Analytic Models to Identify Patients at Risk for Prescription Opioid Abuse

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Objective: To assess the feasibility of using medical and prescription drug claims data to develop models that identify patients at risk for prescription opioid abuse or misuse.

Study Design: Deidentified prescription drug and medical claims for approximately 632,000 privately insured patients in Maine from 2005 to 2006 were used. Patients receiving prescription opioids were divided into 2 mutually exclusive groups, namely, prescription opioid abusers and nonabusers.

Methods: Potential risk factors for prescription opioid abuse were incorporated into logistic models to identify their effects on the probability that a prescription opioid user was diagnosed as having prescription opioid abuse. Different models were based on data available to prescription-monitoring programs and managed care organizations. Best-fitting models were identified based on statistical significance ($P \leq .05$), parsimony, clinical relevance, and area under the receiver operating characteristic curve.

Results: The drug claims models found that the following factors (measured over a 3-month period) were associated with risk for prescription opioid abuse: age 18 to 34 years, male sex, 4 or more opioid prescriptions, opioid prescriptions from 2 or more pharmacies, early prescription opioid refills, escalating morphine sulfate dosages, and opioid prescriptions from 2 or more physicians. The model integrating drug and medical claims found that the following factors (measured over a 12-month period) were associated with risk for prescription opioid abuse or misuse: age 18 to 24 years, male sex, 12 or more opioid prescriptions, opioid prescriptions from 3 or more pharmacies, early prescription opioid refills, escalating morphine dosages, psychiatric outpatient visits, hospital visits, and diagnoses of nonopioid substance abuse, depression, posttraumatic stress disorder, and hepatitis.

Conclusion: Using drug and medical claims data, it is feasible to develop models that could assist prescription-monitoring programs, payers, and healthcare providers in evaluating patient characteristics associated with elevated risk for prescription opioid abuse.

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For author information and disclosures, see end of text.

Prescription opioid abuse or misuse (ie, intentional exposure to prescription opioids in a manner inconsistent with the use they were prescribed for) has become a major societal issue.[1-6] The negative health consequences resulting from prescription opioid abuse or misuse include emergency department visits, hospitalizations, and substance abuse treatment admissions. The National Survey on Drug Use and Health estimates that from 2002 to 2007 an annual mean of 11.8 million Americans used prescription pain relievers for nonmedical purposes.[7] The number of patients admitted for inpatient treatment of prescription opioid abuse or misuse has increased from approximately 46,000 in 2002 to more than 81,000 in 2007.[8] Furthermore, the number of emergency department visits related to nonmedical use of opiates or opioid analgesics has jumped from fewer than 180,000 in 2004 to more than 250,000 in 2006.[9] These increases in prescription opioid abuse or misuse underscore its importance as a major public health issue.[10]

Programs that combat the rise of prescription opioid abuse or misuse (such as prescription-monitoring programs [PMPs]) exist in various forms.[11] As of December 2007, a total of 26 states had launched PMPs; 9 more had legislation requiring their creation, while several others were considering similar legislation.[12-15] Many speculate about the benefits of PMPs, but little empirical evidence exists.[16-19] Hypothesized advantages include identification of potentially inappropriate prescribing or dispensing practices and effective ongoing monitoring of patients receiving prescription opioid therapy, including identification of at-risk patients to physicians via warning letters. Other benefits may include the ability to provide better care and reduce costs associated with abuse-related events (eg, emergency department visits). Prescription-monitoring programs have recognized the limitations inherent in interpreting their data and have set up external professional committees to limit unintended negative consequences (eg, false positives). Nevertheless, some concern exists that PMPs may produce a "chilling effect" as discussed by Wastila and Bishop.[20] For example, further research by Simoni-Wastila et al[19] demonstrated that the requirement by New York that physicians use state-monitored prescription forms for benzodiazepines led to reduced benzodiazepine use.

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Although risk factors associated with drug abuse have been studied, few published studies have used data simi-

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Take-Away Points

It is feasible to use claims data to develop models that estimate risk of prescription opioid abuse. Prescription-monitoring programs and managed care organizations have data that may be used to implement such models. Consequently, there is potential for early identification of patients at risk, which may improve patient outcomes through earlier detection and treatment.

