	0.63	1.87	<.001	0.67	1.95	<.001	0.84	2.33	<.001
Male	-0.16	0.86	.02	0.00	1.00	.99	-0.35	0.70	<.001
Northeast region	-0.21	0.81	.02	-0.04	0.96	.76	0.08	1.08	.57
Southeast region	-0.31	0.73	<.001	-0.01	0.99	.95	0.10	1.11	.43
West region	-0.23	0.80	.02	-0.03	0.97	.87	-0.08	0.93	.60
Age	0.01	1.01	<.001	0.04	1.04	<.001	-0.02	0.98	<.001
Charlson Comorbidity Index score	0.18	1.19	.25	0.17	1.18	.30	0.19	1.21	.23
Preindex period value	0.00	1.00	<.001	0.00	1.00	.22	0.00	1.00	<.001
Constant	-0.42	0.66	.02	-3.35	0.03	<.001	-1.22	0.30	<.001

ED indicates emergency department.

■ **Table 3B.** Gamma Models of Outpatient, Inpatient, and ED Costs

Predictor	Outpatient Costs			Inpatient Hospital Costs			ED Costs		
	β	Exp(B)	P	β	Exp(B)	P	β	Exp(B)	P
Constant	9.37	0.00	<.001	11.42	0.00	<.001	8.61	0.00	<.001
Potentially problematic use	0.13	1.14	.04	0.02	1.02	.91	0.18	1.20	.10
Suboxone	0.00	1.00	.99	-0.56	0.57	.09	0.35	1.43	.09
Male	0.09	1.10	.14	0.13	1.14	.33	0.02	1.02	.82
West region	0.02	1.03	.79	0.21	1.23	.29	0.01	1.01	.97
Southeast region	-0.22	0.80	.01	-0.29	0.75	.10	-0.25	0.78	.08
Northeast region	0.01	1.01	.91	-0.07	0.93	.69	-0.21	0.81	.15
Age	-0.30	0.74	.01	-0.19	0.83	.16	-0.23	0.79	.27
Charlson Comorbidity Index score	0.00	1.00	.31	-0.01	0.99	.32	-0.01	0.99	.07
Preindex period value	0.00	1.00	<.001	0.00	1.00	.23	0.00	1.00	<.001

ED indicates emergency department.

■ **Table 3C.** Gamma Models of Pharmacy, Office, and Total Healthcare Costs

Predictor	Pharmacy Costs			Office Costs			Total Costs		
	β	Exp(B)	P	β	Exp(B)	P	β	Exp(B)	P
Constant	7.65	0.00	<.001	8.53	0.00	<.001	9.53	0.00	<.001
Potentially problematic use	0.12	1.12	<.001	0.30	1.35	<.001	0.43	1.54	<.001
Suboxone	0.42	1.52	<.001	0.23	1.26	<.001	0.22	1.24	.01
Male	-0.09	0.92	<.001	-0.07	0.93	.04	-0.04	0.96	.23
West region	0.03	1.03	.38	-0.11	0.90	.04	0.04	1.04	.48
Southeast region	0.02	1.02	.59	0.01	1.01	.91	-0.17	0.84	<.001
Northeast region	0.03	1.03	.44	-0.03	0.97	.51	-0.03	0.97	.59
Age	0.08	1.08	.14	-0.03	0.97	.58	-0.04	0.96	.53
Charlson Comorbidity Index score	0.00	1.00	.07	0.00	1.00	.03	0.01	1.01	<.001
Preindex period value	0.00	1.00	<.001	0.00	1.00	<.001	0.00	1.00	<.001

lization and costs with those of the group of OAT-CP patients without evidence of these behaviors. Just more than 5% of the OAT-CP sample had a prescription fill for buprenorphine/naloxone, which was used as a proxy for opioid abuse and addiction.¹⁰ Intriguingly, 39% of the sample showed signs of PPOU, defined as either doctor shopping or rapid opioid dose escalation in the absence of opioid abuse/addiction, or a buprenorphine/naloxone fill. The rate of PPOU behavior found in the current analyses is consistent with rates of behavioral markers of opioid abuse and dependence as high as 50%.²⁰ The remainder of the sample (56%) showed no evidence of either addiction or PPOU based on their claims. Results of both bivariate and adjusted multivariate models of health service utilization and expenditure showed statistically significant differences between study groups on most outcomes, with the PPOU group generally having the largest rate of service utilization and highest average costs. Overall, when controlling for patient characteristics, the PPOU group incurred 54% greater total healthcare costs than the control group, while the buprenorphine/naloxone group incurred 24% greater costs.

Implications for Patients

The Institute of Medicine estimates that roughly 116 million Americans affected with chronic pain are undertreated.²¹ However, long-term opioid treatment is complicated, as illustrated by the wide range of published rates of addiction and problematic use among OAT-CP patients.^{6,20} Further, the limitations inherent in the use of the ICD-9 opioid dependence/abuse diagnostic criteria combined with our finding that nearly 40% of an OAT-CP sample showed evidence of PPOU underscores the importance of heightened patient awareness regarding the delicate balance between the benefits and potential risks of chronic opioid treatment. A continuous dialogue between patients and their treating physicians is necessary to optimize pain management and functioning while minimizing the risk of opioid abuse and addiction.