- Age 18 to 34 years and male sex were significant demographic risk factors.
- Filling opioid prescriptions at multiple pharmacies and refilling opioid prescriptions early were significant drug use–related risk factors.
- Clinicians should be cautious in applying such statistical models to individual patients, who should each be considered individually in light of such risk factors.

lar to those available to PMPs and managed care organizations (MCOs) to develop models that identify patients at risk for prescription opioid abuse or misuse.[21,22] While some PMPs use basic algorithms or thresholds to identify potential at-risk patients, combining more detailed claims-based algorithms with clinical measures of abuse may enhance their ability to identify those at risk. Our objective was to assess the feasibility of using medical and prescription drug claims data to develop models that identify patients at risk for prescription opioid abuse or misuse using observed outcomes measures (ie, based on *International Classification of Diseases, Ninth Revision, Clinical Modification* [*ICD-9-CM*] codes).

METHODS

Data

This study used deidentified medical and prescription drug claims data provided by the Maine Health Data Organization[23] for approximately 632,000 privately insured residents of Maine (from 2005 to 2006). Data on the prescribing physician were only available beginning in September 2006. Patients aged 12 to 64 years with at least 1 claim for a prescription opioid and at least 1 medical claim from 2005 to 2006 were identified (ie, the prescription opioid user population). This population was further divided into 2 mutually exclusive groups, namely, prescription opioid abusers and nonabusers. Prescription opioid abusers were defined as the subset of all prescription opioid users having at least 1 medical claim associated with any of the following *ICD-9-CM* codes from 2005 to 2006: 304.0 (opioid-type dependence), 304.7 (combinations of opioid type with any other), 305.5 (opioid abuse), or 965.0 (poisoning by opiates or related narcotics but excluding 965.01 [heroin poisoning]). The nonabusers consisted of the remaining prescription opioid users, who had no claims associated with the 4 abuse codes.

This approach of using *ICD-9-CM* codes to identify opioid abusers is consistent with prior research.[24] However, there are other instances of abuse-related phenomena (eg, "nonmedical use of prescription drugs" as measured by the National Survey on Drug Use and Health) that this study does not identify and which may occur in the nonabuser sample.

Statistical Analysis

Potential risk factors for prescription opioid abuse were incorporated into models based on prior analyses of prescription opioid utilization patterns and clinical knowledge of comorbidities associated with prescription opioid abuse.[25-27] Stepwise logistic regression models were used to evaluate the effects of independent variables corresponding to these risk factors. Each model began with a core set of demographic variables that categorized patients by sex and age group. Then, additional variables related to drug use, comorbidities, and medical services were added based on their statistical or clinical significance. Independent variables are listed and described in more detail in eAppendices A and B (available at **www.ajmc.com**).

The models took the following general form:

$$\text{Log}\left(\frac{p_i}{1-p_i}\right) = \alpha + \sum_{j=1}^{J} \beta_j X_{ij}$$

where p_i is the probability that patient i is a prescription opioid abuser, α and β_j are variables of the model to be estimated, and X_{ij} are the J risk factors for the i patients. Note that the general model describes associations rather than causation.

Three general logistic models were developed, namely, 2 based on drug claims alone and 1 that integrates data from drug and medical claims. The drug claims models serve as approximations for the data available to a PMP director, whereas the integrated model represents the data available to MCOs. For the models based only on drug claims, drug utilization behavior was assessed during the 3-month period following the index date (because many PMPs review data on a quarterly basis). The first variation excludes information on prescribing physicians, while the second variation incorporates such information but requires the use of an abbreviated time frame because the Maine data did not identify prescribing physicians until the last quarter of 2006. The third (integrated) model builds on the first by also including information on healthcare services and comorbidities from medical claims to estimate a more comprehensive model. Patient characteristics were measured over the 12-month period following the index date. To identify the best-fitting models, the following 4 criteria were used:

Area Under the Receiver Operating Characteristic Curve. The performance of different algorithms was evaluated by comparing the area under the receiver operating characteristic (ROC) curves using SAS (Version 9.1, SAS Institute, Inc, Cary, NC). The ROC curves were used to assess overall fit (eg, a model that has a greater area under the ROC curve will have a better fit). This study sought to optimize the tradeoff between sensitivity and specificity. That is, a curve with the highest sensitivity (ie, the most correct identifications of abuse) for any given level of specificity (ie, false positives) was preferred. The C statistic was used to evaluate the area under the ROC curve.

Parsimony. A model with a smaller set of relevant independent variables was desired. A parsimonious model is more practical and places lesser data burden on potential users.

Statistical Significance. Variables with $P \leq .05$ were preferred so that the model would focus on variables with the most statistical power. The 5% level was used in initial model building to identify potentially relevant risk factors. However, demographic variables were included regardless of their P value for purposes of comparison.

Clinical Relevance. The model focused on independent variables that were clinically relevant based on existing literature and expert opinion. We generally adopted a $P < .05$ criterion but considered all 4 selection criteria in arriving at a final decision. Therefore, there were times when the model included variables with an odds ratio (OR) close to 1 because we believed a priori that the variable was clinically relevant.