Implications for Providers

There is considerable variability in and controversy about the prescribing practices of physicians who treat chronic pain with opioids.^{22,23} Apparent dose escalation was a qualifier for inclusion in the PPOU group in the current study, and 25% of the sample met that criterion. While dose titration is often appropriate according to the package insert of many opioid products, it is unclear whether this titration is necessary to adequately control pain or is simply a response to tolerance and hyperalgesia. However, in either case, titration or dose escalation may increase the likelihood of developing addiction²⁴ and therefore requires close monitoring. The level of doctor shop-

ping observed (21%) was also not inconsequential. The implementation of state-level prescription monitoring programs may facilitate more informed prescribing practices for physicians who choose to participate, which may in part curtail this behavior.²⁵ Other recommendations for improving prescriber awareness include addiction screening throughout treatment using questionnaires, patient interviews, and lab tests.²⁶

Implications for Payers

Early identification of OAT-CP patients at risk for PPOU may provide payers with an opportunity to avoid unnecessary healthcare costs.²⁷ In the present study, the per member per year total healthcare cost for PPOU group members was nearly \$13,000 greater than the per member per year cost for nonproblematic OAT-CP members. Assuming that present results are similar to those of other managed care organizations, health plans can expect to expend significant amounts of resources on the management of chronic pain without knowing how the costs partition between nonaddiction, PPOU, and addiction cases. Specifically within the PPOU group, it will be important to distinguish between those patients exhibiting true problematic opioid use and those with more severe pain conditions that require additional pharmaceutical and medical interventions. With further exploration and confirmation of the problematic use definition and process, health plans may soon be able to partition costs and implement interventions that are matched to the needs of each of these segments of the OAT-CP population.

Effective care management may be part of the solution. Utilization reviewers and case managers within health plans routinely monitor patients at the greatest risk for utilization of avoidable high-cost-venue services, which in theory increases the overall quality of patient care. It is feasible that increased monitoring of the PPOU group could improve these patients' pain management and daily functioning, while decreasing emergence of opioid abuse/addiction and avoiding unnecessary healthcare spending.

Limitations

One limitation of the present study was the use of administrative claims data, which does not allow for the assessment of clinical outcomes and may include administrative coding errors.²⁸ Furthermore, the between-group factor based on buprenorphine/naloxone fills and PPOU may be endogenous, meaning that other unmeasured factors could drive healthcare service utilization patterns that are proxies for PPOU. Additionally, unmeasured characteristics correlated with both the development of PPOU and healthcare utilization may lead to biased estimates.

A key limitation of note was the operational definitions used to identify patients with PPOU, specifically the defi-

nitions for dose escalation and doctor shopping. Although developed as a proxy for increased tolerance to opioids and drug-seeking behavior, dose escalation as defined here is confounded with the otherwise-sound clinical practice of opioid dose titration.²⁹ As claims data do not provide clinical judgment or visit notes, it is not possible to distinguish between these 2 processes. Additionally, patients in the dose escalation group may be experiencing more severe pain and/or multiple comorbidities warranting rapid titration, although there were no between-group differences on the Charlson Comorbidity Index score or on the distribution of indexed pain diagnoses. As patients with more severe or complex clinical presentations tend to require more medical resources, it cannot be determined from this study what portion of the cost was truly avoidable or unnecessary. Additional work is needed to better understand how results would have changed if different definitions had been used. Finally, although the doctor-shopping definition applied in the current study was based on published work,¹⁷ little agreement exists in the literature on what constitutes true opioid doctor-shopping behavior, with evidence supporting a wide range of criteria: more than 5 prescribers,³⁰ 4 or more prescribers,²⁵ filling of 2 or more prescriptions by different prescribers within 1 day,³¹ and 1 or more prescribers and at least 3 pharmacies.³² Analyses applying varying definitions of doctor shopping to test the robustness of the results should be considered in future research.

Future Directions

Additional studies are needed to validate the operational definitions of the elements of PPOU used here: doctor shopping and rapid dose escalation. The latter metric was developed for this study based on the assumption that rapid dose increases indicate possible increased tolerance to opioids for some OAT-CP patients and are a marker of potentially emerging opioid abuse, misuse, or addiction. The definitions used here should be explored and differentiated from accepted titration patterns in order to effectively develop a correction factor for the algorithm. Additionally, the relationship between patients who utilize multiple prescribers and those who exhibit rapid dose escalation should be further explored. Chronic pain patients on buprenorphine/naloxone also warrant additional investigation. Although Rice and colleagues¹⁰ emphasized that the relationship between buprenorphine/naloxone use and opioid abuse was correlational in their study, removal of this variable from their statistical models led to changes in the statistical significance of other predictors, indicating that a fill for buprenorphine/naloxone may be a marker for some unobserved patient characteristics that are associated with problematic use,

abuse, or addiction. In the current study, a number of service utilization and expenditure outcomes for the buprenorphine/naloxone group were greater than those evidenced by controls but similar to those for the PPOU group, suggesting a possible correlation between these 2 groups that should be explored further.

Future research should also examine general provider knowledge and attitudes regarding opioid addiction. As the present study has indicated, more than one-third of the sample demonstrated PPOU, which resulted in significantly greater healthcare utilization and spending. Given the limitations of claims data, it is unclear whether the prescribers were psychiatrists or other mental health professionals informed and trained in identifying the signs and symptoms of a developing addiction. Exploration of prescriber specialty as it relates to opioid prescribing is needed.

CONCLUSION

More than one-third of a sample of OAT-CP patients were identified as potentially problematic opioid users according to the study definitions applied. Healthcare service utilization and expenditures were significantly greater for this group compared with the control group; the group of patients who filled a prescription for buprenorphine/naloxone were also shown to incur higher service rates and costs. These findings demonstrate a need for closer monitoring of PPOU patients, even in the absence of an opioid abuse or dependence diagnosis, and the use of interventions tailored to mitigate the effect of problematic use on patients and payers. These results suggest that focusing only on the diagnosis of opioid addiction will likely underestimate the impact of problematic use on healthcare service utilization and costs. Broadening the criteria beyond diagnosis codes to include indicators of potentially problematic use may have value to health plans and providers interested in improving outcomes and containing costs.

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