RESULTS

Drug Claims Models

Alternative sets of results are presented that correspond to the 2 models evaluating only drug claims data. The first describes results for the full sample of 116,382 prescription opioid users (alternative A), while the second summarizes results for the subset of 8592 patients for whom sufficient information was available to construct a "physician shopping" variable (alternative B). Because of the short duration of the data, no eligibility criteria were imposed, so patients could have potentially cycled in and out of the data.

Alternative A. There were 116,382 patients who received at least 1 prescription opioid (approximately 15% of the privately insured population of Maine). Of the prescription opioid user sample, 875 patients were diagnosed as being prescription opioid abusers from 2005 to 2006 (ie, 0.8% of users were abusers based on *ICD-9-CM* codes alone) (**Table 1**). The prescription opioid user population was predominantly female (55.7%), while the abuser population was predominantly male (59.1%). Most prescription opioid users (26.7%) were aged 45 to 54 years. In contrast, most prescription opioid abusers (24.6%) were aged 25 to 34 years. Patients aged 18 to 34 years accounted for 48.5% of the abuser population but only 25.0% of the overall sample. Several utilization behaviors were significantly more prevalent among abusers than nonabusers, including filling prescriptions at 2 or more pharmacies (39.4% vs 7.7%), having 1 or more early refills (36.0% vs 3.7%), and demonstrating 2 or more consecutive months of dose escalation (4.7% vs 0.4%).

The best-fitting model for alternative A included the following variables: age, sex, number of pharmacies, number of prescriptions, early prescription opioid refills, and dose escalation (**Table 2**). The ROC curve had a C statistic of 0.840, and the pseudo r^2 was 0.21. All variables were significant at the 5% level except for age 35 to 44 years (included for purposes of comparison). Variables indicating that a patient was aged 18 to 24 years, received 4 or more opioid prescriptions, filled opioid prescriptions at 2 or more pharmacies, or exhibited early refill behavior all had ORs above 2.00, meaning that each factor at least doubled the odds of a patient being at risk for prescription opioid abuse. Because the model controls for the number of opioid prescriptions, the ORs for the other variables indicate that those measures were associated with prescription opioid abuse diagnoses and were not merely statistical consequences of long-term opioid therapy.

Alternative B. As already mentioned, because Maine did not require third-party payers to record the prescribing physician's identifier until June 30, 2006, this analysis was limited to the final quarter of 2006.[28] This subsample of patients with a prescriber identifier for a prescription opioid included 8592 patients (7.4% of the total patients from alternative A). The demographic characteristics (**Table 3**) were similar to those in alternative A. Alternative B covers a shorter period to include a metric on physician shopping.

The best-fitting model for alternative B included the following variables: age, sex, number of pharmacies, early prescription opioid refills, and number of physicians (**Table 4**). The physician shopping variable was statistically significant at the 10% level but not at the 5% level. The ROC curve had a C statistic of 0.774, and the pseudo r^2 was 0.15. The lower C statistic and pseudo r^2 values are likely indicative of the shorter interval and more limited data available for this model. All variables were significant at the 10% level (and at the 5% level) except for ages 25 to 34 years and 35 to 44 years, as well as the physician shopping variable. Early prescription opioid refills (OR, 3.31; 95% confidence interval [CI], 2.56-4.28) and the age bracket of 18 to 24 years (OR, 3.53; 95% CI, 1.64-7.61) seemed particularly important. In addition, variables indicating that a patient was male, filled opioid prescriptions at 2 or more pharmacies, or was aged 25 to 34 years all had ORs above 1.50. The number of opioid prescriptions was considered for this model as well but was

■ **Table 1.** Drug Claims Analysis Alternative A Summary Statistics[a]

Variable	No. (%)		
	All Prescription Opioid Users (N = 116,382)	Prescription Opioid Nonabusers (n = 115,507)	Prescription Opioid Abusers (n = 875)
Age at first prescription opioid claim, y			
12-17	9724 (8.4)	9680 (8.4)	44 (5.0)
18-24	11,018 (9.5)	10,809 (9.4)	209 (23.9)
25-34	18,093 (15.5)	17,878 (15.5)	215 (24.6)
35-44	26,684 (22.9)	26,480 (22.9)	204 (23.3)
45-54	31,099 (26.7)	30,957 (26.8)	142 (16.2)
55-64	19,764 (17.0)	19,703 (17.1)	61 (7.0)
Sex			
Female	64,879 (55.7)	64,521 (55.9)	358 (40.9)
Male	51,503 (44.3)	50,986 (44.1)	517 (59.1)
Opioid prescriptions, No.			
1-3	104,642 (89.9)	104,293 (90.3)	349 (39.9)
≥4	11,740 (10.1)	11,214 (9.7)	526 (60.1)
Pharmacies where opioid prescriptions were filled, No.			
1	107,169 (92.1)	106,639 (92.3)	530 (60.6)
≥2	9213 (7.9)	8868 (7.7)	345 (39.4)
Early refills of opioid prescriptions[b]			
0	111,767 (96.0)	111,207 (96.3)	560 (64.0)
≥1	4615 (4.0)	4300 (3.7)	315 (36.0)
Dose escalation[c]			
0	115,873 (99.6)	115,039 (99.6)	834 (95.3)
≥2 Consecutive months	509 (0.4)	468 (0.4)	41 (4.7)

[a]Data for privately insured pharmacy claims from Maine Health Data Organization from 2005 to 2006 (http://mhdo.maine.gov/imhdo/). The index date was defined as the date of each patient's first prescription opioid claim during 2005-2006. The analysis was conducted over the 3-month period following the index date for each patient. All patients in the sample have at least 1 prescription opioid claim.
[b]Early refills were characterized by patients who filled 2 consecutive opioid prescriptions during the study period for which the number of days supply of the first prescription was more than 10% higher than the number of days between prescriptions.
[c]Dose escalation was characterized by patients who had a 50% increase in the mean milligrams of morphine per month twice consecutively during the study period.

omitted from the best-fitting model because it was highly correlated with the physician shopping variable. It is difficult to compare the C statistics of alternatives A and B given the much smaller sample size of the latter (116,382 vs 8592).

Integrated Model

Comorbidities were initially identified based on prior research.[24] The best-fitting integrated model included the following variables: age, sex, nonopioid substance abuse, depression, posttraumatic stress disorder, hepatitis, cancer, mental health outpatient facility visits, hospital visits, number of pharmacies, number of prescriptions, and early prescription opioid refills (Table 5). The ROC curve had a C statistic of 0.926. With a pseudo r^2 of 0.37, this model provided a much better fit to the data than either drug claims model. All variables listed in eAppendix A were considered in the stepwise regression analysis. Early prescription opioid refills was most important (OR, 6.52; 95% CI, 5.39-7.89), followed by nonopioid substance abuse (OR, 5.83; 95% CI, 5.03-6.75). The categorization for the number of pharmacies where opioid prescriptions were filled differs slightly because the data period in Table 5 differs from that in Tables 1 through 4.

DISCUSSION

This study demonstrates the feasibility of developing models derived from claims data variables to identify specific characteristics associated with elevated risk for prescription opioid

Table 2. Drug Claims Analysis Alternative A Results[a]

Variable	Parameter Estimate	Adjusted Odds Ratio (95% Confidence Interval)	*P*
Age at first prescription opioid claim, y			
12-17	1.00	1.00 [Reference]	
18-24	1.07	2.91 (2.08-4.05)	<.001
25-34	0.42	1.52 (1.09-2.12)	.01
35-44	–0.18	0.83 (0.60-1.17)	.29
45-54	–0.73	0.48 (0.34-0.68)	<.001
55-64	–1.10	0.33 (0.22-0.50)	<.001
Sex			
Female	1.00	1.00 [Reference]	
Male	0.54	1.71 (1.49-1.97)	<.001
Opioid prescriptions, No.			
1-3	1.00	1.00 [Reference]	
≥4	1.99	7.34 (6.14-8.76)	<.001
Pharmacies where opioid prescriptions were filled, No.			
1	1.00	1.00 [Reference]	
≥2	0.76	2.14 (1.82-2.51)	<.001
Early refills of opioid prescriptions[b]			
0	1.00	1.00 [Reference]	
≥1	1.22	3.39 (2.86-4.03)	<.001
Dose escalation[c]			
0	1.00	1.00 [Reference]	
≥2 Consecutive months	0.63	1.88 (1.31-2.68)	<.001

[a]Data for privately insured pharmacy claims from Maine Health Data Organization from 2005 to 2006 (http://mhdo.maine.gov/imhdo/). The index date was defined as the date of each patient's first prescription opioid claim during 2005-2006. The analysis was conducted over the 3-month period following the index date for each patient. All patients in the sample have at least 1 prescription opioid claim.
[b]Early refills were characterized by patients who filled 2 consecutive opioid prescriptions during the study period for which the number of days supply of the first prescription was more than 10% higher than the number of days between prescriptions.
[c]Dose escalation was characterized by patients who had a 50% increase in the mean milligrams of morphine per month twice consecutively during the study period.

abuse. Several identified risk factors increased the likelihood that a patient may be at risk for abusing or misusing prescription opioids. The ability of the models to precisely identify patients who received an *ICD-9-CM* diagnosis for abuse or misuse was less robust, which may be explained by the few patients with such clinical diagnoses, as well as other limitations of the data used and of claims data in general for assessing patient risk levels.

Nonetheless, such models may serve as a valuable tool to assist clinicians in monitoring their patients. As Katz et al state, "healthcare providers will feel more comfortable prescribing and dispensing opioids when they are able to better identify patients at risk for abuse, and will be able to intervene in problematic cases to minimize risk."[29] For instance, PMPs could automatically screen all patients receiving prescription opioids using this type of model and generate reports of patients with certain characteristics (eg, physician shopping and multiple opioid prescriptions), or they could notify providers if patients meet certain key risk factors such as those identified in this study (eg, pharmacy shopping and early refills). Several state PMPs have indicated an interest in using drug data as a clinical tool.[30]

In practice, clinicians must carefully balance reducing prescription opioid abuse with supporting appropriate prescription opioid therapy for patients in pain. It is important to avoid falsely identifying patients as having increased risk who do not have prescription opioid abuse problems (the difficulty experienced by physicians in identifying patients with prescription opioid abuse has been discussed in the literature[30]). If claims-based models are used to accomplish this goal, cutoffs with high specificity (low false-positive rates) should be chosen. For example, using the best-fitting alternative A model set at 95% specificity, the sensitivity (proportion of individuals with prescription opioid abuse identified

Table 3. Drug Claims Analysis Alternative B Summary Statistics[a]

Variable	No. (%) All Prescription Opioid Users (N = 8592)	Prescription Opioid Nonabusers (n = 8289)	Prescription Opioid Abusers (n = 303)
Age at first prescription opioid claim, y			
12-17	230 (2.7)	222 (2.7)	8 (2.6)
18-24	435 (5.1)	375 (4.5)	60 (19.8)
25-34	1042 (12.1)	960 (11.6)	82 (27.1)
35-44	2120 (24.7)	2051 (24.7)	69 (22.8)
45-54	2996 (34.9)	2936 (35.4)	60 (19.8)
55-64	1769 (20.6)	1745 (21.1)	24 (7.9)
Sex			
Female	5004 (58.2)	4872 (58.8)	132 (43.6)
Male	3588 (41.8)	3417 (41.2)	171 (56.4)
Pharmacies where opioid prescriptions were filled, No.			
1	6884 (80.1)	6696 (80.8)	188 (62.0)
≥2	1708 (19.9)	1593 (19.2)	115 (38.0)
Early refills of opioid prescriptions[b]			
0	7178 (83.5)	6999 (84.4)	179 (59.1)
≥1	1414 (16.5)	1290 (15.6)	124 (40.9)
Physicians, No. of prescription opioid prescribers			
1	6350 (73.9)	6171 (74.4)	179 (59.1)
≥2	2242 (26.1)	2118 (25.6)	124 (40.9)

[a]Data for privately insured pharmacy claims from Maine Health Data Organization from 2005 to 2006 (http://mhdo.maine.gov/imhdo/). The index date was defined as the date of each patient's first prescription opioid claim during 2005-2006. The analysis was conducted over the 3-month period following the index date for each patient. All patients in the sample have at least 1 prescription opioid claim.
[b]Early refills were characterized by patients who filled 2 consecutive opioid prescriptions during the study period for which the number of days supply of the first prescription was more than 10% higher than the number of days between prescriptions.

by the model) was 54%. Based on the Maine data population, a PMP director sending out "warning letters" using this cutoff would send 8792 letters, of which only 473 would be true positives. The implication of this is that almost 95% of the letters (8319 of 8792) sent out would be false positives. Drug data alone (all that are available to PMPs) could identify more than half of the abusers in this population. Although the number of false positives may seem large in absolute terms, it represents only about 5% of all prescription opioid users (some of whom may be abusers or misusers who have not received an *ICD-9-CM* diagnosis or patients potentially at future risk). Low base rates of diagnosed abuse or misuse (only 0.8% of this population was diagnosed as having prescription opioid abuse) also contribute to the high absolute number of false positives.

By comparison, the integrated model illustrates the potential for improving these models by constructing and validating more refined algorithms. It also highlights the potential role for MCOs (which have access to patient medical claims in addition to drug claims) in the monitoring process. The increase in sensitivity of the integrated model best illustrates the improved accuracy in identifying at-risk patients produced by combining medical and drug data. At 95% specificity, the integrated model yields a sensitivity of 71%, a substantial improvement over the 54% sensitivity achieved using drug claims alone. Compared with the drug claims model, a program administrator using the same 95% specificity would correctly identify an additional 143 abusers (a 31% improvement). Therefore, combining medical and drug claims is significantly more effective at identifying prescription opioid abuse or misuse than using drug claims alone. Still, from the perspective of a PMP, creating algorithms based on drug claims data may be an important first step toward identifying potential prescription opioid abusers or misusers.

In any event, physicians using such algorithms would need to take great care to incorporate this information into the full

Table 4. Drug Claims Analysis Alternative B Results[a]

Variable	Parameter Estimate	Adjusted Odds Ratio (95% Confidence Interval)	*P*
Age at first prescription opioid claim, y			
12-17	1.00	1.00 [Reference]	
18-24	1.26	3.53 (1.64-7.61)	.001
25-34	0.53	1.70 (0.80-3.62)	.17
35-44	−0.42	0.66 (0.31-1.40)	.27
45-54	−0.87	0.42 (0.20-0.90)	.02
55-64	−1.19	0.31 (0.13-0.69)	.005
Sex			
Female	1.00	1.00 [Reference]	
Male	0.57	1.77 (1.39-2.24)	<.001
Pharmacies where opioid prescriptions were filled, No.			
1	1.00	1.00 [Reference]	
≥2	0.61	1.83 (1.41-2.39)	<.001
Early refills of opioid prescriptions[b]			
0	1.00	1.00 [Reference]	
≥1	1.20	3.31 (2.56-4.28)	<.001
Physicians, No. of prescription opioid prescribers			
1	1.00	1.00 [Reference]	
≥2	0.25	1.28 (0.99-1.67)	.06

[a]Data for privately insured pharmacy claims from Maine Health Data Organization from 2005 to 2006 (http://mhdo.maine.gov/imhdo/). The index date was defined as the date of each patient's first prescription opioid claim during 2005-2006. The analysis was conducted over the 3-month period following the index date for each patient. All patients in the sample have at least 1 prescription opioid claim. The receiver operating characteristic curve had a C statistic of 0.774, and the pseudo r^2 was 0.149 (N = 8592).
[b]Early refills were characterized by patients who filled 2 consecutive opioid prescriptions during the study period for which the number of days supply of the first prescription was more than 10% higher than the number of days between prescriptions.

clinical picture to avoid taking inappropriate action. From a clinician's perspective, reports generated based on claims data could serve as an additional data point for consideration in light of other sources (eg, patient histories, physical examinations, laboratory test results, and ongoing monitoring).[31,32] Physicians would still require diagnostic confirmation through a comprehensive clinical assessment. Used in conjunction with these other assessment tools, claims-based models have the potential to aid in detecting prescription opioid abuse or misuse and allow physicians to prescribe prescription opioids to patients more confidently.

There are some limitations to our study and other directions for future research. Although they are the only option for claims data analysis, the use of *ICD-9-CM* codes to identify prescription opioid abuse has important limitations. First, these codes are likely to identify a mixture of individuals with heroin and prescription opioid abuse, with an unknown proportion of each. To mitigate this problem, the analysis required that all patients have at least 1 prescription opioid claim; however, heroin abusers may also be prescription opioid users. Second, the true extent of prescription opioid abuse is likely understated because many patients who are abusers may not receive an abuse diagnosis for several reasons (such as the stigma associated with the condition).[24] Moreover, PMPs always understate the true prevalence of prescription opioid abuse or misuse because they focus on practitioners and patients and do not characterize the many other sources of illicit use of prescription drugs.

In addition, the integrated model could be further improved. The duration of the data was short (2-year maximum). Furthermore, the prescribing physician identifier was only available for 3 months. Algorithms based on several years of claims data may have more explanatory power. Also, drug data were only available for prescriptions that were paid for by private insurance; individuals who paid using cash or by other payers were not included. Linking medical claims data with more comprehensive prescription data could yield a more robust algorithm. Moreover, given the short period covered by the data, it was not possible to assess the sequencing of medical comorbidities (eg, to test the hypothesis that

Table 5. Integrated Analysis Results[a]

Variable	Parameter Estimate	Adjusted Odds Ratio (95% Confidence Interval)	*P*
Age at first prescription opioid claim, y			
12-17	1.00	1.00 [Reference]	
18-24	0.82	2.27 (1.64-3.14)	<.001
25-34	–0.08	0.92 (0.66-1.28)	.62
35-44	–0.83	0.44 (0.31-0.61)	<.001
45-54	–1.32	0.27 (0.19-0.38)	<.001
55-64	–1.66	0.19 (0.13-0.28)	<.001
Sex			
Female	1.00	1.00 [Reference]	
Male	0.78	2.19 (1.89.2.53)	<.001
Pharmacies where opioid prescriptions were filled, No.			
1-2	1.00	1.00 [Reference]	
≥3	0.67	1.96 (1.66-2.33)	<.001
Early refills of opioid prescriptions[b]			
0	1.00	1.00 [Reference]	
≥1	1.87	6.52 (5.39-7.89)	<.001
Dose escalation[c]			
0	1.00	1.00 [Reference]	
≥2 Consecutive months	0.46	1.59 (1.33-1.89)	<.001
Opioid prescriptions, No.			
1-11	1.00	1.00 [Reference]	
≥12	0.75	2.12 (1.73-2.61)	<.001
≥1 Nonopioid substance abuse diagnoses			
No	1.00	1.00 [Reference]	
Yes	1.76	5.83 (5.03-6.75)	<.001
≥1 Depression diagnoses			
No	1.00	1.00 [Reference]	
Yes	0.93	2.52 (2.17-2.93)	<.001
≥1 Posttraumatic stress disorder diagnoses			
No	1.00	1.00 [Reference]	
Yes	0.90	2.45 (1.88-3.19)	<.001
≥1 Hepatitis diagnoses			
No	1.00	1.00 [Reference]	
Yes	0.94	2.57 (1.84-3.58)	<.001
≥1 Cancer diagnoses			
No	1.00	1.00 [Reference]	
Yes	–0.55	0.58 (0.44-0.76)	<.001
≥1 Mental health outpatient facility visits			
No	1.00	1.00 [Reference]	
Yes	0.69	1.99 (1.23-3.23)	.005
≥1 Hospital visits			
No	1.00	1.00 [Reference]	
Yes	0.48	1.61 (1.39-1.87)	<.001

[a]Data for privately insured pharmacy claims from Maine Health Data Organization from 2005 to 2006 (http://mhdo.maine.gov/imhdo/). The index date was defined as the date of each patient's first prescription opioid claim during 2005-2006. The analysis was conducted over the 3-month period following the index date for each patient. All patients in the sample have at least 1 prescription opioid claim. The receiver operating characteristic curve had a C statistic of 0.926, and the pseudo r^2 was 0.370 (N = 134,542).
[b]Early refills were characterized by patients who filled 2 consecutive opioid prescriptions during the study period for which the number of days supply of the first prescription was more than 10% higher than the number of days between prescriptions.
[c]Dose escalatioin was characterized by patients who had 50% increase in the mean milligrams of morphine per month twice consecutively during the study period.

a specific prior diagnosis such as alcohol abuse would lead to a future opioid abuse diagnosis). Such enhancements would further improve our understanding of the risk factors. Finally, the ability to generalize the data to other geographic areas is unknown. The behavioral patterns of prescription opioid abusers may vary across geographic and demographic groups.

A possible interpretation of the data is that the patients classified as prescription opioid abusers also have pain that is undertreated and are engaging in aberrant behaviors because of pseudoaddiction. Given the notable comorbidity of pain and psychiatric disorders (including addiction and abuse), it is possible that high-risk behaviors such as early refills and physician shopping are palliation attempts rather than true abuse or dependence. This scenario would increase the likelihood of a false-positive identification using these data. Such a consideration is beyond the scope of the present research.

CONCLUSIONS

Models such as those used in this study can help successfully identify patients at risk for prescription opioid abuse or misuse. Identifying characteristics of patients who abuse or misuse prescription opioids may help true abusers get treatment sooner, which could yield substantial improvements in patient outcomes and reduced costs. In this way, PMPs and MCOs can have an important role in assisting healthcare providers and their patients to minimize risk of prescription opioid abuse or misuse.

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eAppendix A. Key Variables Considered

Drug Claims	Medical Claims
Demographic features	**Demographic features**
Age	Age
Sex	Sex
Utilization variables	**Medical resource utilization**
No. of opioid prescriptions	Hospital visits
	Mental health inpatient facility visits
High-risk behavior	**Comorbidities**
Pharmacy shopping	Nonopioid substance abuse
Physician shopping	Depression
Refilling opioid prescriptions early	Posttraumatic stress disorder
Escalating dosage	Hepatitis
	Cancer
	Fibromyalgia

■ **eAppendix B.** All Variables Considered

Variable	Description
Drug Utilization	
Mean prescription opioid dosage	Mean dosage of prescription opioid per day (in milligrams of morphine)
Distinct LAO count	No. of distinct LAOs used by a patient
Distinct SAO count	No. of distinct SAOs used by a patient
Dose escalators	Patients who had 2 consecutive increases in their mean monthly prescription opioid dosage (in milligrams of morphine) of ≥50%
Early refillers	Patients who filled 2 consecutive opioid prescriptions for which the number of days of supply of the first prescription was more than 10% greater than the number of days between the 2 prescriptions
Frequent prescription opioid users	Patients who filled ≥4 opioid prescriptions
Multiple concurrent prescription opioid users	Patients who used ≥2 opioid prescriptions at the same time for ≥30 total days (not necessarily consecutively)
Multiple LAO users	Patients who filled ≥3 prescriptions for the same LAO
Multiple SAO users	Patients who filled ≥3 prescriptions for the same SAO
Pharmacy shoppers	Patients who filled opioid prescriptions at ≥2 pharmacies (based on sensitivity analysis of the effect of the No. of prescriptions on the statistical power of this variable)
Physician shoppers	Patients who received opioid prescriptions from ≥2 physicians
Total days supply of LAOs	Total No. of days supply of LAOs for a patient
Total days supply of opioid prescriptions	Total No. of days supply of opioid prescriptions for a patient
Total days supply of SAOs	Total No. of days supply of SAOs for a patient
Total LAO prescriptions	Total No. of LAO prescriptions filled by a patient
Total SAO prescriptions	Total No. of SAO prescriptions filled by a patient
Comorbidities	
Antisocial personality disorder	≥1 Claims associated with *ICD-9-CM* code 301.7
Arthritis	≥1 Claims associated with *ICD-9-CM* codes 711.xx-716.xx
Bipolar disorder	≥1 Claims associated with *ICD-9-CM* codes 296.0 or 296.4-296.8
Burns	≥1 Claims associated with *ICD-9-CM* codes 940.xx-949.xx
Cancer	≥1 Claims associated with *ICD-9-CM* codes 014.xx-020.xx or 023.xx
Chronic back pain	≥2 Claims associated with *ICD-9-CM* codes 711.xx-716.xx, 721.3, 722.32, 722.52, 722.93, 724.02, 724.2, 724.3, 724.5, 724.6, 724.70, 724.71, 724.79, 738.5, 739.3, 739.4, 846.1-846.3, 846.8, 846.9, or 847.2
Depression	≥1 Claims associated with *ICD-9-CM* codes 296.2, 296.3, or 311.xx
Endocarditis	≥1 Claims associated with *ICD-9-CM* codes 421.xx
Fibromyalgia	≥1 Claims associated with *ICD-9-CM* code 729.1
Gastrointestinal bleeding	≥1 Claims associated with *ICD-9-CM* codes 578.xx
Hepatitis	≥1 Claims associated with *ICD-9-CM* codes 070.xx, 571.4, or 573.3
Herpes	≥1 Claims associated with *ICD-9-CM* codes 054.xx
Human immunodeficiency virus or AIDS	≥1 Claims associated with *ICD-9-CM* codes 042.xx
Liver disease or cirrhosis	≥1 Claims associated with *ICD-9-CM* codes 570.xx-571.xx
Nonopioid substance abuse	≥1 Claims associated with *ICD-9-CM* codes 304.xx-305.xx, excluding 304.0, 304.7, and 305.5
Pancreatitis	≥1 Claims associated with *ICD-9-CM* codes 577.0-577.1 or 072.3
Posttraumatic stress disorder	≥1 Claims associated with *ICD-9-CM* code 309.81
Schizophrenia	≥1 Claims associated with *ICD-9-CM* codes 295.xx
Sexually transmitted diseases	≥1 Claims associated with *ICD-9-CM* codes 090.xx-099.xx
Skin infections	≥1 Claims associated with *ICD-9-CM* codes 681.xx, 682.xx, or 683.xx
Medical Resource Utilization	
Emergency department visit	≥1 Claims associated with a visit to an emergency department
Hospital visit	≥1 Claims associated with a visit to a hospital
Mental health inpatient facility visit	≥1 Claims associated with a visit to a mental health inpatient facility
Mental health outpatient facility visit	≥1 Claims associated with a visit to a mental health outpatient facility
Substance abuse visit	≥1 Claims associated with a visit to a substance abuse treatment center

ICD-9-CM indicates *International Classification of Diseases, Ninth Revision, Clinical Modification*; LAO, long-acting opioid; SAO, short-acting opioid.